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El tiempo frente a las pantallas: la nueva variable en la salud infantil y juvenil

Screen-time: a new stakeholder in children and adolescent health

Los niños comienzan cada vez antes a utilizar dispositivos basados en pantallas, y pasan cada vez más tiempo delante de las mismas (1). Esta conducta se asocia con patrones de dieta insanos, una pobre calidad del sueño, un aumento en el riesgo de padecer una enfermedad cardiovascular y a mayor frecuencia de obesidad en niños (2). Tiene también consecuencias negativas para la salud mental, en especial problemas de inatención en los más pequeños (3), y en adolescentes (4), en los que tienen especial protagonismo las redes sociales (5). Hay suficiente información disponible que apunta a que el tiempo de consumo de pantallas se asocia de una forma negativa a mayor adiposidad, peor condición física, pero calidad de vida, menor autoestima, pero rendimiento académico y pérdida de habilidades sociales, mayor grado de ansiedad y de depresión (6). Por el contrario, la práctica regular de actividad física se asocia a un mayor bienestar y a un mejor estado de salud mental (7,8).

De forma paralela, hemos asistido a un aumento en la tasa de obesidad infanto-juvenil, en la que el sedentarismo juega un papel relevante. Niveles bajos de actividad física, junto con tiempos de ocio prolongados delante de una pantalla y la presencia de obesidad se asocian a peores puntuaciones en escalas de bienestar en niños (9), aunque el número de estudios que correlacionan todas estas variables es escaso.

Delgado-Floody y cols. publican en el último número de *Nutrición Hospitalaria* (10) un estudio original en una muestra de escolares chilenos, en la que correlacionan el estado de bienestar en función del patrón de actividad física, su estado nutricional y el tiempo dedicado a actividades de ocio frente a una pantalla. Los autores encuentran que los escolares con más horas de tiempo ante una pantalla y menor número de horas de actividad física fuera del horario escolar puntúan peor en las escalas de valoración de bienestar utilizadas (en este estudio el Inventario de Autoestima de Coppersmith). Además, a mayor tiempo de exposición a las pantallas puntuaciones mayores en las escalas de depresión (valorada con el Inventario de Depresión Infantil, CDI) y peor autoestima. Por otra parte, los niños con obesidad puntuaban peor en las escalas de sensación de bienestar y de depresión. En su estudio, Delagado-Floody y cols. encuentran diferencias significativas en el número de horas ante las pantallas en el grupo de niños con sobrepeso y obesidad, y un número menor de horas de actividad física extraescolar. Si bien es cierto que el estudio presenta limitaciones por el tamaño muestral y que se circunscribe a una población concreta, probablemente sus resultados pueden extrapolarse a otras poblaciones similares.

Las sociedades científicas han señalado claramente en los últimos años las recomendaciones de uso (de consumo) de tiempo de pantallas en función de la edad: así la Academia Americana de Pediatría recomienda evitar el uso de pantallas en < 18 meses, excepto para reuniones familiares (*video-chatting*), entre 18 y 24 meses los padres deben escoger programaciones de muy elevada calidad y estar con los niños explicándoles los contenidos, entre los 2 y los 5 años el límite debe ser 1 hora diaria y siempre en compañía de los hijos y por encima de esa edad su uso en periodos limitados y siempre que se garantice que no sustituyen al sueño, al juego o la actividad física u otras acciones esenciales para la salud. Recomienda también disponer de tiempos juntos libres de dispositivos, como por ejemplo el tiempo de las comidas y espacios sin pantallas, como es el caso del dormitorio (11). En la misma línea se han manifestado la Asociación Pediátrica Canadiense (12) o la Asociación Española de Pediatría (AEP).

Sin embargo, a pesar de la creciente evidencia de la asociación entre conductas sedentarias (p. ej. tiempo antes una pantalla) y resultados de salud peores en niños y adolescentes, cada vez es mayor el número de niños que las usan a edades más tempranas y por periodos más prolongados. Menos de la mitad de niños y adolescentes pasan < 2 horas al día ocupados en esta actividad, fuera del uso escolar. Faltan, sin embargo, estudios

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longitudinales o de intervención que permitan conocer mejor las consecuencias de estas conductas. También es preciso mejorar la calidad de los estudios, generalmente basados en cuestionarios autorreportados, disponiendo de herramientas objetivas que permitan conocer el tiempo real de actividades sedentarias o de actividad física.

Para abordar esta situación hace falta no solo disponer de recomendaciones claras de las sociedades científicas, sino también medidas de las autoridades sanitarias y educativas (quizá haya que valorar si considerando el tiempo que ya usan los dispositivos en su tiempo libre. Hay que seguir potenciando el uso de tabletas en las aulas). Y, por supuesto, hay que señalar el papel de los padres no solo en el establecimiento de mensajes claros sobre su uso por parte del niño y del adolescente, sino también en la propia conducta del individuo adulto en relación con los mismos dispositivos.

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Bibliografía

1. Ferrari GLM, Pires C, Solé D, Matsudo V, Katzmarzyk PT, Fisberg M. Factors associated with objectively measured total sedentary time and screen time in children aged 9-11 years. J Pediatr (Rio J). 2019;95(1):94-105. DOI: 10.1016/j.jped.2017.12.003
2. Tremblay MS, Chaput JP, Adamo KB, Aubert S, Barnes JD, Choquette L, et al. Canadian 24-Hour Movement Guidelines for the Early Years (0-4 years): An Integration of Physical Activity, Sedentary Behaviour, and Sleep. BMC Public Health 2017;17(Suppl 5):874. DOI: 10.1186/s12889-017-4859-6
3. Tamana SK, Ezeugwu V, Chikuma J, Lefebvre DL, Azad MB, Moraes TJ, et al. Screen-time is associated with inattention problems in pre-schoolers: results from the CHILD birth cohort study PLOS ONE 2019;14(4):e0213995.
4. Suchert V, Pedersen A, Hanewinkel R, Isensee B. Relationship between attention-deficit/hyperactivity disorder and sedentary behavior in adolescence: a cross-sectional study. Atten Defic Hyperact Disord 2017;9(4):213-8. DOI: 10.1007/s12402-017-0229-6.
5. Riehm KE, Feder KA, Tormohlen KN, Crum RM, Young AS, Green KM, et al. Associations Between Time Spent Using Social Media and Internalizing and Externalizing Problems Among US Youth. JAMA Psychiatry 2019:1-9. DOI: 10.1001/jamapsychiatry.2019.2325
6. Saunders TJ, Vallance JK. Screen time and health indicators among children and youth: current evidence, limitations and future direction. Appl Health Econ Health Policy 2017;15:323-31.
7. Donnelly JE, Hillman CH, Castelli D, Etnier JL, Lee S, Tomporowski P, et al. Physical Activity, Fitness, Cognitive Function, and Academic Achievement in Children: A Systematic Review. Med Sci Sports Exerc 2016;48(6):1197-222. DOI: 10.1249/MSS.0000000000000901
8. Fromel K, Kudlacek M, Groffik D, Svozil Z, Simunek A, Garbaciak W. Promoting Healthy Lifestyle and Well-Being in Adolescents through Outdoor Physical Activity. Int J Environ Res Public Health 2017;14(5). DOI: 10.3390/ijerph14050533
9. Ikävalko T, Lehto S, Lintu N, Väistö J, Eloranta A, Haapala E, et al. Health-related correlates of psychological well-being among girls and boys 6-8 years of age: The Physical Activity and Nutrition in Children study. Journal of Paediatrics and Child Health 2018;54(5):506-9. DOI:10.1111/jpc.13891
10. Delgado-Floody P, Jerez-Mayorga D, Caamaño-Navarrete F, Cofré-Lizama A, Álvarez C. Psychological well-being related to screen time, physical activity after school and weight status in Chilean Schoolchildren. Nutr Hops 2019;36(6):1254-60. DOI: 10.20960/nh.02751
11. Council on Communication and media. American Academy of Pediatrics. Media Use in School-Aged Children and Adolescents. Pediatrics 2016;138(5):e20162592. DOI: https://doi.org/10.1542/peds.2016-2592
12. Digital media: Promoting healthy screen use in school-aged children and adolescents. Disponible en: https://www.cps.ca/en/documents/position/digital-media (consultado por última vez el 1/11/2019).

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Nutrición Hospitalaria

Trabajo Original

Nutrición artificial

All-in-one *versus* lipid-free parenteral nutrition for premature infants: visual, pH, and particle size analyses

Comparación de nutrición parenteral "todo-en-uno" frente a nutrición parenteral sin lípidos en prematuros: análisis visual, de pH y tamaño de partículas

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Abstract

Objective: this study aims to investigate the physical stability of standard formulations for parenteral nutrition, with and without lipids, in one bag for preterm babies.

Method: standard formulations for first-day and for second-day parenteral nutrition of preterm babies weighing 1,000 grams were prepared in triplicate. Standard all-in-one formulas for first-day and for second-day parenteral nutrition were compared with equivalent standard lipid-free formulations. The standard formulas contain glucose, amino acids, lipids, calcium gluconate, potassium chloride, sodium chloride, and vitamins. Stability was evaluated using visual inspection, particle size analysis, and pH measurement. The physical instability of the all-in one parenteral nutrition formulas was reported as creaming, coalescence, or cracking, whereas the instability of the lipid-free parenteral nutrition formulas was described as turbidity, precipitation, gas formation, or colour changes. Two independent evaluators assessed the visual changes under light and against a dark-light background, as well as using the Tyndall beam effect. Particle size was measured using a particle size analyzer. Chemical compatibility was checked using a pH-meter.

Result: the result showed that the all-in-one (AIO) parenteral nutrition formulas develop reversible creaming on day three, while the lipid-free ones remain clear. As regards pH and particle size, none of the four AIO and lipid-free formulas developed significant changes ($\Delta pH < 0.05$ and particle size < 400 nm) until after seven days.

Conclusion: all four formulas are stable following examination with visual inspection, a pH-meter, and a particle size analyzer.

Key words:

AIO-parenteral nutrition. Lipid-free parenteral nutrition. Preterm baby. Physical stability.

Resumen

Objetivo: el objetivo del estudio es investigar la estabilidad de las formulaciones estandarizadas de nutrición parenteral, con y sin lípidos, para prematuros.

Métodos: se prepararon por triplicado las formulaciones estandarizadas del 1º y 2º día para prematuros de menos de 1000 gramos. Se compararon las soluciones preparadas "todo-en-uno" con las soluciones estandarizadas equivalentes que no contenían lípidos. Las soluciones estandarizadas contenían glucosa, aminoácidos, lípidos, gluconato cálcico, cloruro potásico, cloruro sódico y vitaminas. La estabilidad se evaluó mediante inspección visual, medición del tamaño de las partículas, y medición del pH. Se interpretó como inestabilidad física de las soluciones ternarias la presencia de separación de fases, coalescencia o la formación de una capa grasa, mientras que en las preparaciones sin lípidos se describió como turbidez, precipitación, formación de gas o cambios de coloración. Dos evaluadores independientes comprobaron los cambios visuales bajo luz directa o en contraste con un fondo oscuro, así como mediante el uso del efecto Tyndall. El tamaño de las partículas se midió mediante un analizador de partículas. La compatibilidad química se comprobó con el Phmetro.

Resultados: todas las nutriciones parenterales todo-en-uno (AIO) desarrollaron una capa grasa (*creaming*) al tercer día, mientras que las mezclas sin lípidos permanecieron transparentes. Con respecto al pH y el tamaño de las partículas, ninguna de las cuatro emulsiones AIO y nutrición parenteral sin lípidos mostraron cambios significativos (incremento de pH < 0,03 y tamaño de las partículas < 400 nm) en los siete primeros días.

Conclusión: las cuatro formulaciones fueros estables tras inspección visual, medición del pH y análisis del tamaño de las partículas.

Palabras clave:

Nutrición parenteral "todo-en-uno". Nutrición parenteral sin lípidos. Prematuro. Estabilidad física.

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INTRODUCTION

Provision of total parenteral nutrition for preterm infants is paramount, especially for very low-weight babies at birth (less than 1.5 kg). Preterm babies often cannot achieve the minimum rate of growth since the requirements of energy expenditure in extrauterine life are higher than those of intrauterine life (1). In addition, preterm babies are often unable to suck or swallow well before 34 weeks of age (2). Therefore, early parenteral nutrition should be added and gradually given along with enteral feeding or breast milk (2,3). In order to get sufficient macronutrients and micronutrients, nutrition should contain dextrose, amino acids, lipids, electrolytes, and vitamins. Currently, ready-to-use parenteral nutrition formulas contain one type of nutrient. However, the administration of each nutrient separately via a different line may become a burden for any hospital. Mixing all those macro- and micro-nutrients in one intravenous (IV) bag will reduce the number of venous lines. Besides, the administration of parenteral nutrition in one bag is also paramount for prematures with volume restriction. Therefore, provision of a high concentrated solution in a low-volume formulation is often preferred. This confirmed why requests for total parenteral nutrition admixtures have currently increased in the hospital pharmacy (4).

Even though the administration of a total parenteral nutrition formula is common practice, the mixing of an all-in-one formulation for administration in one bag remains unusual. Practitioners remain unsure about the stability of added lipids for parenteral nutrition (5). Thus, parenteral nutrition is commonly administered through separate lines, which is then called two-bag parenteral nutrition. However, an issue may arise in the critical care setting, where the patient receives many intravenous medications and venous access is limited (4). The administration of two-bag parenteral nutrition, with a separate lipid route, needs an additional port or access. This situation arouses debate on the benefits of mixing all nutrients into one bag.

The concern when adding lipids into a parenteral nutrition formula is instability, which results in creaming, coalescence, and cracking. The main hazard of macronutrient stability is not a chemical but rather a physical issue associated with particle size distribution. A previous study that assessed total parenteral nutrition in one bag had quite a different result (6-8). Additionally, no studies comparing mixed lipid and lipid-free parenteral nutrition using similar formulas for prematurity have been found. This study discusses and compares two types of solution–first, an all-in-one or one-bag parenteral nutrition formula; second, a lipid free or two-bag parenteral nutrition formula.

METHOD

The nutrition components were acquired from standard hospital stock: Aminosteril® Infant 6% (Fresenius Kabi Combiphar), Dextrose 5% (Otsuka), Dextrose 40% (Otsuka), NaCl 3% (Otsuka), Potassium Chloride injection 7,46% (Otsuka), Calcium Gluconate Injection (Generik, Ethica Industri Farmasi), Magnesium Sulfate 20% injection (Otsuka), Lipofudin® 20% (Braun), Nutrient Pad Set Standard TTC Media, Membrane Filter (Satorius), and Pepton Water (OXOID).

FORMULA

This study investigated the standard parenteral nutrition of preterm babies with a weight of 1,000 mg. The composition of nutrients was based on the first-day and second-day guidelines used by practitioners in the hospital (9). A stability study was carried out on four formulas, where formulas 1a and 2a are all-in-one parenteral nutrition (AIO-PN) and formulas 1b and 2b are lipid-free parenteral nutrition (lipid-free-PN) formulas, as stated below:

1. Formula 1a is a first-day standard formulation in one bag containing 5% glucose (28.85 mL), 40% glucose (25 mL), 6% amino acids (25 mL), 10% calcium gluconate (10 mL), 20% magnesium sulfate (0.36 mL), and 20% lipids (5 mL) (Day-1 AIO PN).
2. Formula 1b is a first-day standard formulation in one bag containing 5% glucose (28.85 mL), 40% glucose (25 mL), 6% amino acids (25 mL), 10% calcium gluconate (10 mL), and 20% magnesium sulfate (0.36 mL) (Day-1 Lipid free PN).
3. Formula 2a is a second-day standard formulation in one bag containing 5% glucose (30 mL), 40% glucose (33.33 mL), 6% amino acids (25 mL), 10% calcium gluconate (10 mL), 20% magnesium sulfate (0.36 mL), and 20% lipids (7.5 mL) (Day-2 AIO PN).
4. Formula 2b is a second-day standard formulation in one bag containing 5% glucose (30 mL), 40% glucose (33.33 mL), 6% amino acids (25 mL), 10% calcium gluconate (10 mL), and 20% magnesium sulfate (0.36 mL) (Day-2 Lipid-free PN).

Four formulas were prepared to be aseptic in triplicate under laminar air flow (LabTech International, Indonesia). After preparation, the four formulas were kept in a refrigerator (2-8 °C). Physical stability was investigated every 24 hours during 7 days following the principle of compatibility justification – visual inspection, particle size, and pH. Each solution was observed by a trained pharmaceutical technician against a black and a white background to detect visual changes including discoloration, effervescence, turbidity, emulsion instability, creaming, and cracking. A particle size analyzer (Horiba, Germany) was used to measure particle size distribution in the sample. The distribution of lipid droplet diameters was also confirmed using a microscope (Olympus CX21, Japan). Chemical detection was evaluated with a calibrated surface pH-meter (Horiba, Germany) and osmometer (Horiba, Germany).

RESULTS

The AIO PN formulas showed that osmolarity was within the 500-700 mOsm range as shown in table I. Based on visual inspection the AIO PN formulas changed visually during testing. Table II shows that creaming developed in AIO PN (F1a and F2a) formulas from the third day after preparation. Particle size was measured as in table III. It was in the range < 600 nm. Table IV shows that the pH of all four formulas did not change significantly during the assay.

Table I. Osmolarity of four parenteral nutrition formulas after preparation

Replication	Osmolarity (mOsm/L)			
	F1a	F1b	F2a	F2b
1	716	612	664	589
2	714	617	668	583
3	718	617	667	584
Mean ± SD	716.0 ± 2.01	615.33 ± 2.35	666.33 ± 2.08	585.33 ± 2.62

F1a: standard first-day AIO PN formula for preterm babies; F1b: standard first-day lipid-free PN formula for preterm babies; F2a: standard second-day AIO PN formula for preterm babies; F2b: standard second-day lipid-free PN formula for preterm babies.

Table II. Evaluation on physical stability of four formulas based on visual examination

Day testing	Visual examination			
	F1a	F1b	F2a	F2b
Day 1	White, milky	Clear	White, milky	Clear
Day 2	White, milky	Clear	White, milky	Clear
Day 3	Creaming	Clear	Creaming	Clear
Day 4	Creaming	Clear	Creaming	Clear
Day 5	Creaming	Clear	Creaming	Clear
Day 6	Creaming	Clear	Creaming	Clear
Day 7	Creaming	Clear	Creaming	Clear

F1a: standard first-day AIO PN formula for preterm babies; F1b: standard first-day lipid-free PN formula for preterm babies; F2a: standard second-day AIO PN formula for preterm babies; F2b: standard second-day lipid-free PN formula for preterm babies.

Table III. Particle size of four parenteral nutrition formulas using a particle size analyzer (PSA)

Day testing	Particle Size (nm)			
	F1a	F1b	F2a	F2b
Day 1	351.30 ± 7,3	< 5	313.23 ± 1,2	< 5
Day 2	344.90 ± 0,8	< 5	356.63 ± 2,1	< 5
Day 3	329.90 ± 3,9	< 5	300.03 ± 6,6	< 5
Day 4	349.00 ± 0,5	< 5	342.43 ± 0,9	< 5
Day 5	335.87 ± 2,8	< 5	361.13 ± 1,0	< 5
Day 6	352.10 ± 3,7	< 5	362.20 ± 0,3	< 5
Day 7	369.20 ± 1,1	< 5	303.63 ± 2,6	< 5

F1a: standard first-day AIO PN formula for preterm babies; F1b: standard first-day lipid-free PN formula for preterm babies; F2a: standard second-day AIO PN formula for preterm babies; F2b: standard second-day lipid-free PN formula for preterm babies.

Table IV. pH value of four parenteral nutrition formulas using a pH-meter

Day testing	pH values			
	F1a	F1b	F2a	F2b
Day 1	6.06 ± 0.09	6.83 ± 0.05	5.75 ± 0.04	6.80 ± 0.07
Day 2	5.76 ± 0.02	6.85 ± 0.01	5.80 ± 0.04	6.85 ± 0.03
Day 3	5.52 ± 0.09	6.81 ± 0.04	6.04 ± 0.03	6.98 ± 0.05
Day 4	5.94 ± 0.02	6.81 ± 0.05	6.04 ± 0.03	6.99 ± 0.02
Day 5	6.13 ± 0.04	6.78 ± 0.07	6.15 ± 0.10	6.98 ± 0.4
Day 6	5.90 ± 0.02	6.80 ± 0.05	5.98 ± 0.06	6.89 ± 0.02
Day 7	5.82 ± 0.01	6.80 ± 0.06	6.22 ± 0.06	6.81 ± 0.03
Mean	5.87 ± 0.09	6.81 ± 0.07	6.14 ± 0.09	6.90 ± 0.07
ΔpH	1.06	1.24		

F1a: standard first-day AIO PN formula for preterm babies; F1b: standard first-day lipid-free PN formula for preterm babies; F2a: standard second-day AIO PN formula for preterm babies; F2b: standard second-day lipid-free PN formula for preterm babies.

DISCUSSION

The osmolarity value, which is higher than 600, may be categorized as hyperosmolar. It showed that these four standard formulas should not be administered through peripheral routes, to prevent vein problems such as phlebitis or extravasation. A central route or PICC is best for these formulas, especially in babies or young children. Of all four options, AIO PN formulas had a higher osmolarity around 80-100 mOsm as compared to the Lipid-free PN ones.

Emulsion instability is marked by creaming, cracking, and inversion phase. Cracking is due to particle fusion to form larger particles. Creaming indicates physical instability and is reversible with shaking. Irreversible instability occurs when coalescence or cracking develops. During seven days in observation no visual signs of coalescence or cracking appeared. Coalescence and cracking typically occur when fat globules are larger than 500 nm (10). As regards the particle size analysis, the four formulas remained within the normal range (300-400 nm) for seven days, though physical changes were seen. To better qualify results we chose PSA rather than visual inspection. PSA measured the particles following a principle of dynamic light scattering, which is more sensitive and specific compared to the eye ability to differentiate emulsion changes. PSA is able to detect particles accurately in a range of 0.01-5,000 µm, and is also reliable to measure lipid size distribution. Furthermore, the microscopic analysis revealed no particles larger than 1 µm, and the naked eye is limited to sizes larger than 50 microns (5). Therefore, it was confirmed that judgment of lipid physical instability within 24 hours as based on naked eye evaluation is inaccurate.

Evidence of particulate hazards has been reported, such as deaths in newbors associated with embolism. Therefore, such formulations should be avoided for parenteral or intravascular administration (11). Table II shows that all four formulas remain within the acceptable range. The particle sizes obtained are able to freely circulate through the microvascular network. Particle sizes larger than the microvascular diameter (600 nm-1,000 nm) are dangerous since particles would be trapped inside these veins and induce embolism (12,13). Any particles larger than the vasculature's diameter may block a vein or artery. They also may occlude the capillary bed since the particles be larger than capillary diameter. During intravenous delivery, particulate contaminants enter the vein and travel through the venous system to the heart and lung. Particles larger than 5 µm tend to become trapped in the lung, whereas those smaller than 5 µm are usually retained in the liver, spleen, or kidney (14). In order to achieve a safe particle size, intravenous medication or parenteral nutrition particles should not be larger than 1 µm (15). Particle sizes smaller than 600 nm are physically safe to be introduced and circulate in the blood vessels.

Furthermore, the results of pH-metry show that the addition of fat into a parenteral nutrition formula causes a pH decrease (1.06 units for the first formula, 1.24 units for the second formula), even though the pH of the four formulas, including the ones for AIO PN, did not change significantly during seven days in a refrigerator. In theory, any lipids (6-8,11) added to glucose as an acid compound will reduce the lipid pH but increase the PN pH. However, the value of the final PN pH, around 6, is commonly stable; instability may begin when the PN pH is lower than 5.

AIO PN stability was influenced by composition, concentration, and environment, as well as by storage conditions. This study confirmed the causes of physical stability in AIO PN formulas. Both AIO and lipid-free parenteral nutrition formulas remained physically stable to visual inspection, pH-metry, and particle size analysis. Although the formula developed creaming, this was easy to disperse after soft shaking. Hence, it was considered to be safe, without no large globules. This result differs from that of a previous study that used different lipid sources and formulas (16). That study identified AIO PN instability within minutes (16). In addition, previous studies did not add vitamin to the parenteral nutrition formula. Vitamins such as Vitalipid® act as fat-soluble vitamins with antioxidant activity to prevent peroxide formation, but do not influence particle size. Therefore, they may enhance stability. Meanwhile, this current research is similar to the previous study that stated AIO PN was stable when fat-soluble vitamins were added (17), with stability persisting for up to seven days (6). The provision of AIO parenteral nutrition in one single bag will be beneficial for patients; it will also be cheaper, with fewer venous accesses required, and simpler to administrate.

This study assessed physical changes such as particle size, as larger sizes indicate physical instability, threaten the microvascular tree, and may result in death. However, it has not solved the chemical stability issue, which is related to concentrations.

CONCLUSION

This study confirmed that both AIO PN and lipid-free PN formulas are physically stable using visual, pH, and PS analyses. The creaming that occurred in the AIO PN formulas on the third day was reversible after re-shaking.

REFERENCES

1. Sauer PJ. Can Extrauterine Gapproximate Intrauterine Growth? Should it? The American Journal of Clinical Nutrition 2007;85(2):608S-13S. DOI: 10.1093/ajcn/85.2.608S.
2. Goldberg DL, Becker PJ, Brigham K, Carlson S, Fleck L, Gollins L, et al. Identifying Malnutrition in Preterm and Neonatal Populations: Recommended Indicators. Journal of the Academy of Nutrition and Dietetics 2018;118(9):1571-2. DOI: 10.1016/j.jand.2017.10.006.
3. Olsen SL, Park ND, Tracy K, Younger D, Anderson B. Implementing Standardized Feeding Guidelines, Challenges, and Results. Neonatal Network 2018;37(4):218-23. DOI: 10.1891/0730-0832.37.4.218.
4. Hanifah S, Ball P, Kennedy R. Medication incompatibility in intravenous lines in a Paediatric Intensive Care Unit (PICU) of Indonesian hospital. Critical Care & Shock 2018;21(3).
5. Staven V, Wang S, Grønlie I, Tho I. Physical stability of an all-in-one parenteral nutrition admixture for preterm infants upon mixing with micronutrients and drugs. Eur J Hosp Pharm 2018:ejhpharm-2018-001562. DOI: 10.1136/ejhpharm-2018-001562.
6. De Cloet J, Van Biervliet S, Van Winckel M. Physicochemical stable standard all-in-one parenteral nutrition admixtures for infants and children in accordance with the ESPGHAN/ESPEN guidelines. Nutrition 2018;49:41-7. DOI: 10.1016/j.nut.2017.11.019.
7. Yailian A-L, Serre C, Fayard J, Faucon M, Thomaré P, Filali S, et al. Production and stability study of a hospital parenteral nutrition solution for neonates. Journal of pharmaceutical analysis 2019;9(2):83-90. DOI: 10.1016/j.jpha.2018.01.002.
8. Watrobska-Swietlikowska D, Szlagatys-Sidorkiewicz A. Evaluation of physical stability of all in one parenteral admixtures for pediatric home care with high electrolytes concentrations. Nutricion hospitalaria 2015;31(1).
9. Wandita, S. Nutrisi pada Bayi Prematur. Kumpulan Makalah Pertemuan Ilmiah Tahunan Ilmu Kesehatan Anak VIII 2016;180-6.
10. Slattery E, Rumore MM, Douglas JS, Seres DS. 3-in-1 vs 2-in-1 parenteral nutrition in adults: A review. Nutrition in Clinical Practice 2014;29(5):631-5. DOI: 10.1177/0884533614533611.
11. Bradley JS, Wassel RT, Lee L, Nambiar S. Intravenous Ceftriaxone and Calcium in the Neonate: Assessing the Risk for Cardiopulmonary Adverse Events. Pediatrics 2009;123(4):e609-e13. DOI: 10.1542/peds.2008-3080.
12. Turmezei J, Jávorszky E, Szabo E, Dredán J, Kallai-Szabo B, Zelko R. Effect of storage temperature ont he stability of total parenteral nutrition admixtures prepared for infants. Acta Poloniae Pharmaceutica 2015;72(5):843-9.
13. Athanasiou C, Hatziantoniou S, Skouroliakou M, Markantonis-Kyroudis S. Assessment of the physicochemical stability of all-in-one parenteral emulsions for neonates according to USP specifications. Journal of Parenteral and Enteral Nutrition 2014;38(7):867-72. DOI: 10.1177/0148607113499589.
14. Bohrer D. Particulate Matter: Willey Online Library; 2012.
15. Singer P, Berger MM, Van den Berghe G, Biolo G, Calder P, Forbes A, et al. ESPEN guidelines on Parenteral Nutrition: Intensive Care. Clinical Nutrition 2009;28(4):387-400. DOI: 10.1016/j.clnu.2009.04.024.
16. Murphy S, Craig D, Murphy A. An Investigation into the Physical Stability of a Neonatal Parenteral Nutrition Formulation. Acta Paediatrica 1996;85(12):1483-6. DOI: 10.1111/j.1651-2227.1996.tb13956.x.
17. Skouroliakou M, Matthaiou C, Chiou A, Panagiotakos D, Gounaris A, Nunn T, et al. Physicochemical stability of parenteral nutrition supplied as all-in-one for neonates. Journal of Parenteral and Enteral Nutrition 2008;32(2):201-9. DOI: 10.1177/0148607108314768.

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Trabajo Original

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Assessment of nutritional status and bone health in neurologically impaired children: a challenge in pediatric clinical practice

Valoración del estado nutricional y de la salud ósea en niños con afectación neurológica: un reto en la práctica clínica

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Abstract

Introduction: neurologically impaired children frequently experience nutritional disorders and bone health complications. Our aim was firstly to analyze a method to interpret bone mineral density (BMD) accurately in neurologically impaired children. Secondly, to determine its relationship with the nutritional status and micronutrient levels in order to identify which factors are associated with low BMD.

Methods: a observational multicenter study was conducted in children with moderate-to-severe neurological impairment. Data collected included: medical records, anthropometric measures, hematologic and biochemical evaluation. BMD was measured with Dual-energy X-ray absorptiometry and z-scores were calculated adjusting for sex and chronological age. Secondly, BMD z-scores were calculated applying height age (age at which the child's height would be in 2nd percentile) instead of chronological age.

Results: fifty-two children were included (aged 4-16 years). Seventeen patients (32.7%) received feeding by gastrostomy tube. Height and BMI z-score were below 2SD in 64% and 31% of patients respectively, with normal mid upper arm circumference and skinfold thickness measurements. Low vitamin-D levels were found in 42% of cases. 50% of patients evidenced low BMD when calculated for chronological age, whereas only 34.5% showed BMD z-score <-2 when calculated for height age. No correlation was observed between BMD and vitamin-D levels, weight and height z-scores or age when BMD was calculated applying height age.

Conclusions: the prevalence of low BMD is high in neurologically impaired children, and it is probably multifactorial. In these children, we suggest adjusting BMD for height age, in order not to over diagnose low BMD.

Key words:

Disabled children. Cerebral palsy. Nutritional assessment. Bone mineral density. Bone health.

Resumen

Introducción: los niños con afectación neurológica con frecuencia presentan trastornos nutricionales y complicaciones óseas. Nuestro objetivo fue, en primer lugar, analizar un método para interpretar la densidad mineral ósea (DMO) de forma adecuada en estos pacientes. En segundo lugar, determinar la relación de la DMO con el estado nutricional y los niveles de micronutrientes, para determinar qué factores se asocian con baja DMO.

Métodos: estudio observacional multicéntrico, se incluyeron niños con afectación neurológica moderada-severa. Se recogieron datos clínicos, medidas antropométricas y una evaluación hematológica y bioquímica. La DMO fue evaluada mediante densitometría, y se calcularon los z-scores según la edad y sexo. En segundo lugar, se recalcularon los z-scores de DMO para la edad talla (edad en la cual la talla del niño se encontraría en el percentil 2) en vez de la edad cronológica.

Resultados: se incluyeron 52 niños (4-16 años). Diecisiete pacientes (32,7%) recibían alimentación por gastrostomía. Los z-scores de peso y talla estaban por debajo de 2 desviaciones estándar (DE) en el 64% y 31% de los pacientes respectivamente, con normalidad de las mediciones de perímetro braquial y pliegues tricipital y subescapular. Los niveles de vitamina D estaban bajos en el 42% de los casos. La mitad de los pacientes tenían baja DMO cuando se calculó para la edad cronológica, mientras que solo el 34,5% presentaron DMO por debajo de 2 DE cuando se calculó para la edad talla. No observamos correlación entre z-scores de DMO calculados para la edad talla y los niveles de vitamina D, la edad o los z-scores de peso y talla.

Conclusiones: la prevalencia de baja DMO es alta en niños con discapacidad neurológica, y probablemente es multifactorial. En estos niños, sugerimos ajustar DMO para la edad talla, para evitar sobrediagnosticar baja DMO.

Palabras clave:

Niños discapacitados. Parálisis cerebral. Seguimiento nutricional. Densidad mineral ósea. Salud ósea.

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INTRODUCTION

Patients with severe neurologic diseases frequently experience nutritional and growth disorders and bone health complications of multifactorial origin, being these more evident with increasing motor disorder (1,2). Almost half of these children show problems with feeding and malnutrition, frequently under-recognized (1,3). Undernutrition can have adverse consequences, including growth failure, greater motor disorder, poor bone health, recurrent pneumonia and neurologic worsening with increasing cognitive delay and abnormal behavior (4).

Among factors that contribute to nutritional disorders in children with neurologic disease are oromotor dysfunctions that result in insufficient intake, increased losses and feeding behavior disorders (5). A frequent problem in these patients is osteoporosis related to immobility, undernutrition, insufficient intake of calcium, limited solar exposure and treatment with antiepileptic drugs. All of them often favor fractures after minimal trauma (6-8). As a consequence, all of these conditions negatively affect the quality of life of the children and their caregivers or family (3,9).

In order to assess bone health, the recommended method and most widely available is to evaluate BMD using Dual-energy X-ray absorptiometry scan (DXA). During childhood, BMD changes according age and sex, so we need to express the results as z-score. Because BMD is a two-dimensional measurement, it is a problem to interpret the results in the growing skeleton, as BMD measurements are affected by body size (10). Currently, there is no consensus about which method we must apply to adjust BMD for height in order to avoid over and under diagnosis of low BMD. There have been several approaches, but most of them are difficult to perform in clinical practice.

With this perspective, the aim of our study was firstly to analyze a method to determine bone mineral density (BMD) accurately in neurologically impaired children. Secondly, to determine the relationship between BMD, the nutritional status and micronutrient levels, in order to identify which factors are associated with low BMD.

MATERIAL AND METHODS

An observational multicenter study was conducted. Data was collected between September 2014 and September 2016.

PATIENTS

Patients under 16 years of age with neurological impairment were recruited. They were controlled in Pediatric Gastroenterology and Nutrition outpatient clinics of five hospitals. Patients with the following moderate or severe motor affectation were included: a) cerebral palsy (CP) grade III, IV or V classified according to the Gross Motor Function Classification System (GMFCS) (11); b) patients with severe neurological disorders that could not walk around without help (Table I). In both cases, written parental consent and approval from the Hospitals' Ethics Committee were obtained.

Parameters recorded were: age, gender, underlying disease, medications, questions to assess swallowing problems, and feeding method (oral or tube-feeding). Factors related with BMD, mineral and vitamin D supplementation, history of bone fractures and treatment with antiepileptic drugs were assessed. The intellectual delay was classified according to the diagnostic criteria of the DSM-IV-TR, categorizing children with or without severe mental retardation (12).

Table I. Patients' characteristics

	Patients (n = 52)
Mean age (range)	9.9 (4-16)
Gender male n (%)	33 (63.5%)
Diagnosis n (%)	
Cerebral palsy	40 (77%)
GMFCS III	4 (10%)
GMFCS IV	11 (27.5%)
GMFCS V	25 (62.5%)
Genetic diseases	6 (11.5%)
Neuromuscular diseases	2 (4%)
Epileptic encephalopathies	1 (2%)
Others	3 (5.5%)
Anticonvulsive treatment n (%)	33 (63.5%)
Treatment with PPI n (%)	30 (58%)
Previous fractures n (%)	8 (15.4%)
Severe mental retardation n (%)	44 (85%)
Nutritional variables n (%)	
Oral feeding	35 (67.3%)
Supplement with polymeric enteral formula	17 (48.5%)
Tube feeding	17 (33%)

PPI: proton pump inhibitors.

ANTHROPOMETRIC ASSESSMENT

The weight was obtained from the child either naked or in underwear. Given that these children are not capable of standing with stability, they were weighed together with the caregiver, whose weight was later subtracted (Clinical electronic scales Seca® model 769, Germany) (4,5). Length was measured in a supine position using an anthropometer or horizontal measuring table (Holtain® stadiometer, United Kingdom). In children who showed contractures, spasticity or severe scoliosis, as the measurement could not be obtained this way, measurement of segmental lengths was recorded on the left side of the body and repeated, achieving the average of both measurements. In children with some disparities, the measurements were obtained from the least affected side. The upper arm length (UAL) (distance from the acromion to the radial head) and the tibial length (TL) (distance from the supermedial edge of the tibia to the inferior edge of the medial malleolus) were measured (13). In these children, the stature (S) was calculated from the TL using the following formula: S = (3.26 x TL) +30.8 (14). In these patients, the body mass index (BMI) was not calculated so as not to magnify the possible error of the estimated S calculation when squared.

Other measurements recorded were mid upper arm circumference (MUAC) (with inextensible tape measure) and triceps and subscapular skinfolds thickness using a skinfold caliper (0.2 mm precision) (Holtain®, United Kingdom), obtaining the average of three measurements.

The anthropometric data was converted into z-score for age and sex according to the references of the WHO for children under 5 years of age (15). For those older than 5, the weight, size and BMI z-score were calculated according to references of the WHO (16), applying references of Frisancho for MUAC and skinfold thickness (17).

HEMATOLOGIC AND BIOCHEMICAL EVALUATION

During the initial evaluation of each patient, hematologic and biochemical analyses were performed. The biochemical evaluation included measuring levels of albumin, prealbumin, calcium, phosphorous, magnesium, alkaline phosphatases, 25OH vitamin D, parathyroid hormone (PTH), vitamin B12, folate, iron, ferritin and zinc. A concentration of 25OH vitamin D below 30 ng/mL was considered insufficient, and marked as deficiency if below 20 ng/mL (18). Zinc was considered below normal when the levels were under 70 µg/dL (19).

ASSESSMENT OF BONE HEALTH

BMD was evaluated at lumbar spine (L2-L4) through DXA (Norland DXA®). Firstly, the measurements obtained (g/cm^2) were converted into z-scores normalized by chronological age and sex according to the previously published data (20). Secondly, BMD z-score were calculated substituting chronological age for height age. Height age was calculated for children with height below z-score <-2 as the age at which the child's height would be in 2nd percentile. For children with height greater than 2nd percentile, height age was assigned the same as chronological age.

DATA ANALYSIS

Descriptive statistics were calculated for the demographic, clinical characteristics, and biochemical analysis. Independent sample one-way ANOVAs were undertaken to determine the differences in anthropometric characteristics between patients with or without gastrostomy. Pearson's correlations were calculated to determine the level of association between BMD (calculated in the two ways: chronological age and height age), age, anthropometric z-scores and vitamin D levels. Hierarchical multiple regression analyses were conducted with the BMD and anthropometric z-scores. Statistics were generated with a standard statistical package IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA). The two-sided threshold for statistical significance was set at $p < 0.05$.

RESULTS

A total of 52 patients were included (patients' main characteristics in table I). The mean age was 9.9 years (range 4-16), and 63.5% of sample were boys. Among these patients, the majority presented severe motor impairment, whereas 85% suffered from profound mental retardation. The main diagnostic obtained was CP (77%). Anticonvulsive drugs were prescribed in 63.5% of cases, and proton pump inhibitors (PPI) in 58%. Most children (67.3%) received oral feeding, 17 of them (48.5%) with supplement in the form of polymeric formula. Seventeen patients (33%) were fed by gastrostomy tube. Twelve children (23%) received oral supplement with vitamin D at the time of the study.

ANTHROPOMETRIC RESULTS

The anthropometric results are showed in table II. In 63% of children, the weight z-score was below 2SD; height z-score was below 2SD in 64% patients; and BMI resulted below 2SD in 31% children. No differences between patients with or without GT were shown except in height for age. The stature was not possible to obtain in a direct way in 16 children and had to be calculated by estimating from the TL.

Table II. Anthropometric characteristics

Z-score	Orally-fed patients (n = 35)	Gastrostomy-fed patients (n = 17)	p-value
Weight for age, M (SD)	-2.70 (1.50)	-2.29 (1.71)	0.413
Height for age, M (SD)	-2.12 (1.54)	-2.97 (1.50)	0.038
BMI for age, M (SD)	-1.43 (1.82)*	-0.84 (1.95)**	0.327
Arm circumference, M (SD)	-0.86 (1.16)	-0.32 (1.30)	0.192
Triceps skinfold, M (SD)	-0.36 (0.96)	0.26 (1.30)	0.142
Subscapular skinfold, M (SD)	0.08 (0.64)	0.24 (0.86)	0.184

*M: mean; SD: standard deviation. *n = 22; **n = 14.*

HEMATOLOGICAL AND BIOCHEMICAL RESULTS

Iron deficiency anemia was detected in 3 patients (2 of them at a pubertal age). The biochemical study showed that 19 children (36.5%) had vitamin D levels lower than recommended (25% insufficiency and 11.5% deficiency), while levels of calcium, phosphorus, magnesium, alkaline phosphatase, vitamin B12 and folate remained normal in every case. PTH levels were not included in the results because we have results only in 40% of the patients, showing normal levels in all of them. The albumin was normal, while the prealbumin was diminished in 18% of patients. Levels of zinc were found to be diminished in 20% of patients (Table III).

BONE HEALTH

A total of 15.4% of patients included in the study had a history of bone fractures. BMD was lower in patients with history of bone fractures, but it was not statistically significant (p = 0.277).

When calculated for chronological age, 26 patients (50%) showed a BMD z-score <-2 (mean -1.73 ± 1.25), whereas only 18 (34.5%) showed BMD z-score <-2 when calculated for height age (mean -1.44 ± 1.27).

The associations between BMD and other variables are presented in table IV. When calculated for chronological age, BMD was significantly correlated with z-score weight (r = 0.453, p = 0.001), and z-score height (r = 0.340, p = 0.042), but not with BMI z-score. However, no correlation was found when BMD calculated applying height age. No relation was observed between BMD and the levels of vitamin D or age.

Table III. Biochemical analysis

Micronutrient	Mean	SD	Children presenting deficiency (%)
Calcium (mg/dL)	9.9	0.5	0
Phosphorous (mg/dL)	4.5	0.7	0
Magnesium (mg/dL)	1.8	0.6	0
Alkaline phosphatase (UI/L)	190	54	0
Vitamin B12 (pg/mL)	973	538	0
Albumin (g/dL)	4.3	0.4	0
Iron (µg/dL)	74.7	35	6
Ferritin (ng/mL)	46.5	45	6
Folate (ng/mL)	11.8	5.5	0
25OH-vitamin D (ng/mL)	36.7	15.5	36.5
Prealbumin (mg/dL)	19.3	4.6	18
Zinc (µg/dL)	86.8	38	20

SD: standard deviation.

Table IV. Pearson's correlations between BMD, anthropometric z-score, age and vitamin D level

Variables	BMD for chronological age	BMD for age height
Z-score Height for age	0.866**	0.082
Z-score Weight for age	0.453**	0.206
Z-score BMI for age	0.229	0.139
Age	-0.113	0.125
Vitamin D level	0.214	0.084

***Correlation is significant at 0.01 level (two-tailed). *Correlation is significant at the 0.05 level (two-tailed).*

DISCUSSION

Nutritional support in children with neurological disabilities is considered an important factor to improve global outcome, reduce complications and promote the quality of life of both the patient and their parents/caregivers. As a part of their nutritional assessment, bone health should be evaluated, because children with disability of a neurological origin frequently feature lower BMD compared with healthy children of the same age and gender, resulting in an increased risk of fractures (21,22). The objective of bone health assessment in clinical practice is to determine whose children are at risk, in order to establish a treatment before suffering fractures. The recommended method is measuring BMD with DXA. BMD values must be expressed in age and sex specific z-scores. Additionally, it is well known that DXA measures of BMD are confounded by short stature (23), but there is no consensus about how to adjust these results for bone size.

It has been proven that neurologically impaired children grow slower than children of the same age and gender without chronic pathology (24-26), and these differences increase with age (8). This is due to both nutritional and non-nutritional factors, such as genetic and endocrine factors. Our anthropometric results show average z-scores for height under 2 SD, suggestive of stunting, so the need to adjust the results for body size becomes even more important.

Some authors suggest adjusting BMD for height age, which is the age at which child's height is the median height-for-age on the growth chart (27). A limitation of this procedure is that it doesn't consider pubertal maturation. The calculation of bone mineral apparent density (BMAD) adjusted for age is also proposed, but this is a complicated procedure to perform in clinical practice (28). We suggest adjusting BMD for height age, but taking the age corresponding to 2nd percentile, because it is the lower limit of normality considered by WHO. In our opinion, taking the median (50th percentile) as a reference is an unrealistic goal because these children have a height well below this parameter, thus the height for 50th percentile is far from reality.

In our findings, half of the sample features exhibited low BMD according to chronological age, with a z-score less than -2 SD. However, when calculated for height age (age at which the child's height would be in 2nd percentile), this percentage decreased to 34.5%. These results show that not adjusting for height may result in over diagnosing low BMD.

Low BMD is known to be associated with a higher risk of fractures (29), thus monitoring and follow up are important. As previously mentioned, fractures are frequent in patients with severe or moderate neurological affectation, and those that have indeed had a fracture have an increased risk of having subsequent ones (7,30). In our series we have found 15.4% of patients who experienced a fracture in the past, which is similar to previously published data (30,31) and it is probably due to multiple factors that can influence bone health in a negative way (32). Some risk factors that these patients present are undernutrition, feeding disorders, age, history of previous fractures, immobility, and antiepileptic treatment (10,33-35).

In our patients, it was noted a high prevalence of epilepsy (63.5%), which requires specific drugs that can contribute to bone disorders. Feeding problems in children with neurological diseases can produce deficiencies at micronutrient level. Thus, their deficiencies in many cases can be subclinical, being able to affect different areas (36). Therefore, it is crucial to carry out a periodic monitoring and control of these aspects. In our study, we have found a high prevalence of vitamin D and zinc deficiency. Regarding the definition of lack of vitamin D in infancy, in 2013 the ESPGHAN Committee on Nutrition considered levels of 250H-vitamin D below 50 nmol/L (equivalent to 20 ng/ml) as deficient and levels below 25 nmol/L (10 ng/ml) as severe deficiency, taking into account that these recommendations are for healthy children (37). In the same way, Munns et al., in a global consensus recommendations on prevention and management of nutritional rickets published in 2016, consider levels below 50 nmol/L as insufficiency, and below 30 nmol/L as deficiency (38). Nevertheless, other authors consider insufficient levels between 50-80 nmol/L (20-30 ng/ml) and deficiency levels below 50 nmol/L (< 20 ng/ml) (18). Considering the multiple risk factors for bone health in these children, it seems more convenient to contemplate the latter. It should be noted the normality at biochemical level of the minerals (calcium, phosphorus, magnesium), alkaline phosphatase, vitamin B12 and folate in all cases, supporting what was described in other series (39). However, it has to be taken into account that the normality of the levels of these minerals in blood do not reflect fully the state of the entire organism, given that it deals with important components at blood level and that they are strongly regulated by homeostasis (36).

It should be considered that many of the risk factors for bone health that these patients have are interrelated, which makes it difficult to determine their contribution in an isolated way. In our patients, after performing Pearson's correlation, we found association between the BMD z-score and the z-score of weight and height. However, this relation is not maintained after adjusting BMD for height. The association we observed between height, weight and BMD is most likely an artefact of the short stature in these children, rather than a true effect of undernutrition. Consequently, it disappears after adjusting BMD measurements for height age. No association with age or vitamin D levels were found, despite being described previously in the literature (6).

To this effect, accurate reporting of these patients' clinical and laboratory data throughout their follow-up can be of interest to paediatricians responsible for these patients.

Despite the relevance of this study's findings, several limitations must be acknowledged. Firstly, the transversal nature of this study limits the ability to withdraw causational or directional conclusions. Secondly, since the sample comprises children suffering from neurological diseases, results may not be readily applicable to children with other underlying diseases. Finally,

the relatively small sample size imposes an overall limitation to result extrapolation.

In conclusion, these results suggest the need to perform a periodic follow up of the nutritional status of children with neurological impairment as an integral part of their health care, aiding to early detect nutritional disorders so that they will benefit from precocious treatment (5). During the follow up it is important to monitor the levels of vitamin D and zinc, as their lack is frequent but can be corrected, and to perform periodic controls of DXA to try to early detect changes in the BMD before they suffer fractures. We suggest calculating BMD z-score according sex and adjusting age at which height is at 2nd percentile if lower, to avoid to over diagnose low BMD.

REFERENCES

1. Kuperminc MN, Gottrand F, Samson-Fang L, Arvedson J, Bell K, Craig GM, et al. Nutritional management of children with cerebral palsy: a practical guide. Eur J Clin Nutr 2013;67:S21-3. DOI: 10.1038/ejcn.2013.227
2. Martínez-Costa C, Borraz S, Benlloch C, López-Sáiz A, Sanchiz V, Brines J. Early decision of gastrostomy tube insertion in children with severe developmental disability: a current dilemma. J Hum Nutr Diet 2011;24(2):115-21. DOI: 10.1111/j.1365-277X.2010.01146.x
3. Sullivan PB, Lambert B, Rose M, Ford-Adams M, Johnson A, Griffiths P. Prevalence and severity of feeding and nutritional problems in children with neurological impairment: Oxford Feeding Study. Dev Med Child Neurol 2000;42(10):674-80. DOI: 10.1017/S0012162200001249
4. Kuperminc MN, Stevenson RD. Growth and nutrition disorders in children with cerebral palsy. Dev Disabil Res Rev 2008;14(2):137-46. DOI: 10.1002/ddrr.14
5. Marchand V, Motil KJ; NASPGHAN Committee on Nutrition. Nutrition support for neurologically impaired children: a clinical report of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr 2006;43(1):123-35. DOI: 10.1097/01.mpg.0000228124.93841.ea
6. Henderson RC, Lark RK, Gurka MJ, Worley G, Fung EB, Conaway M, et al. Bone density and metabolism in children and adolescents with moderate to severe cerebral palsy. Pediatrics 2002;110(1):e5. DOI: 10.1542/peds.110.1.e5
7. Mus-Peters CTR, Huisstede BMA, Noten S, Hitters MWMGC, van der Slot WMA, van den Berg-Emons RJG. Low bone mineral density in ambulatory persons with cerebral palsy? A systematic review. Disabil Rehabil 2018;22:1-11.
8. Stevenson RD, Conaway M, Chumlea WC, Rosenbaum P, Fung EB, Henderson RC, et al. Growth and Health in Children With Moderate-to-Severe Cerebral Palsy. Pediatrics 2006;118(3):1010-8. DOI: 10.1542/peds.2006-0298
9. Holenweg-Gross C, Newman CJ, Faouzi M, Poirot-Hodgkinson I, Bérard C, Roulet-Perez E. Undernutrition in children with profound intellectual and multiple disabilities (PIMD): its prevalence and influence on quality of life. Child Care Health Dev 2014;40(4):525-32. DOI: 10.1111/cch.12085
10. Kecskemethy HH, Harcke HT. Assessment of bone health in children with disabilities. J Pediatr Rehabil Med 2014;7(2):111-24.
11. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997;39(4):214-23. DOI: 10.1111/j.1469-8749.1997.tb07414.x
12. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. In: Diagnostic and statistical manual of mental disorders, 4. 4a ed. Washington, DC; 2000.
13. Bell KL, Davies PSW, Boyd RN, Stevenson RD. Use of Segmental Lengths for the Assessment of Growth in Children with Cerebral Palsy. In: Preedy VR, editor. Handbook of Anthropometry [Internet]. New York, NY: Springer New York; 2012. pp. 1279-97. [cited 2015 Dec 31]. Available from: http://link.springer.com/10.1007/978-1-4419-1788-1_78. DOI: 10.1007/978-1-4419-1788-1_78
14. Stevenson RD. Use of segmental measures to estimate stature in children with cerebral palsy. Arch Pediatr Adolesc Med 1995;149(6):658-62. DOI: 10.1001/archpedi.1995.02170190068012
15. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards based on length/height, weight and age. Acta Paediatr 2006;450:76-85. DOI: 10.1111/j.1651-2227.2006.tb02378.x
16. De Onis M. Growth curves for school age children and adolescents. Indian Pediatr 2009;46(6):463-5.
17. Frisancho AR. New norms of upper limb fat and muscle areas for assessment of nutritional status. Am J Clin Nutr 1981;34(11):2540-5. DOI: 10.1093/ajcn/34.11.2540
18. Wacker M, Holick M. Vitamin D - Effects on Skeletal and Extraskeletal Health and the Need for Supplementation. Nutrients 2013;5(1):111-48. DOI: 10.3390/nu5010111
19. Gibson RS, Hess SY, Hotz C, Brown KH. Indicators of zinc status at the population level: a review of the evidence. Br J Nutr 2008;99:S14-23. DOI: 10.1017/S0007114508006818
20. Kalkwarf HJ, Zemel BS, Gilsanz V, Lappe JM, Horlick M, Oberfield S, et al. The bone mineral density in childhood study: bone mineral content and density according to age, sex, and race. J Clin Endocrinol Metab 2007;92(6):2087-99. DOI: 10.1210/jc.2006-2553
21. Fehlings D, Switzer L, Agarwal P, Wong C, Sochett E, Stevenson R, et al. Informing evidence-based clinical practice guidelines for children with cerebral palsy at risk of osteoporosis: a systematic review. Dev Med Child Neurol 2012;54(2):106-16. DOI: 10.1111/j.1469-8749.2011.04091.x
22. Romano C, van Wynckel M, Hulst J, Broekaert I, Bronsky J, Dall'Oglio L, et al. ESPGHAN- Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children with Neurological Impairment. J Pediatr Gastroenterol Nutr 2017;65:242-64. DOI: 10.1097/MPG.0000000000001646
23. Kalkwarf HJ, Abrams SA, DiMeglio LA, Koo WWK, Specker BL, Weiler H, et al. Bone densitometry in infants and young children: the 2013 ISCD Pediatric Official Positions. J Clin Densitom 2014;17(2):243-57. DOI: 10.1016/j.jocd.2014.01.002
24. Brooks J, Day S, Shavelle R, Strauss D. Low weight, morbidity, and mortality in children with cerebral palsy: new clinical growth charts. Pediatrics 2011;128(2):e299-307. DOI: 10.1542/peds.2010-2801
25. Day SM, Strauss DJ, Vachon PJ, Rosenbloom L, Shavelle RM, Wu YW. Growth patterns in a population of children and adolescents with cerebral palsy. Dev Med Child Neurol 2007;49(3):167-71. DOI: 10.1111/j.1469-8749.2007.00167.x
26. Samson-Fang L, Stevenson RD. Linear growth velocity in children with cerebral palsy. Dev Med Child Neurol 1998;40(10):689-92. DOI: 10.1111/j.1469-8749.1998.tb12329.x
27. Zemel BS, Leonard MB, Kelly A, Lappe JM, Gilsanz V, Oberfield S, et al. Height adjustment in assessing dual energy x-ray absorptiometry measurements of bone mass and density in children. J Clin Endocrinol Metab 2010;95(3):1265-73. DOI: 10.1210/jc.2009-2057
28. Bachrach LK, Hastie T, Wang MC, Narasimhan B, Marcus R. Bone mineral acquisition in healthy Asian, Hispanic, black, and Caucasian youth: a longitudinal study. J Clin Endocrinol Metab 1999;84(12):4702-12. DOI: 10.1210/jc.84.12.4702
29. Bianchi mL, Leonard MB, Bechtold S, Högler W, Mughal MZ, Schönau E, et al. Bone health in children and adolescents with chronic diseases that may affect the skeleton: the 2013 ISCD Pediatric Official Positions. J Clin Densitom 2014;17(2):281-94. DOI: 10.1016/j.jocd.2014.01.005
30. Henderson RC. Bone density and other possible predictors of fracture risk in children and adolescents with spastic quadriplegia. Dev Med Child Neurol 1997;39(4):224-7. DOI: 10.1111/j.1469-8749.1997.tb07415.x
31. Kilpinen-Loisa P, Paasio T, Soiva M, Ritanen UM, Lautala P, Palmu P, et al. Low bone mass in patients with motor disability: prevalence and risk factors in 59 Finnish children. Dev Med Child Neurol 2010;52(3):276-82. DOI: 10.1111/j.1469-8749.2009.03464.x
32. Henderson RC, Kairalla JA, Barrington JW, Abbas A, Stevenson RD. Longitudinal changes in bone density in children and adolescents with moderate to severe cerebral palsy. J Pediatr 2005;146(6):769-75. DOI: 10.1016/j.jpeds.2005.02.024
33. Cheng SW, Ko CH, Lee CY. The effect of anticonvulsant use on bone mineral density in non-ambulatory children with cerebral palsy. Hong Kong Med J 2016;22:242-8. DOI: 10.12809/hkmj154588

34. Mergler S, Evenhuis HM, Boot AM, De Man SA, Bindels-De Heus KGCB, Huijbers WAR, et al. Epidemiology of low bone mineral density and fractures in children with severe cerebral palsy: a systematic review. Dev Med Child Neurol 2009;51(10):773-8. DOI: 10.1111/j.1469-8749.2009.03384.x
35. Ozel S, Switzer L, Macintosh A, Fehlings D. Informing evidence-based clinical practice guidelines for children with cerebral palsy at risk of osteoporosis: an update. Dev Med Child Neurol 2016;58(9):918-23. DOI: 10.1111/dmcn.13196
36. Schoendorfer MC, Vitetta L, Sharp N, DiGeronimo M, Wilson G, Coombes JS, et al. Micronutrient, Antioxidant, and Oxidative Stress Status in Children With Severe Cerebral Palsy. JPEN J Parenter Enteral Nutr 2013;37:97-101. DOI: 10.1177/0148607112447200
37. Braegger C, Campoy C, Colomb V, Decsi T, Domellof M, Fewtrell M, et al. Vitamin D in the healthy European paediatric population. J Pediatr Gastroenterol Nutr 2013;56(6):692-701. DOI: 10.1097/MPG.0b013e31828f3c05
38. Munns CF, Shaw N, Kiely M, Specker BL, Thacher TD, Ozono K, et al. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. J Clin Endocrinol Metab 2016;101(2):394-415. DOI: 10.1210/jc.2015-2175
39. Papadopoulos A, Ntaios G, Kaiafa G, Girtovitis F, Saouli Z, Kontoninas Z, et al. Increased incidence of iron deficiency anemia secondary to inadequate iron intake in institutionalized, young patients with cerebral palsy. Int J Hematol 2008;88(5):495-7. DOI: 10.1007/s12185-008-0191-3

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Pediatría

Interleukine 6 and C-reactive protein predict growth impairment and acute malnutrition in children and adolescents with chronic kidney disease

La interleucina 6 y la proteína C-reactiva predicen el retraso del crecimiento y la desnutrición aguda en niños y adolescentes con enfermedad renal crónica

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Abstract

Objective: secondary malnutrition and systemic inflammation may impair growth and body composition in children and adolescents with chronic kidney disease (CKD). This association has been scantily studied, particularly in pre-dialytic stages. Our aim was to correlate growth and nutritional status indicators with the serum concentration of interleukine 6 (IL-6) and ultrasensitive C-reactive protein (CRP) in children with CKD.

Methods: this was a prospective cross-sectional study in 29 children and adolescents aged 3-16 years with CKD, stages 3 or 4, in two third-level general hospitals. The outcome variables were height for age, body mass index, arm anthropometric indicators, plus lean mass/fat percentage by bioelectrical impedance. The independent variables were IL-6 and CRP. This study was reviewed and approved by the Health Research and Ethics Committees of both hospitals.

Results: height for age, body mass index, subscapular skinfold, arm fat area, and lean mass had a significant negative correlation with IL-6. The height-for-age z-score had a negative correlation with CRP. IL-6 explained 15% to 35% of the variance in height for age and nutritional status indicators. CRP predicted 22% of height for age. One fifth of the patients had acute malnutrition, and one third were stunted. Muscle was the most affected compartment.

Conclusion: IL-6 and CRP in children and adolescents with CKD in the pre-dialytic stage predicted one fifth and one third of the variance in acute and chronic malnutrition indicators. The frequency of acute malnutrition and impaired growth was considered clinically significant. Muscular mass deficit was a central component of malnutrition.

Key words:

Children. Chronic kidney disease. Inflammation. Malnutrition. Interleukine 6.

Resumen

Objetivo: correlacionar indicadores de crecimiento y del estado nutricional con la concentración sérica de interleucina 6 (IL-6) y proteína C-reactiva ultrasensible (PCR) en niños con enfermedad renal crónica (ERC).

Métodos: estudio transversal analítico de 29 niños y adolescentes de 3 a 16 años de edad con ERC, estadios 3 o 4, en dos hospitales generales de tercer nivel. Las variables dependientes fueron indicadores antropométricos de crecimiento y del estado nutricional y la composición corporal por impedancia bioeléctrica. Las variables independientes fueron IL-6 y PCR. Este estudio fue revisado y aprobado por los Comités de Ética y de Investigación de ambos hospitales.

Resultados: la talla para la edad (T/E), el índice de masa corporal, el pliegue cutáneo subescapular, el área de grasa del brazo y la masa magra obtuvieron una correlación negativa con la IL-6. La T/E obtuvo una correlación negativa con la PCR. La IL-6 explicó el 15% y 35% de la varianza de la T/E y de los indicadores del estado nutricional. La CRP predijo el 22% de la T/E. Una quinta parte de los pacientes tenía desnutrición aguda y una tercera parte desmedro. El compartimento corporal más afectado fue el muscular.

Conclusión: la IL-6 y la PCR en niños y adolescentes con ERC en etapa predialítica explicaron una quinta y una tercera parte de la varianza de los indicadores de desnutrición aguda y crónica, respectivamente. La frecuencia de la desnutrición aguda y el desmedro fueron clínicamente significativos. El déficit de masa muscular fue un componente central de la desnutrición.

Palabras clave:

Niños. Enfermedad renal crónica. Inflamación. Desnutrición. Interleucina 6.

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INTRODUCTION

Secondary malnutrition in chronic kidney disease (CKD) is a complex, multifactorial process associated with a number of conditions: inadequate intake of energy, macro, and micronutrients; hyporexia; electrolyte imbalance; acidosis; anemia; uremia; abnormal loss of protein in the urine; loss of nutrients during peritoneal dialysis and hemodialysis; hormonal disorders; and increased basal energy expenditure (1-3). Some consequences of malnutrition in the early stages of life may be its impact on linear growth and body composition, particularly on fat reserves and muscle mass (4,5).

Systemic inflammation, particularly through proinflammatory cytokines, has been associated with malnutrition in adults with stage-3 or -4 CKD (6). The proposed mechanisms for this association are decreased appetite, muscle proteolysis, increased catabolism, and decreased albumin synthesis (7,8). This association has been sparsely studied in children and adolescents with CKD, particularly in the pre-dialytic stages. The aim of this study was to correlate anthropometric indicators of growth and nutritional status with the serum concentrations of interleukin-6 (IL-6) and ultrasensitive C-reactive protein (CRP) in children with CKD in stages 3 and 4.

MATERIALS AND METHODS

PATIENTS

In this prospective, cross-sectional study 29 consecutive children and adolescents with stages 3 or 4 of CKD who were taken care of in two third-level general hospitals were studied from February through December 2014. Inclusion criteria were CKD stages 3 or 4 (glomerular filtration rate, 15–59 mL/min/1.73 m^2) and age 3 to 16 years. Patients with systemic or autoimmune diseases, primary tubular acidosis, acute or chronic infections, and treatment with anti-inflammatory drugs were not included.

ANTHROPOMETRY

- *Standardization:* before data collection, the authors performed an anthropometrical standardization trial (9). Consistency (intragroup individual measurements) and validity (comparison with a gold standard) were evaluated with Pearson's bivariate correlations. When the correlation coefficient was below 0.8 the anthropometric technique was reviewed and corrected until intragroup and intergroup correlations above 0.8 were achieved.
- *Weight:* patients were weighed with a movable-weight, platform-beam scale (ATCO mechanical height and weight scale, WSE40032), without shoes and with minimal clothing. Weight was recorded to the nearest 100 grams (10).
- *Height:* height was measured and recorded to the nearest 0.1 cm with a standiometer fitted with a movable block (ADE/Germany, MZ10023). The subjects were measured while standing, without shoes, heels together, back as straight as possible, and arms hanging freely; the head was positioned in the Frankfort horizontal plane (10).
- *Mid-upper arm circumference (MUAC):* to obtain the MUAC the patient's left arm was bent at a 90-degree angle at the elbow, with the upper arm held parallel to the side of the body. The distance between the acromion and olecranon was measured with a fiberglass metric tape, and the midpoint between these two points was marked. The children's arm was then relaxed, hanging loosely by the side. The fiberglass tape was positioned at the marked midpoint, and the circumference was recorded to the nearest 0.1 cm (10).
- *Triceps skinfold (TSF):* the TSF was measured with a Lange skinfold caliper (Cambridge, Maryland, USA) at the previous posterior mark in the left upper-arm midpoint. The arm was extended in the same relaxed position used for the MUAC. The examiner grasped a vertical pinch of skin and subcutaneous fat between the thumb and forefinger, approximately 1 cm above the marked midpoint, gently pulling away from the underlying muscle. The skinfold caliper was placed at the midpoint mark while maintaining the skinfold grasp. Readings were measured in millimeters when the caliper came in contact with the skin and the dial reading was stabilized (9-12).
- *Total arm area (TAA); arm muscle area (AMA); and arm fat area (FAA):* arm areas were calculated according to the formulas described by Frisancho; the results were expressed in square centimeters (10).
- *Reference patterns and indicators of nutritional status:* the z-scores for height for age and body mass index (BMI) for age were calculated with the World Health Organization (WHO) 2006 reference pattern (11). Z-scores of the mid-upper arm circumference, triceps skinfold, and arm areas for age were calculated with the Frisancho reference patterns (10-13). Z-scores for each arm measurement and area were classified into two groups: < -2 SD and -2 to +2 SD.

BIOELECTRICAL IMPEDANCE (BIE)

The estimation of lean body mass and fat percentage was performed with the analyzer BODYSTAT® QuadScan 4000, with the subject fasting for three hours, avoiding moderate and vigorous physical activity before measurement, and without metal objects (watch, chains, earrings, etc.). The children were placed in a supine position over a non-electrically conductive surface at room temperature. Two electrodes were positioned in the right hand (one behind the knuckles, one on the wrist next to the ulnar head), and two electrodes on the right foot (one behind the toes, one at the ankle). The black measuring leads were connected to the electrodes on the wrist and ankle, and the red leads to the distal electrodes. Then the measuring device was turned on to introduce the necessary data (age, weight, and height), and subsequently allow the passage of electric current; the data were printed after five seconds and then transferred via Bluetooth to the QuadScan software (14) (Clasey JL, 2011).

HEMATOLOGY AND CLINICAL CHEMISTRY

Routine laboratory tests included serum hemoglobin (g/dL), serum creatinine (mg/dL), and serum albumin (g/dL). The glomerular filtration rate was estimated with the Schwartz formula and reported as mL/min/m^2 (15).

Interukine-6: the quantification of serum IL-6 was performed by high-sensitivity enzyme-linked immunosorbent assay (ELISA) kits (KHC0064, Invitrogen®) with 96-well plates and a microplate reader. This assay recognizes both the natural and recombinant forms of this target with a sensitivity < 2 pg/mL and a standard curve range of 7.8-500 pg/mL. The sample volume required was 100 µL with a total assay time of 3 hours.

Ultrasensitive C-reactive protein: the quantification of highly sensitive CRP was performed using the latex-turbidimetry method with detection starting from 0.06 mg/L (Linear Chemicals® SL).

STATISTICS

Quantitative demographic, anthropometric, and laboratory data had a normal distribution and were reported as mean and standard deviation (SD); the comparison of means was performed with an independent Student's *t*-test. IL-6 and CRP had an abnormal distribution and were reported as median and interquartile range. The correlation between inflammation markers and anthropometrical indicators was calculated using Spearman's rho. The comparison of serum concentrations for inflammatory markers and nutritional status as a categorical value was performed with the Kruskal-Wallis H analysis. A linear regression analysis was performed with the anthropometric indicators of growth and nutritional status as dependent variables, and with serum interleukine 6 and C-reactive protein concentrations as independent variables.

ETHICAL ASPECTS

This work was done using the resources of the institutions involved – Hospital Civil de Guadalajara Dr. Juan I. Menchaca, Hospital Civil de Guadalajara Fray Antonio Alcalde, and Universidad de Guadalajara. The protocol was reviewed and approved by the Health Research and Ethics Committees of both hospitals (1347/14). Parents or legal guardians provided their informed consent in writing prior to study enrollment. Children older than 12 years signed a written assent.

RESULTS

PATIENTS

Seventeen patients (58.6%) were males and 12 were females. Mean age was 11.3 (± 4.7) years, with a minimum and maximum of 3 and 16 years.

CHRONIC KIDNEY DISEASE

The etiology of CKD was multiple. The diagnoses in descending order were renal hypoplasia or agenesis (n = 7), obstructive uropathy (n = 3), prematurity (n = 3), glomerular diseases (n = 2), and single cases of tubule-interstitial nephropathy, cystic disease, toxicity by cisplatin, neurogenic bladder, and nephroblastoma; in 9 cases the etiology was unknown. The time between CKD diagnosis and inclusion in the study was 5.5 (± 4.3) years.

The biochemical and hematological variables, classified according to CKD stage, are listed in table I. Serum creatinine was higher and glomerular filtration rate was lower in stage-4 patients. Hemoglobin concentration was higher in patients in stage 3.

Table I. Biochemical and hematological variables measured in 29 children and adolescents with chronic kidney disease (CKD)

Laboratory variables	Units	Stage 3		Stage 4		p
		Mean	(SD)	Mean	(SD)	
Serum creatinine	(mg/dL)	1.5	(0.3)	2.8	(1.0)	*< 0.001*
Glomerular filtration rate	(mL/min/m^2)	41.0	(9.3)	20.6	(5.1)	*< 0.001*
Plasma HCO_3^-	(mmol/L)	23.4	(1.5)	22.7	(1.5)	0.319
Urinary protein	(mg/dL)	38.1	(98.7)	106.7	(107.4)	0.133
Hemoglobin	(g/dL)	13.6	(2.3)	11.5	(1.7)	*0.009*
Albumin	(g/dL)	3.9	(0.8)	3.9	(0.7)	0.992

The results are classified according to CKD stages 3 or 4. Data are presented as mean and standard deviation (SD).
Statistics: Student's t-test for independent variables.

No differences in plasma HCO_3^-, proteinuria, and serum albumin were observed.

ANTHROPOMETRY

Height for age: the location trend of the height-for-age z-scores was in the negative region of the distribution curve (-1.6 ± 1.3 SD). Eleven patients were located below -2 SD and four below -3 SD; the proportion of stunting was 37.9%. No difference was found in the frequencies of chronic malnutrition between patients in stages 3 and 4.

Body mass index for age: the BMI-for-age z-score distribution also showed a trend to be located in the negative area of the curve (-0.8 ± 1.6). Six patients (20.7%) were located below -2 SD and two below -3 SD; the proportion of acute malnutrition was 20.7%. No difference was found in frequency of acute malnutrition between patients in stages 3 and 4.

Arm anthropometrics: the results of arm anthropometrical measurements and areas are shown in table II. The z-score means of all indicators were located in the negative area of the distribution curve. MUAC and TAA were below -2 SD in one fifth of patients. AMA was below -2 SD in 17.2% of cases; FAA and TSF were within the assigned normal limits in all cases.

Subscapular skinfold: the subscapular skinfold was within normal limits in all cases.

The comparison of frequencies and means for arm indicators between patients in stage 3 and in stage 4 showed no statistical differences.

BIOELECTRICAL IMPEDANCE

The correlation coefficients of IL-6 (pg/mL) with lean mass values (g) and body fat percentage as estimated by BIE are shown in table IV. Lean mass showed a significant negative linear relationship, and percentage of fat showed no relationship between both variables.

INTERLEUKINE 6 AND ULTRASENSITIVE C-REACTIVE PROTEIN

Interleukine 6: the median value of serum IL-6 concentrations in the overall group was 0.8, interquartile range (IQR) 0.5 to 2.2 pg/mL. In 15 patients (51.7%) this value was above the parameter (2.03 pg/mL, IQR = 1.1-5.1). The comparison of serum IL-6 concentrations between patients in stage 3 and stage 4 showed no differences.

Ultrasensitive C-reactive protein: the median value of CRP in the overall group was 1.8 (IQR = 1.2 to 3.4) mg/mL. In 8 patients (27.6%) CRP concentration was above the reference value (8.5 mg/mL, IQR = 3.9-12.4). The comparison of CRP concentrations between the stage-3 and stage-4 subjects showed no differences.

IL-6, CRP, HEIGHT AND NUTRITIONAL STATUS

Table III shows the median and IQR values for IL-6 and CRP, grouped according to the WHO classification of height for age. The values of both markers were higher in the presence of stunting,

Table II. Arm anthropometric indicators and subscapular skinfold calculated on 29 children and adolescents with chronic kidney disease

Anthropometric variables	Z-score mean	(SD)	± 2 SD		< -2 SD	
			n	(%)	n	(%)
Medium upper arm circumference	-.1	(1.3)	23	(79.3)	6	(20.7)
Triceps skinfold	-0.4	(1.0)	29	100)	0	(0)
Subscapular skinfold	-0.05	(1.1)	29	(100)	0	(0)
Total arm area	-0.9	(1.2)	23	(79.3)	6	(20.7)
Arm fat area	-0.4	(1.0)	29	(100)	0	(0)
Arm muscular area	-1.0	(1.3)	24	(82.8)	5	(17.2)

Data are presented as numerical variables (z-score mean and standard deviation) and as categorical variables (frequencies and percentages). Assigned normal limits: -2 to +2 SD.

Table III. Medians and interquartile ranges (IQR) for serum interleukine 6 (IL-6) and ultrasensitive C-reactive protein (CRP) as measured in 29 children and adolescents with CKD

Height for age (SD)	n	CRP[a]		IL-6[b]	
		Median	(IQR)	Median	(IQR)
Normal (± 2)	4	1.7	(1.2-2.4)	0.7	(0.5-1.7)
Moderate stunting (< -2 to -3)	7	1.9	(1.0-3.2)	0.7	(0.3-1.8)*
Severe stunting (< -3)	18	6.8	(1.7-12.4)	8.0	(3.0-11.5)*

[a]CRP, p = 0.032. [b]IL-6, p = 0.016. The results are grouped according to the World Health Organization (WHO) classification of height for age. Statistics: Kruskal-Wallis test.

particularly in severe cases. The comparison of concentrations for both IL-6 and CRP according to degree of height-for-age impairment was significantly higher, particularly in cases with severe stunting.

The correlation coefficients of serum IL-6 and CRP concentrations with height or nutritional status anthropometric indicators are shown in table IV. Z-scores of height for age, body mass index, subscapular skinfold, and arm fat area showed significant negative correlations with serum IL-6 levels; the indicators of adiposity, triceps skinfold and arm fat area, despite their not exceeding -2 SD, showed a negative linear relation with IL-6. Height-for-age z-scores also showed a negative and significant correlation with serum CRP concentration. Lean body mass also showed a significant negative correlation with IL-6. Both indicators of adiposity, arm fat area and fat percentage by BIA did not show a significant linear relationship.

A regression analysis showed that IL-6, assigned as independent variable, independently predicted 35% and 33% of the variance of height for age and BMI as indicators of growth and nutritional status, respectively. The subscapular skinfold explained 15% of the variance of height for age. CRP predicted 22% of the variance of height (Table V).

DISCUSSION

The driving hypothesis of this work was the demonstration of a relationship between two indicators of inflammation and nutritional status. We showed a negative linear correlation of IL-6 and CRP with anthropometric indicators of growth and body composition, both by anthropometry and by bioelectrical impedance. These observations were strengthened by the linear regression analysis, which allowed us to predict these indicators from IL-6 and CRP. These findings provide a partial statistical explanation for the growth and nutritional impairment observed in our patients; because it is a correlation of random variables, the results can be extrapolated to CKD patients in similar conditions.

Systemic inflammation is a condition that occurs with a certain frequency in patients with renal disease, and has been associated with malnutrition, morbidity, and mortality (16,17). The reported evidence of this association is robust in adult patients with renal diseases but in children is not entirely clear (18). Sylvester et al. measured IL-6 levels in 10- and 15-year-old healthy children, and found a mean of 0.7 ± 0.2 pg/mL (19); in the current study, slightly higher values were observed in the pre-dialysis stage. The value of this interleukin has been studied in children with CKD

Table IV. Correlation coefficients of interleukin 6 and C-reactive protein serum concentrations with anthropometric indicators of growth and nutritional status plus lean body mass and fat percentage as assessed by electric bioimpedance on 29 children and adolescents with CKD stages 3 and 4

Inflammation indicator	Dependent variables	Correlation coefficient		p
Interleukin 6 (pg/mL)	Anthropometric indicators	Height for age (z-score)	-0.452	*0.018*
		BMI for age (z-score)	-0.389	*0.045*
		Subscapular skinfold (z-score)	-0.479	*0.011*
		Muscle arm area (cm^2)	-0.452	*0.018*
		Fat arm area (cm^2)	-0.312	0.113
C-reactive protein (mg/mL)	Bioelectrical impedance	Lean body mass (g)	-0.390	*0.049*
		Fat percentage (%)	-0.046	0.824
		Height for age (z-score)	-0.467	*0.011*

Statistics: Spearman's bivariate correlation. BMI: body mass index.

Table V. Lineal regressions performed in 29 children and adolescents with chronic kidney disease through the z-score of anthropometric indicators of growth and nutritional status as dependent variables, and serum concentrations of interleukin 6 (pg/mL) and C-reactive protein (mg/dL) as independent variables

Independent variables	Dependent variables	R^2	SE	β	t	p
Interleukin 6	Height for age	0.355	1.1	-0.596	-3.707	*0.001*
	Body mass index for age	0.330	1.4	-0.574	-3.509	*0.002*
	Subscapular skinfold for age	0.151	1.1	-0.388	-2.106	*0.045*
Ultrasensitive C-reactive protein	Height for age	0.219	1.2	-0.476	-2.748	*0.011*

Anthropometric indicators were handled as z-scores. SE: standard error.

on dialysis, when the inflammatory process is more noticeable with values > 10.1 pg/mL (20). The serum concentration of CRP in our study was similar to the values obtained by Sozeri *et al.* in pre-dialysis children (21). The association of chronic inflammation and CKD is controversial. The proposed mechanisms include a decrease in the clearance of pro-inflammatory cytokines, a decrease in antioxidant levels (vitamin C, vitamin E, carotenoids, selenium), an impairment of the energy–protein and food intake equilibrium, comorbidities, dialysis membranes with low biocompatibility, and peritonitis episodes (22).

The assessment of current nutritional status by means of anthropometry has been controversial when fluid retention may occur, as in chronic liver disease, heart disease, or CKD, because body weight – the usual axis of anthropometric indicators for BMI or weight for height – is altered by edema (23). However, fluid retention tends to be distal and affects little or almost nothing proximal arm segments (9,24,25). In our study, the z-scores of both arm indicators and BMI were in negative values; however, no difference in the frequency of acute malnutrition was shown between them. This means that the higher the concentration of serum markers for systemic inflammation, the more negative the the z-scores for growth and nutritional status indicators, moving away from zero in a linear and statistically significant relationship.

Mean serum albumin concentration was normal in both groups; this variable, together with the hemoglobin level, is involved, among other factors, in fluid retention. It is possible that in patients with hypoalbuminemia and anemia fluid retention would be greater, and that arm anthropometry would be useful in the diagnosis of current nutritional status.

Arm indicators were also located in the negative values of the parameter and allowed to estimate fat and/or muscle deficit in about one-fifth of cases; the finding that the most severe arm impairment, below -2 SD, was in the muscular area could indicate that there is a selective presence of protein malnutrition that could be related to reduced intake and urinary losses. In our study, arm anthropometry results were similar to those published by Sylvestre et al. (19).

In contrast to the frequency of acute malnutrition, height for age was below -2 SD in one third of our patients. Growth impairment has been demonstrated by other authors, mainly in patients on hemodialysis and peritoneal dialysis; this probably is the nutritional condition with greater implications for growth and development (19,21,23,26). Growth failure has been associated with an increase of 14% in the risk of death for each decrease in one standard deviation of height for age (27).

The weaknesses of the present work are a limited sample size and the diversity of diagnoses encompassed with CKD, which implies a great diversity of pathophysiological mechanisms. Its strengths include the finding of a linear and negative predictive relationship between IL-6 and CRP with anthropometric indicators of growth and nutritional status, which may add information to secondary malnutrition mechanisms in CKD, and the estimate of a clinically significant frequency of acute and chronic malnutrition with growth impairment and muscular mass deficit as central components of the malnutrition syndrome.

REFERENCES

1. Romero E, Placito A, Pérez E, Vázquez E. Estado de nutrición en niños con insuficiencia renal crónica en fase terminal en tratamiento sustitutivo. Bol Med Hosp Infant Mex 2002;59:104-11.
2. Atkinson MA, Warady BA. Anemia in chronic kidney disease. Pediatr Nephrol 2018;33:227-38.
3. Zha Y, Qian Q. Protein nutrition and malnutrition in CKD and ESRD. Nutrients 2017;9:1-19.
4. Sultana S, Rahman MH, Paul SK, Hossain MM. Impact of etiology of chronic renal failure on growth in children. Mymensingh Med J 2007;16:S34-43.
5. Bacchetta J, Harambat J, Cochat P, Salusky IB, Wesseling-Perry K. The consequences of chronic kidney disease on bone metabolism and growth in children. Nephrol Dial Transplant 2012;27:3063-71.
6. Eustace J, Astor B, Munter P, Ikizler A, Coresh J. Prevalence of acidosis and inflammation and their association with low serum albumin in chronic kidney disease. Kid Int 2004;65:1031-40.
7. Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. Sem Dial 2004;17:425-6.
8. Kalantar-Zadeh K, Block G, McAllister C, Humphreys M, Kopple J. Appetite and inflammation, nutrition, anemia, and clinical outcome in hemodialysis patients. Am J Clin Nutr 2004;80:299-307.
9. Hurtado-López EF, Larrosa-Haro A, Vásquez-Garibay E, Macías-Rosales, Troyo-Sanromán R, Bojórquez-Ramos MC. Liver function tests predict the nutritional status evaluated by arm anthropometrical indicators. J Pediatr Gastroenterol Nutr 2007;45:451-7.
10. Frisancho AR. Anthropometric standards for the assessment of growth and nutritional status. Michigan: The University of Michigan Press, 1990:9-30.
11. WHO Multicentre Growth Reference Study Group. WHO Child Growth standards based onl ength/height weight and age. Acta Paediatr (Suppl) 2006;450:76-85.
12. Butte NF, Hopkinson JM, Wong WW. Body composition during the first 2 years of life: an updated reference. Pediatr Res 2000;47:578-85.
13. Fomon S, Haschke F, Ziegler E, Nelson SE. Body composition of reference children from birth to age 10 years. Am J Clin Nutr 1982;35:1169-75.
14. Clasey JL, Bardley KD, Bardley JW, Long DE, Groiffith JR. A New BIA Equation estimating the body composition of young children. Obesity 2011;19:1813-7.
15. Schwartz G.J. Height: the missing link in estimating glomerular filtration rate in children and adolescents. Nephrol Dial Transpl 2014;29:944-7.
16. Stenvinkel P, Heimburger O, Paultre F, Diczfalusy U, Wang T, Berglund L, et al. Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. Kidney Int 1999;55:1899-911.
17. Jankowska M, Cobo G, Lindholm B, Stenvinkel P. Inflammation and Protein-Energy Wasting in the Uremic Milieu. Contrib Nephrol 2017;191:58-71.
18. Pecoits-Filho R, Lindholm B, Stenvinkel P. The malnutrition, inflammation, and atherosclerosis (MIA) syndrome-the heart of the matter. Nephrol Dial Transplant 2002;17:28-31.
19. Sylvester FA, Wyzga N, Hyams JS, Gronowicz GA. Effect of Crohn's disease on bone metabolism in vitro: a role for interleukin-6. J Bone Miner Res 2002;17:695-702.
20. Goldstein SL, Leung JC, Silverstein DM. Pro- and anti-inflammatory cytokines in chronic pediatric dialysis patients: effect of aspirin. Clin J Am Soc Nephrol 2006;1:979-86. DOI: 10.2215/CJN.02291205
21. Sozeri B, Mir S, Kara OD, Dincel N. Growth impairment and nutritional status in children with chronic kidney disease. Iran J Pediatr 2011;21:271-7.
22. Kalantar-Zadeh K, Ikizler A, Block G, Avram MM, Kopple JD. Malnutrition-inflammation complex syndrome in dialysis patients: causes and consequences. Am J Kidney Dis 2003;42:864-81. DOI: 10.1016/j.ajkd.2003.07.016
23. Foster B, Leonard M. Measuring nutritional status in children with chronic kidney disease. Am J Clin Nutr 2004;80:801-14. DOI: 10.1093/ajcn/80.4.801
24. Sokol RJ, Stall C. Anthropometric evaluation of children with chronic liver disease. Am J Clin Nutr 1990;52:203-8. DOI: 10.1093/ajcn/52.2.203
25. Hurtado-López EF, Vásquez-Garibay EM, Trujillo X, Larrosa-Haro A. Body composition predicts growth in infants and toddlers with chronic liver disease. J Pediatr Gastroenterol Nutr 2017;65:117-9. DOI: 10.1097/MPG.0000000000001746
26. Abitbol CL, Warady BA, Massie MD, Baluarte HJ, Fleischman LE, Geary DF. Linear growth and anthropometric and nutritional measurements in children with mild to moderate renal insufficiency: a report of the Growth Failure in Children with Renal Diseases Study. J Pediatr 1990;116:S46-54. DOI: 10.1016/S0022-3476(05)82925-7
27. Wong CS, Gipson DS, Gillen DL, Emerson S, Koepsell T, Sherrard DJ, et al. Anthropometric measures and risk of death in children with end-stage renal disease. Am J Kidney Dis 2000;36:811-9. DOI: 10.1053/ajkd.2000.17674

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ARÁN

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Trabajo Original

Pediatría

Psychological well-being related to screen time, physical activity after school, and weight status in Chilean schoolchildren

Bienestar psicológico relacionado con el tiempo de pantalla, la actividad física después de la escuela y el peso corporal en escolares chilenos

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Abstract

Background: the relationship between physical activity (PA) patterns and mental health in children is receiving considerable attention.

Aims: the aim of this study was to compare psychological well-being in groups of schoolchildren according to PA patterns and weight status, and to determinate the association between psychological well-being and both screen time and PA after school.

Material and methods: in a cross-sectional sample of girls (n = 272, aged 11.93 ± 0.94 years) and boys (n = 333, aged 12.09 ± 1.00 years), we assessed body mass index (BMI), waist circumference and body fat. Self-esteem, body image dissatisfaction, depression, screen time, and after-school PA were also included.

Results: according to PA patterns, there were significant differences between good PA and bad PA groups in self-esteem (p = 0.013) and depression (p = 0.035). BMI was associated with depression (β: 0.36; 95% CI: 0.19, 0.53; p < 0.001). Screen time was positively associated with depression (β: 0.88; 95% CI: 0.32, 1.44; p = 0.002) and inversely associated with self-esteem (β: -1.12; 95% CI: -1.79, -0.45; p < 0.001). Finally, after-school PA had an inverse association with depression levels (β: -0.55; 95% CI: 0.10, 1.00; p = 0.016).

Conclusion: psychological well-being was associated with screen time, after-school PA and weight status in schoolchildren.

Key words:

Screen time. Physical activity. Mental health. Schoolchildren. Obesity.

Resumen

Antecedentes: la relación entre los patrones de actividad física (AF) y la salud mental en los niños está recibiendo una atención considerable.

Objetivos: el objetivo de este estudio fue comparar el bienestar psicológico en grupos de escolares de acuerdo con los patrones de AF y el estado de peso, y determinar la asociación entre el bienestar psicológico con el tiempo frente a pantalla y la AF después de la escuela.

Material y métodos: en una muestra transversal de niñas (n = 272, de 11,93 ± 0,94 años) y niños (n = 333, de 12,09 ± 1,00 años), evaluamos el índice de masa corporal (IMC), la circunferencia de la cintura y la grasa corporal. También se incluyeron la autoestima, la insatisfacción con la imagen corporal, la depresión, el tiempo frente a la pantalla y la AF después de la escuela.

Resultados: de acuerdo con los patrones de AF, hubo diferencias significativas entre los buenos niveles de AF y la malos niveles de AF en la autoestima (p = 0,013) y la depresión (p = 0,035). El IMC de los participantes se asoció con depresión (β: 0,36; IC 95%: 0,19 a 0,53; p < 0,001). El tiempo de pantalla se asoció positivamente con la depresión (β: 0,88; IC 95%: 0,32 a 1,44; p = 0,002) e inversamente con la autoestima (β: -1,12; IC 95%: -1,79 a -0,45; p < 0,001). Finalmente, la AF después de la escuela tuvo una asociación inversa con los niveles de depresión (β: -0,55; IC 95%: 0,10 a 1,00; p = 0.016).

Conclusión: el bienestar psicológico se asoció con el tiempo frente a la pantalla, la AF después de la escuela y el estado de peso de los escolares.

Palabras clave:

Tiempo de pantalla. Actividad física. Salud mental. Escolares. Obesidad.

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INTRODUCTION

Mental health is a multidimensional state of well-being, with negative indicators such as body image dissatisfaction (1), depression, and positive indicators such as self-esteem (2). Mental illness and the negative consequences of poor mental health among children and the youth are particularly a public health priority.

In this sense, regular physical activity (PA) has been found to have a positive association with mental health (3). Likewise, evidence suggests that participation in PA programmes may support young people's current and future mental health (4). Some studies have reported negative associations between bad PA patterns and poor psychosocial well-being (5), as excessive screen time is strongly associated with depressive disease (6). However, these associations have not been extensively studied (7) and thus need to be investigated more thoroughly.

In the same way, school-age obesity is associated with psychosocial alterations, including deficiencies in social coexistence, with consequences for quality of life (8). It has been observed that obese children tend to have affective problems, which may negatively affect their academic performance (9). Therefore, the relationship between mental illness (i.e., with psychosocial origin) and well-being is an important area of public concern (10).

Various studies have reported that self-esteem is associated with children's social, emotional, behavioural, and mental health (11). Self-esteem plays an important role during childhood and adolescence (12), with low self-esteem being recognized as being strongly associated with different risk factors for mental health issues that affect childhood development (11). In contrast, high self-esteem has been associated with better cognitive development (13) and quality of life (14).

Body image dissatisfaction in children and adolescents has negative implications for psychological and physical well-being (1). Previous studies have stressed the importance of exploring factors that influence body image dissatisfaction in order to avoid future psychosocial problems, along with other health-related consequences, for children (15). Additionally, depression is a serious psychiatric illness in children (16), often persisting into adolescence and young adulthood, and with severe negative consequences—including self-harm and suicide (17).

A growing proportion of children's leisure time is spent as 'screen time,' including the use of smartphones, tablets, gaming consoles, and televisions—a pattern that has raised concerns about its effect on their psychological well-being (18). Lower levels of PA and higher levels of screen time and obesity are associated with impaired psychological well-being in children (19,20). However, research exploring screen time, after-school PA, weight status and psychological effects (i.e., self-esteem, body image and depression) among children need to be studied deeply. Therefore, the hypothesis of the study was that good PA patterns and normal weight status are associated with psychological well-being, and the aim of this study was to compare psychological well-being in groups of schoolchildren according to PA patterns and weight status, and to determinate the association between psychological well-being and both screen time and after-school PA.

MATERIALS AND METHODS

PARTICIPANTS

The sample for this cross-sectional study comprised girls (n = 272; aged 11.93 ± 0.94 years) and boys (n = 333; aged 12.09 ± 1.00 years) attending a public primary school in Chile, and selected using convenience criteria. Sample size is similar to that of previous studies (21,22). Inclusion criteria were as follows: a) informed parental consent and participant consent; b) attending school, and c) aged between 11 and 13 years. Exclusion criteria were: a) the presence of musculoskeletal disorders or any other medical condition that might affect health and PA levels, and b) physical, sensory or intellectual disabilities. The tests were explained to all participants before the study began, and they were asked to abstain from intense exercise for 48 hours prior to the study.

Parents and guardians were informed about the study and provided their written consent for their children's participation. In addition, all children provided a written assent on the day of the assessment. The investigation complied with the Helsinki Declaration and was approved by the Ethical Committee at Universidad de La Frontera (DFP16-0013), Temuco, Chile.

MEASUREMENTS

Anthropometric assessment

Body mass (kg) was measured using an electrical TANITA™ scale (Scale Plus UM-028; Tokyo, Japan) while wearing underclothes, without shoes. Height (m) was measured with a SECA™ stadiometer (Model 214; Hamburg, Germany) graduated in millimetres. The nutritional status of the participants was assessed according to obesity categories, estimated from the body mass index (BMI) and calculated by dividing body weight by the square of their height in meters (kg/m^2). Based on the growth table published by the Centers for Disease Control and Prevention, Overweight and Obesity (CDC) for children of the same age and sex, "overweight" was defined as a BMI at or above the 85th percentile but below the 95th percentile, and "obesity" was defined as a BMI at or above the 95th percentile (23,24).

Waist circumference (WC) was measured at the height of the umbilical scar using a SECA™ tape measure (Model 201; Hamburg, Germany) (25). The waist-to-height ratio (WtHR) was subsequently obtained by dividing the WC by height in order to estimate the accumulation of fat in the central zone of the body, consistent with international norms (26). The percentage (%) of body fat (BF) was estimated from measurements of the subcutaneous tricipital and subscapular folds using a Lange™ skinfold calliper (102-602L; Minneapolis, USA) and calculated using Slaughter's formula (27): Girls: %BF = 1.33 (tricipital + subscapular) - 0.013 (tricipital + subscapular)^2 - 2.5. Boys: %BF = 1.21 (tricipital + subscapular) - 0.008 (tricipital + subscapular)^2 - 1.7. The research assistant was submitted to the test-retest (n = 62) protocol to verify the technical measurement error with an intra-class correlation coe-

fficient (ICC), in WC (ICC = 0.94), tricipital fold (ICC = 0.91) and subscapular fold (ICC = 0.91).

Psychosocial outcomes

The Body Shape Questionnaire (BSQ) was used to identify body image dissatisfaction (28). This questionnaire is comprised of 34 items; answers are given using a 6-point Likert scale (1, never; 2, rarely; 3, sometimes; 4, often; 5, very often; and 6, always). The maximum score is 204 points and the minimum is 34 points. Higher scores indicate 'higher dissatisfaction' with one's body image. Scores were categorized as follows: < 81, 'no dissatisfaction'; 81-110, 'mild dissatisfaction'; 111-140, 'moderate dissatisfaction'; and > 140, 'extreme dissatisfaction.' The level of internal consistency reached in this questionnaire presented a Cronbach's alpha = 0.84.

For the self-esteem measurement we used the Coppersmith Self-Esteem Inventory (29). This self-report questionnaire is designed to measure attitudes toward the self in a variety of areas (family, peers, school, and general social activities). The instrument is one of the most commonly used assessment of self-esteem in both research and clinical practice. The scores for self-esteem were categorized as follows: < 22 points, 'very low'; 22-26, 'low'; 26-35, 'normal'; 35-39, 'high'; > 39, 'very high.' The inventory has been validated in Chilean children (30). The level of internal consistency reached in this questionnaire presented a Cronbach's alpha = 0.86.

Depressive symptoms were assessed using the Child Depression Inventory (CDI) (31), which consists of 27 groups of three statements relating to depressive symptoms over the previous 2 weeks. A score ≥ 18 points indicates the probable presence of clinically significant depression. The CDI has been validated in Chilean children (32). The level of internal consistency reached in this questionnaire presented a Cronbach's alpha = 0.85.

Screen time and after-school PA

The PA patterns were evaluated with the Krece Plus test (33). The Krece Plus test is a quick questionnaire that classifies lifestyle based on the daily average of hours spent watching television or playing video games (screen time) and the hours of PA after school per week. The classification is made according to the number of hours devoted to each activity. The total points are added, and the person is classified as good (men: ≥ 9, women ≥ 8), regular (men: 6-8; women: 5-7) or bad (men: ≤ 5 and women: ≤ 4) according to the lifestyle score.

Procedure

Previously-trained research technicians visited selected schools during the 2018 Chilean school year and gave oral and written information to parents/tutors about participation in the research. Anthropometric assessments were carried out in a private room of the school at a comfortable temperature. The questionnaires were administered in classrooms on different days from the anthropometric evaluations. Only one questionnaire was administered per day. All measurements were taken in the morning between 09:00 and 11:00 am.

Statistical analysis

Statistical analyses were performed with the SPSS version 23.0 software (SPSS™ IBM Corporation, NY, USA). The continuous variables all showed a parametric distribution and are reported as the mean and standard deviation. Group differences were assessed by one-way ANOVA, and the *post-hoc* analysis was carried out using Bonferroni's method. The p_{trend} was calculated by linear-by-linear association to establish a trend between h/day of screen time and psychological well-being. To determine the association between psychological well-being with screen time and PA after school, a multivariate logistic regression was used. Values of $p < 0.05$ were considered statistically significant.

RESULTS

Table I shows the descriptive characteristics of the schoolchildren. There were sex differences in percentage of BF (girls 25.33 ± 7.31%, boys 24.00 ± 7.51%; p = 0.029) and body image dissatisfaction (girls 59.88 ± 31.92, boys 53.49 ± 27.42; p = 0.008).

Table II shows the results according to PA patterns. There were significant differences between the 'good PA' and 'bad PA' pattern groups on the variables of self-esteem (34.82 ± 7.01 and 30.79 ± 8.57, respectively; p = 0.013) and depression (10.16 ± 5.09 and 12.91 ± 6.64, respectively; p = 0.035). The schoolchildren who reported screen times of 5 or more hrs/day reported higher depression levels (p_{trend} = 0.003) than their peers (4 or less hrs/day) (Table III). Moreover, the group of schoolchildren with bad PA patterns reported higher screen time (3.92 ± 0.82 h/day) and lower levels of after-school PA per day (1.79 ± 1.04 h/week) in comparison to the 'regular' and 'good PA' pattern groups ($p < 0.001$) (Table II).

As shown in table IV, the normal-weight group was significantly different from the obese group in levels of self-esteem (33.41 ± 8.20 and 26.71 ± 7.79, respectively; $p < 0.001$), body image dissatisfaction (48.84 ± 16.76 and 91.29 ± 43.66, respectively; $p < 0.001$) and depression (10.29 ± 6.30 and 16.56 ± 5.56, respectively; $p < 0.001$). Likewise, there were significant differences between the normal-weight, overweight and obese groups in screen time (3.03 ± 1.16 *vs.* 3.37 ± 1.04 *vs.* 3.66 ± 1.01 h/day, $p < 0.001$) and PA after school (3.00 ± 1.46 *vs.* 2.54 ± 1.31 *vs.* 2.03 ± 1.21 h/week, $p < 0.001$).

Gender had an association with body image dissatisfaction (β: -19.52, 95% CI: -23.94, -15.10, $p < 0.0001$). BMI was associated with body image dissatisfaction (β: 3.20, 95% CI: 2.44, 3.96, $p < 0.001$) and depression (β: 0.36, 95% CI: 0.19, 0.53, $p < 0.001$).

Table I. Descriptive characteristics of the schoolchildren

	Total (n = 605)	Girls (n = 272)	Boys (n = 333)	p-value
Anthropometric parameters				
Age (y)	12.02 ± 0.98	11.93 ± 0.94	12.09 ± 1.00	p = 0.307
Body mass (kg)	51.65 ± 13.84	51.38 ± 12.39	51.88 ± 14.94	p = 0.664
BMI (kg/m^2)	21.41 ± 4.53	21.74 ± 4.39	21.14 ± 4.64	p = 0.109
Normal weight n (%)	323 (53.4)	143 (52.6)	180 (54.1)	
Overweight n (%)	153 (25.3)	75 (27.6)	78 (23.4)	p = 0.485
Obese n (%)	129 (21.3)	54 (19.9)	75 (22.5)	
WC (cm)	73.18 ± 11.42	72.61 ± 10.60	73.65 ± 12.04	p = 0.269
WtHR (WC/height)	0.47 ± 0.07	0.47 ± 0.07	0.47 ± 0.07	p = 0.737
BF (%)	24.60 ± 7.44	25.33 ± 7.31	24.00 ± 7.51	p = 0.029
Psychosocial variables				
Self-esteem (score)	31.27 ± 8.62	31.65 ± 9.44	30.96 ± 7.85	p = 0.369
Body image (score)	62.36 ± 32.68	73.77 ± 31.92	53.49 ± 27.42	p < 0.001
Depression (score)	12.56 ± 6.40	13.11 ± 6.87	12.11 ± 5.97	p = 0.056
Physical activity patterns				
PA after school (h/week)	2.68 ± 1.40	2.53 ± 1.39	2.80 ± 1.42	p = 0.284
Screen time (h/day)	3.25 ± 1.14	3.30 ± 1.17	3.20 ± 1.11	p = 0.200

The data shown represent mean ± DS, and n (%). p < 0.05 was considered statistically significant. BMI: body mass index; WC: waist circumference; WtHR: waist-to-height ratio; BF: body fat; PA: physical activity.

Table II. Comparison of variables according to physical activity patterns (screen time and PA after school)

	Good PA (n = 51) A	Regular PA (n = 204) B	Bad PA (n = 350) C	p-value	*Post hoc*
Psychosocial variables					
Self-esteem (score)	34.82 ± 7.01	31.98 ± 8.88	30.79 ± 8.57	0.013	A > C
Body image (score)	52.11 ± 20.52	61.06 ± 32.32	64.04 ± 34.46	0.088	
Depression (score)	10.16 ± 5.09	12.29 ± 6.13	12.91 ± 6.64	0.035	A < C
Physical activity patterns					
Screen time (h/day)	1.03 ± 0.162	2.50 ± 0.61	3.92 ± 0.82	p < 0.001	A < B < C
PA after school (h/week)	4.95 ± 0.23	3.79 ± 0.69	1.79 ± 1.04	p < 0.001	A > B > C

The data shown are represented as mean ± SD. p < 0.05 was considered statistically significant. A denotes good PA groups, B denotes regular PA groups, and C denotes bad PA groups in the post hoc *analysis.*

Table III. Psychological well-being according to screen time

Screen time, h/day						
	1 (n = 42)	2 (n = 116)	3 (n = 179)	4 (n = 171)	5 or + (n = 88)	P-Trend
Body image (score)	55.1 ± 24.16	57.8 ± 31.57	63.4 ± 32.84	63.92 ± 34.75	66.01 ± 35.55	p = 0.212
Self-esteem (score)	34.12 ± 7.88	32.2 ± 9.01	30.25 ± 8.27	31.44 ± 7.88	31.61 ± 10.27	p = 0.076
Depression (score)	10.52 ± 5.52	11.2 ± 5.56	12.87 ± 6.05	12.65 ± 6.57	14.25 ± 7.65	p = 0.003

The data shown are represented as mean ± SD. p < 0.05 was considered statistically significant.

Table IV. Comparison of variables according to nutritional status

	Normal Weight (n = 323) A	Overweight (n = 153) B	Obesity (n = 129) C	p-value	*Post hoc*
Psychosocial variables					
Self-esteem	33.41 ± 8.23	30.97 ± 8.51	26.71 ± 7.79	p < 0.001	A > B > C
Body image	48.79 ± 16.63	66.50 ± 32.42	91.29 ± 43.80	p < 0.001	A < B < C
Depression	10.29 ± 6.30	14.08 ± 5.35	16.56 ± 5.55	p < 0.001	A < B < C
Physical activity patterns					
Screen time (h/day)	3.03 ± 1.16	3.37 ± 1.04	3.66 ± 1.01	p < 0.001	A < B < C
PA after school (h/week)	3.00 ± 1.46	2.54 ± 1.31	2.03 ± 1.21	p < 0.001	A > B > C

The data shown are represented as mean ± SD. p < 0.05 was considered statistically significant. A denotes the normal weight group, B denotes the overweight group, and C denotes the obesity group in the post hoc *analysis.*

Length of screen time was found to be associated with depression (β: 0.88, 95% CI: 0.32, 1.44, p = 0.002) and inversely associated with self-esteem (β: -1.12, 95% CI: -1.79, -0.45, p < 0.001). After-school PA was found to be inversely associated with depression (β: -0.55, 95% CI: 0.10, 1.00, p = 0.016) (Table V).

DISCUSSION

The aim of this study was to compare levels of psychological well-being, as reflected in self-esteem, body image and depression, between groups of schoolchildren according to PA patterns (consisting of screen time, after-school PA and weight status).

The schoolchildren with higher screen time and lower after-school PA reported worse psychosocial well-being than their counterparts. Moreover, screen time duration was positively associated with depression and inversely associated with self-esteem. These findings are consistent with another investigation that also found an association between excessive screen exposure and poor psychosocial well-being in children (5). Likewise, screen time – in particular, watching television – has been negatively associated with the development of physical and cognitive abilities and positively associated with obesity, sleep problems, depression and anxiety (6). Along these lines, the evidence shows small but consistent associations between screen time and poor mental health (7). A study reported that children and adolescents who spent more time using screens showed worse psychological well-being than low-screen time users (34). Moreover, increased sedentary time is associated with more peer problems in children whereas PA, generally, is beneficial for peer relations in children (35).

In our sample, psychological well-being was lower in the obese group than in the normal-weight group; furthermore, BMI levels were associated with body image dissatisfaction and depression. A study of Australian students of a similar age found that obesity affects the self-perception of children, particularly girls, during early adolescence (36). Hesketh et al. (37) reported that children who were overweight or obese at 5-10 years of age had lower self-esteem when compared to non-overweight children. Moreover, a previous investigation indicated that children with adiposity were more likely to report higher body dissatisfaction (38). An investigation reported that overweight/obese children (aged 6-13 years) were significantly more likely to suffer from depression than normal-weight children (39). A study of Korean schoolchildren found that obese children with higher body dissatisfaction had lower self-esteem and more depressive symptoms than normal-weight children (17). In children, a differential effect of obesity on self-esteem has been

Table V. Association of mental health variables with gender, anthropometric parameters and physical activity patterns

	Body image dissatisfaction	Depression	Self-esteem
Gender	-19.52 (-23.94, -15.10) p < 0.001	-0.71 (-1.68, 0.25) p = 0.147	0.91 (-0.26, 2.09) p = 0.126
BMI	3.20 (2.44, 3.96) p < 0.001	0.36 (0.19, 0.53) p < 0.001	0.06 (-0.15, 0.26) p = 0.585
WC	0.24 (-0.05, 0.53) p = 0.110	0.06 (-0.01, 0.12) p = 0.080	-0.01 (-0.09, 0.07) p = 0.841
BF	-0.16 (-0.48, 0.17) p = 0.335	0.04 (-0.03, 0.11) p= 0.225	-0.03 (-0.11, 0.06) p = 0.538
Screen time	0.38 (-2.17, 2.93) p = 0.770	0.88 (0.32, 1.44) p = 0.002	-1.12 (-1.79, -0.45) p < 0.001
Physical activity after school	0.74 (-1.33, 2.80) p = 0.484	-0.55 (0.10, 1.00) p = 0.016	0.01 (-0.54, 0.56) p = 0.977

The data shown represent beta values (95% CI) p-value. Values of p < 0.05 were considered statistically significant. BMI: body mass index; WC: waist circumference; BF: body fat.

observed in problems of externalization and social perception related to bullying behaviors (40).

In the present study, after-school PA was inversely associated with depression. In this sense, the evidence indicated that low PA levels are associated with poor psychological well-being (41,42). These associations are worrisome, as we found that PA levels were lower in obese students than in overweight and normal-weight schoolchildren. These associations imply that obese children are at greater risk of a depressive episode or symptoms of depression (43). The literature suggests that higher levels of PA can help reduce symptoms of depression in childhood (44,45), which is accompanied by changes in self-esteem (46). Likewise, the evidence suggests that daily TV watching in excess of 2 hours is associated with reduced psychosocial health (47).

LIMITATIONS

This study has some limitations. Although we used standardized PA questionnaires, we did not use accelerometer devices, which would have provided a more precise quantification of PA patterns and sedentary behaviour. The strengths of this study are that we examined several variables that affect the academic performance and mental health of children, contributing to a better understanding of the serious problem of excessive screen time, physical inactivity, and childhood obesity. The information available regarding the psychological well-being in obesity children is important, especially for professionals in the Nutrition and Physical Activity Sciences, given the current study provides some insights into this field.

CONCLUSION

In conclusion, schoolchildren with bad PA patterns such as higher screen time per day, lower after-school PA, and obesity status presented poor psychological well-being compared to their peers with good PA levels and normal weight status. Moreover, screen time duration, after-school PA, and BMI were associated with psychological well-being (i.e., in terms of depression, body image, and self-esteem). This suggests that prevention strategies for childhood sedentary behaviour need to begin early in order to minimize its psychological impact during adolescence and adulthood.

REFERENCES

1. Wang K, Liang R, Ma ZL, Chen J, Cheung EF, Roalf DR, et al. Body image attitude among Chinese college students. PsyCh journal 2018;7(1):31-40. DOI: 10.1002/pchj.200.
2. Dale LP, Vanderloo L, Moore S, Faulkner G. Physical activity and depression, anxiety, and self-esteem in children and youth: an umbrella systematic review. Ment Health Phys Act 2018;16:66-79.
3. Donnelly, Hillman C, Castelli D, Etnier J, Lee S, Tomporowski P, et al. Physical activity, fitness, cognitive function, and academic achievement in children: a systematic review. Med Sci Sports Exerc 2016;48(6):1197. DOI: 10.1249/MSS.0000000000000901.
4. Rodríguez-Ayllón M, Cadenas-Sánchez C, Estévez-López F, Muñoz NE, Mora-González J, Migueles JH, et al. Role of Physical Activity and Sedentary Behavior in the Mental Health of Preschoolers, Children and Adolescents: A Systematic Review and Meta-Analysis. Sports medicine 2019:1-28.
5. Zhao J, Zhang Y, Jiang F, Ip P, Ho FKW, Zhang Y, et al. Excessive Screen Time and Psychosocial Well-Being: The Mediating Role of Body Mass Index, Sleep Duration, and Parent-Child Interaction. The Journal of pediatrics 2018;202:157-62. e1. DOI: 10.1016/j.jpeds.2018.06.029.
6. Domingues-Montanari S. Clinical and psychological effects of excessive screen time on children. J Paediatr Child Health 2017;53(4):333-8. DOI: 10.1111/jpc.13462.
7. Biddle SJ, Asare M. Physical activity and mental health in children and adolescents: a review of reviews. Br J Sports Med 2011;45(11):886-95. DOI: 10.1136/bjsports-2011-090185.
8. Walker L, Hill A. Obesity: The role of child mental health services. Child and Adolescent Mental Health 2009;14(3):114-20. DOI: 10.1111/j.1475-3588.2008.00522.x.
9. Barmola K. Family Environment, Mental Health and Academic Performance of Adolescents. Sociology 2013;2(12). DOI: 10.15373/22778179/DEC2013/169.
10. Khalid A, Qadir F, Chan SW, Schwannauer M. Adolescents' mental health and well-being in developing countries: a cross-sectional survey from Pakistan. J Ment Health 2018:1-8. DOI: 10.1080/09638237.2018.1521919.
11. Wang F, Wild TC, Kipp W, Kuhle S, Veugelers PJ. The influence of childhood obesity on the development of self-esteem. Health reports 2009;20(2):21-7.
12. McClure AC, Tanski SE, Kingsbury J, Gerrard M, Sargent JD. Characteristics associated with low self-esteem among US adolescents. Academic pediatrics 2010;10(4):238-44. e2. DOI: 10.1016/j.acap.2010.03.007.
13. Wang F, Veugelers P. Self-esteem and cognitive development in the era of the childhood obesity epidemic. Obesity reviews 2008;9(6):615-23. DOI: 10.1111/j.1467-789X.2008.00507.x.
14. Griffiths LJ, Parsons TJ, Hill AJ. Self-esteem and quality of life in obese children and adolescents: a systematic review. International journal of pediatric obesity : IJPO : an official journal of the International Association for the Study of Obesity 2010;5(4):282-304. DOI: 10.3109/17477160903473697.
15. Kerner C, Haerens L, Kirk D. Understanding body image in physical education: Current knowledge and future directions. European Physical Education Review 2017:1356336X17692508. DOI: 10.1177/1356336X17692508.
16. Avanci J, Assis S, Oliveira R, Pires T. Childhood depression. Exploring the association between family violence and other psychosocial factors in low-income Brazilian schoolchildren. Child and adolescent psychiatry and mental health 2012;6(1):26. DOI: 10.1186/1753-2000-6-26.
17. Shin NY, Shin MS. Body dissatisfaction, self-esteem, and depression in obese Korean children. The Journal of pediatrics 2008;152(4):502-6. DOI: 10.1016/j.jpeds.2007.09.020.
18. Twenge JM, Martin GN, Spitzberg BH. Trends in US Adolescents' media use, 1976-2016: The rise of digital media, the decline of TV, and the (near) demise of print. Psychology of Popular Media Culture. 2018. DOI: 10.1037/ppm0000203.
19. Tyson P, Wilson K, Crone D, Brailsford R, Laws K. Physical activity and mental health in a student population. J Ment Health 2010;19(6):492-9. DOI: 10.3109/09638230902968308.
20. Ikävalko T, Lehto S, Lintu N, Väistö J, Eloranta AM, Haapala EA, et al. Health-related correlates of psychological well-being among girls and boys 6–8 years of age: The Physical Activity and Nutrition in Children study. Journal of paediatrics and child health 2018;54(5):506-9. DOI: 10.1111/jpc.13891.
21. Delgado-Floody P, Cofré A, Guzmán I, Mayorga D, Salazar C, Caamaño F. Perception of obese schoolchildren regarding their participation in the Physical Education class and their level of self-esteem: comparison according to corporal status. Nutr Hosp 2018;35(6):1270-4.
22. Delgado-Floody P, Caamaño-Navarrete F, Palomino-Devia C, Jerez-Mayorga D, Martínez-Salazar C. Relationship in obese Chilean schoolchildren between physical fitness, physical activity levels and cardiovascular risk factors. Nutr Hosp 2019;36(1):13-9.
23. Karnik S, Kanekar A. Childhood obesity: a global public health crisis. Int J Prev Med 2012;3(1):1-7.
24. CDC. Centers for Disease Control and Prevention, Overweight and obesity; Defining overweight and obesity. 2010.
25. Schröder H, Ribas L, Koebnick C, Funtikova A, Gomez SF, Fíto M, et al. Prevalence of abdominal obesity in Spanish children and adolescents. Do we need waist circumference measurements in pediatric practice? PLoS One 2014;9(1):e87549. DOI: 10.1371/journal.pone.0087549.
26. Chung IH, Park S, Park MJ, Yoo EG. Waist-to-Height Ratio as an Index for Cardiometabolic Risk in Adolescents: Results from the 1998-2008 KNHANES. Yonsei Med J 2016;57(3):658-63. DOI: 10.3349/ymj.2016.57.3.658.

27. Slaughter MH, Lohman TG, Boileau RA, Horswill CA, Stillman RJ, Van Loan MD, et al. Skinfold equations for estimation of body fatness in children and youth. Hum Biol 1988;60(5):709-23.
28. Cooper PJ, Taylor MJ, Cooper Z, Fairbum CG. The development and validation of the Body Shape Questionnaire. Int J Eat Disord 1987;6(4):485-94. DOI: 10.1002/1098-108X(198707)6:4<485::AID-EAT2260060405>3.0.CO;2-O.
29. Jadue G, Galindo A, Navarro L. Factores protectores y factores de riesgo para el desarrollo de la resiliencia encontrados en una comunidad educativa en riesgo social. Estudios pedagógicos (Valdivia) 2005;31(2):43-55. DOI: 10.4067/S0718-07052005000200003.
30. Brinkmann H, Segure T, Solar M. Adaptación, estandarización y elaboración de normas para el inventario de autoestima de Coopersmith. Revista Chilena de Psicología 1989;10(1):63-71.
31. Kovacs M. The Children's Depression, Inventory (CDI). Psychopharmacology bulletin 1985;21(4):995-8.
32. Coggiola A, Guijón P. Estandarización del Inventario de Depresión en Niños de Kovacs y Beck-CDI: Tesis de grado para optar al Titulo Profesional de Psicólogo Universidad Diego Portales, Santiago; 1991.
33. Majem LS, Barba LR, Bartrina JA, Rodrigo CP, Santana PS, Quintana LP. Obesidad infantil y juvenil en España. Resultados del Estudio enKid (1998-2000). Med Clin 2003;121(19):725-32. DOI: 10.1016/S0025-7753(03)74077-9.
34. Twenge JM, Campbell WK. Associations between screen time and lower psychological well-being among children and adolescents: Evidence from a population-based study. Preventive medicine reports 2018;12:271-83. DOI: 10.1016/j.pmedr.2018.10.003.
35. Ahn JV, Sera F, Cummins S, Flouri E. Associations between objectively measured physical activity and later mental health outcomes in children: findings from the UK Millennium Cohort Study. J Epidemiol Community Health 2018;72(2):94-100.
36. Franklin J, Denyer G, Steinbeck KS, Caterson ID, Hill AJ. Obesity and risk of low self-esteem: a statewide survey of Australian children. Pediatrics 2006;118(6):2481-7. DOI: 10.1542/peds.2006-0511.
37. Hesketh K, Wake M, Waters E. Body mass index and parent-reported self-esteem in elementary school children: evidence for a causal relationship. International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity 2004;28(10):1233-7. DOI: 10.1038/sj.ijo.0802624.
38. Gibson LY, Byrne SM, Blair E, Davis EA, Jacoby P, Zubrick SR. Clustering of psychosocial symptoms in overweight children. The Australian and New Zealand journal of psychiatry 2008;42(2):118-25. DOI: 10.1080/00048670701787560.
39. Bell LM, Curran JA, Byrne S, Roby H, Suriano K, Jones TW, et al. High incidence of obesity co-morbidities in young children: a cross-sectional study. J Paediatr Child Health 2011;47(12):911-7. DOI: 10.1111/j.1440-1754.2011.02102.x.
40. Wu X, Kirk SF, Ohinmaa A, Veugelers P. Health behaviours, body weight and self-esteem among grade five students in Canada. SpringerPlus 2016;5(1):1099.
41. Blashill A, Wilhelm S. Body Image Distortions, Weight, and Depression in Adolescent Boys: Longitudinal Trajectories into Adulthood. Psychol Men Masc 2014;15(4):445-51. DOI: 10.1037/a0034618.
42. Solomon-Krakus S, Sabiston CM, Brunet J, Castonguay AL, Maximova K, Henderson M. Body Image Self-Discrepancy and Depressive Symptoms Among Early Adolescents. Journal of Adolescent Health 2017;60(1):38-43. DOI: 10.1016/j.jadohealth.2016.08.024.
43. Mühlig Y, Antel J, Föcker M, Hebebrand J. Are bidirectional associations of obesity and depression already apparent in childhood and adolescence as based on high-quality studies? A systematic review. Obesity Reviews 2016;17(3):235-49. DOI: 10.1111/obr.12357.
44. Zahl T, Steinsbekk S, Wichstrøm L. Physical Activity, Sedentary Behavior, and Symptoms of Major Depression in Middle Childhood. Pediatrics. 2017. DOI: 10.1542/peds.2016-1711.
45. Fibbins H, Czosnek L, Stanton R, Davison K, Lederman O, Morell R, et al. Self-reported physical activity levels of the 2017 Royal Australian and New Zealand College of Psychiatrists (RANZCP) conference delegates and their exercise referral practices. J Ment Health 2018:1-8. DOI: 10.1080/09638237.2018.1521935.
46. Shriver LH, Harrist AW, Page M, Hubbs-Tait L, Moulton M, Topham G. Differences in body esteem by weight status, gender, and physical activity among young elementary school-aged children. Body Image 2013;10(1):78-84. DOI: 10.1016/j.bodyim.2012.10.005.
47. Tremblay MS, LeBlanc AG, Kho ME, Saunders TJ, Larouche R, Colley RC, et al. Systematic review of sedentary behaviour and health indicators in school-aged children and youth. Int J Behav Nutr Phys Act 2011;8(1):98. DOI: 10.1186/1479-5868-8-98.

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Trabajo Original

Pediatría

Implication of gestational diabetes treatment on maternal weight gain and low neonatal weight: a large retrospective cohort study

Implicación del tratamiento de la diabetes gestacional en el aumento de peso materno y bajo peso neonatal: gran estudio de cohorte retrospectivo

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Abstract

Objective: the treatment for gestational diabetes is based on diet, and this may modify maternal weight gain. The limited maternal weight gain is related to newborns with small weight for their gestational age (SGA), and many studies have found an increase of SGA in women with gestational diabetes (GD), but the reason for this is not clear. The objective of this study is to evaluate the effects of gestational diabetes treatment on maternal weight gain and neonatal weight.

Methods: a retrospective cohort study of 1,765 patients with GD, according to the National Diabetes Data Group (NDDG) criteria. We assessed: pre-pregnancy BMI, total maternal weight gain (MWG), weight gain during the third trimester, gestational week of starting the treatment, and treatment modality (diet or diet plus insulin). Birth weight was adjusted by gestational age and gender: SGA (≤ 10th) and large for gestational age (LGA) (> 90th).

Results: the percentage of newborns with weight percentile ≤ 10 was 14.8%. The diet and the time of initiation of the treatment were related to maternal weight gain (MWG) in the third trimester. For every 1 kcal/kg of variation in the diet (increase or decrease), a MWG variation of 0.03 (0.001-0.06) kg occurred ($p < 0.01$). For each week before the beginning of treatment, the mother did not gain 0.13 ± [(-0.15) - (-0.11)] kg in the third trimester ($p < 0.01$). The SGA was related to the lowest MWG in total gestation: 7.0 (IQR 3.0-10.4) kg *vs.* 8.4 (IQR 5.0-11.6) kg ($p < 0.01$), and in the third trimester: 0.3 (IQR -0.9-1.5) kg *vs.* 0.9 (IQR -0.3-2.2) kg ($p < 0.01$).

Conclusion: the dietary treatment for gestational diabetes leads to a lower maternal weight gain and induces an impact on neonatal weight.

Key words:

Gestational diabetes. Birth weight. Pregnancy. Weight gain. Gestational age.

Resumen

Objetivo: el tratamiento para la diabetes gestacional se basa en la dieta y esto puede modificar el aumento de peso materno. Un aumento de peso materno limitado está relacionado con recién nacidos con bajo peso para su edad gestacional (SGA). Muchos estudios han encontrado un aumento de niños con bajo peso en mujeres con diabetes gestacional, pero la razón de esto no está clara. El objetivo de este estudio es evaluar los efectos del tratamiento de la diabetes gestacional sobre el aumento de peso materno y el peso neonatal.

Métodos: estudio de cohortes retrospectivo en 1765 pacientes con diabetes gestacional, según los criterios de los National Diabetes Data Groups (NDDG). Evaluamos: IMC antes del embarazo, aumento de peso materno total (MWG), aumento de peso durante el tercer trimestre, semana gestacional de inicio del tratamiento y modalidad de tratamiento (dieta o dieta más insulina). El peso al nacer se ajustó por edad gestacional y género: SGA (percentil de ≤ 10) y grande para la edad gestacional (LGA) (percentil de > 90).

Resultados: el porcentaje de recién nacidos con peso percentil de ≤ 10 fue del 14,8%. La dieta y el momento de inicio del tratamiento se relacionaron con el aumento de peso materno en el tercer trimestre. Por cada 1 kcal/kg de variación en la dieta (aumento o disminución) se produjo una variación de aumento del peso materno de 0,03 (0,001-0.06) kg ($p < 0,01$). Por cada semana antes de inicio del tratamiento, la madre dejó de ganar 0,13 ± [(- 0,15) - (- 0,11)] kg en el tercer trimestre ($p < 0,01$). El SGA se relacionó con un aumento de peso materno más bajo en el total de la gestación: 7,0 (IQR 3,0-10,4) kg *vs.* 8,4 (IQR 5,0-11,6) kg ($p < 0,01$), y en el tercer trimestre: 0,3 (IQR -0,9-1,5) kg *vs.* 0,9 (IQR -0,3-2,2) kg ($p < 0,01$).

Conclusión: el tratamiento dietético para la diabetes gestacional puede conducir a un menor aumento de peso materno y a su vez inducir un impacto en el peso neonatal.

Palabras clave:

Diabetes gestacional. Peso neonatal. Gestación. Ganancia de peso. Edad gestacional.

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INTRODUCTION

GD is defined as the diabetes diagnosed in the second or third trimester of pregnancy that is not clearly either type 1 or type 2 diabetes (1).

GD has been associated with many adverse maternal and newborn outcomes, such as large for gestational age (LGA) (2-5). Many systematic reviews and meta-analyses have found that the treatment of GD reduces LGA births (6-8). It is not a questionable result, but several of these studies have shown an increase in the percentage of small for gestational age (SGA) infants (9-12). Thus, it seems that in some cases the treatment of GD had unexpected results.

One of the most important factors in neonatal weight is maternal weight gain during gestation, and this is related to the maternal diet. In fact, nutrition therapy is the cornerstone of treatment in GD management, and its modifications are used to achieve optimal glycemic control. However, the optimal diet (energy content, macronutrient distribution…) remains open to question. The Institute of Medicine (IOM) has published the most widely adopted guidelines for weight gain during pregnancy (13), but it is unclear to what extent they can be influenced by changes in diet and to what extent they in turn influence birth weight. There are several studies that have been carried out on pregnant patients without GD in which there is evidence of an increase in SGA in relation to diet restriction (14). However, there is no evidence of this fact in patients with gestational diabetes.

We conducted this study to evaluate gestational diabetes treatment effects in a large group of gestations complicated with GD, and to identify any weight adverse effects on the newborns.

METHODS

The present retrospective study was conducted using data from our database that contains the records of all gestations complicated with diabetes. We selected women with a singleton pregnancy who had been diagnosed with gestational diabetes using the National Diabetes Data Group (NDDG) criteria from 1994 through to 2014.

At weeks 24–28 of gestation, women with no previous history of diabetes were assessed by means of the O'Sullivan test, after a 12 h fast. If they had any known risk factors for gestational diabetes, a screening test was performed in the first gestational trimester. When plasma glucose levels 1 h after glucose load were ≥ 140 mg/dL, a further 100 g OGTT was performed, and new glucose levels were measured while fasting, at 1, 2, and 3 hour intervals after intake. GD was diagnosed according to NDDG criteria: two or more glucose levels above the following: 105 mg/dL basal, 190 mg/dL in 1 h, 165 mg/dL in 2 h, and 145 mg/dL in 3h. The exclusion criteria were patients with other types of diabetes than GD, multiple gestation, delivery < 20 weeks, and incomplete follow-up to delivery.

The treatment consisted of physical activity and a balanced diet (50-53% carbohydrates, 18-21% protein, and 28-32% fat). Considering pre-pregnancy BMI, 45-50 kcal/kg was prescribed in women with low weight (BMI < 18.5 kg/m^2), 35-40 kcal/kg in women with normal weight (BMI 18.5-24.9 kg/m^2), 30 kcal/kg in women who were overweight (BMI 25-29.9 kg/m^2), and 20 kcal/kg in women with obesity (BMI ≥ 30 kg/m^2). These recommendations are consistent with the 2009 IOM guidelines (13).

Therapy with insulin was commenced if optimal glycemic targets were not reached (fasting blood glucose level ≥ 95 mg/dL and/or 1h postprandial blood glucose level ≥ 140 mg/dL). Patients had to register blood glucose controls, and describe the previous intake if glucose levels were out of the target range.

We assessed:

1. *Maternal data:* age, pre-pregnancy weight (kg) (based on self-reported or first-registered weight at the beginning of gestation) and BMI (kg/m^2), weight gain during the third trimester and the total gestational period, the gestational week of starting treatment, and treatment modality (diet or diet plus insulin).
   Concerning diet, we assessed kcal per pre-gestational weight (kcal/kg) and the total diet prescribed (kcal). Delivery was categorized as eutocic or caesarean delivery.
2. *Neonate data:* gender, neonatal weight adjusted by gestational age and gender, and total neonatal weight (g).

Birth weights were categorized into small for gestational age (≤ 10th percentile) and large for gestational age (> 90th percentile) by reference to Carrascosa et al. (15).

STATISTICAL ANALYSIS

Qualitative variables are presented with their frequency distribution. Quantitative variables are summarized as mean and standard deviation (SD) or median and interquartile range (p25-p75) in case of asymmetry.

The association is made between qualitative variables with the Chi^2 test or Fisher exact test, in the event that more than 25% of the expected quantity of fewer than 5 were evaluated.

The behavior of quantitative variables was analyzed for each of the independent variables categorized using Student's t-test (in comparisons of a variable with two categories) and/or ANOVA. By using this technique, mean differences due to the individual, or the main effect of each factor and/or the effect of their interactions, were evaluated. The significance level was corrected retrospectively (compared to peers) with the Bonferroni test. If there were asymmetry differences with the non-parametric test, the Mann-Whitney test or median (where appropriate) was evaluated. $p < 0.05$ was considered statistically significant.

The software package used for the analysis was the SPSS for Windows.

RESULTS

A total of 1,765 patients were included in the study with a mean age of 32.5 ± 4.3 years (mean ± SD). Table I shows the maternal characteristics.

Table I. Maternal characteristics

Age (years)	32.5 ± 4.3
Pregestational weight (kg)	68.4 ± 14.7
Height (m)	1.59 ± 0.06
Pregestational BMI (kg/m^2)	26.9 ± 5.4
Week of gestation at treatment initiation	29.2 ± 5.9
Diet (kcal)	2050 ± 164.8
Diet, kcal/kg	31.4 ± 7.5
Insulin (%) (n = 354)	20.1
Weight, start of 3rd trimester (kg)	75.6 ± 14.1
Weight, end of 3rd trimester (kg)	76.6 ± 13.9
Total weight gain (kg)	8.2 ± 5.3
3rd trimester weight gain (kg)	1.0 ± 2.3

Table II. Differences between neonatal percentile weight groups (≤ 10 and > 10 percentile) and maternal weight gain

	Neonatal weight p ≤ 10 (n = 251; 14.8%)	**Neonatal weight p > 10 (n = 1443; 85.2%)**	**(p)**
Maternal total weight gain (kg)	7 (3-10.4)	8.4 (5-11.8)	p < 0.01
Maternal 3rd T weight gain (kg)	0.3 (-0.9-1.5)	0.9 (-0.3-2.2)	p < 0.01

The mean pre-gestational BMI (mean ± SD) was 26.9 ± 5.4 kg/m^2, distributed as follows: low maternal weight 1.1%, normal weight 38.9%, overweight 32.6%, and obese 21.6%.

The intervention was started at 29.2 ± 5.9 weeks of gestation. The number of kilocalories prescribed in the initial diet was 2,050 ± 164.8 kcal, with 31.4 ± 7.5 kcal/kg of pre-gestational weight.

According to the pre-gestational BMI, mean kcal/kg was: low weight: 49.1 ± 7.7 kcal/kg, normal weight: 37.2 ± 5.1 kcal/kg, overweight: 29.9 ± 3.7 kcal/kg, and obese: 22.3 ± 3.5 kcal/kg.

The mean total maternal weight gain during gestation was 8.2 ± 5.3 kg; during the third trimester it was 1.0 ± 2.3 kg.

During pregnancy, 20.1% of the women needed insulin therapy.

Concerning neonatal data, mean neonatal birth weight was 3,204.4 ± 531.6 g. In all, 14.8% of births were SGA (weight percentile ≤ 10), 18.4% were in a low weight percentile (p10-25), and 10.1% were LGA (weight percentile > 90). Mean gestational week at birth was 38.8 ± 2.1, and there were 27.1% cesarean interventions.

Concerning neonatal birth weight and preconception and pregnancy-associated factors, we observed the association with maternal pre-gestational BMI as follows: 3,033.4, 3,137.9, 3,238.9 and 3,306.9 g in patients with low weight, normal weight, overweight and obesity, with significant differences between groups ($p < 0.05$).

For SGA neonates, maternal weight gain was less than for non-SGA neonates, both in pregnancy as a whole (7.0 *vs.* 8.4 kg, $p < 0.01$) and during the third trimester: (0.3 *vs.* 0.9 kg, $p < 0.01$) (Table II).

Pre-gestational maternal BMI was lower in women who gave birth to SGA children than in the rest of women (25.9 ± 5.4 kg/m^2 *vs.* 27.1 ± 5.4 kg/m^2, $p < 0.01$). Maternal weight at the beginning of the third trimester and at the end of pregnancy was also lower (70.9 ± 13.6 *vs.* 76.5 ± 14.0 kg, and 71.1 ± 13.5 *vs.* 77.5 ± 13.8 kg, respectively; $p < 0.01$). Fewer mothers with SGA children used insulin (10.0% *vs.* 16.1%, $p < 0.01$).

Treatment with insulin was associated with higher neonatal birth weight (3,267.6 *vs.* 3,188 g, $p = 0.01$) and birth by cesarean section (3,740.8 ± 500.1 *vs.* 3,116.5 ± 477.0, $p < 0.01$), possibly because increased fetal weight is one of the factors that encourage the use of insulin.

Related to maternal weight gain, we observed that, as regards the maternal pre-gestational BMI, there were significant differences between all groups in terms of median maternal weight gain over the entire pregnancy: low weight 12.3 kg (IQR: 11.1-15.1), normal weight 9.6 kg (IQR: 7.0-12.2), overweight 7.8 kg (IQR: 4.7-10.9), and obesity 5.0 kg (IQR: 1.5-9.1) ($p < 0.01$).

In third-trimester weight gain alone, differences were revealed between low-weight patients and the other groups ($p < 0.01$): low weight 2.1 kg (IQR: 1.5-2.8), normal weight 1.0 kg (IQR: -0.2-1.1), overweight 1.0 kg (IQR: -0.4-2.3), and obese patients 0.8 kg (IQR: -0.8-2.2) (Fig. 1).

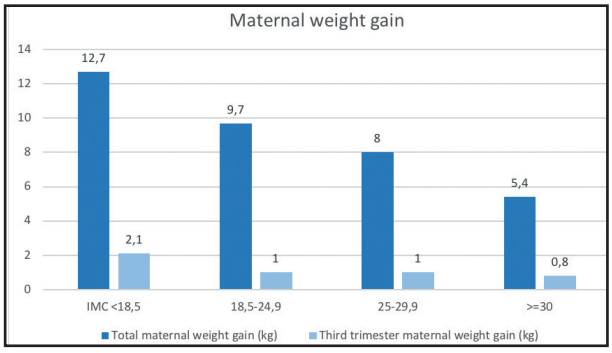

Figure 1.
Maternal weight gain according to maternal pregestational BMI during the total and third trimester gestation.

We observed a relationship between use of insulin and higher weight gain in the third trimester (1.5 kg (0.1-3.3) *vs.* 0.6 kg (-0.5-1.8), $p < 0.01$), with no significant differences in total weight gain for the total gestational period.

In the multivariate analysis of weight gain during the third trimester of gestation we found a relationship between diet and weight gain, with a variation of 0.03 kg per each 1 kcal/kg variation in the prescribed diet ($p < 0.05$).

We also observed that for each week earlier that patient monitoring was started, patients failed to gain 0.13 kg during the third trimester ($p < 0.01$).

Maternal weight gain during the third trimester was linked to the neonatal birth weight percentile, so that in the lowest weight percentile groups ($p < 3$, p3-10, p10-25) there was a difference in maternal weight gain of -1.03, -0.61, and -0.34 kg (respectively, $p < 0.05$) compared to the weight gain seen in the mothers who gave birth to children in weight percentiles considered to be within the normal range (p25-75) (Fig. 2).

DISCUSSION

Uncontrolled GD has a direct consequence on the fetus and increases the risk of macrosomia. Treatment leads to a decrease in birth weight (16). Today this is closer to 10% and thus similar to the general population. Some studies have evidenced a reduction in overall fetal weight linked to decreased macrosomia, which are valued as a positive effect of treatment as it lowers the incidence of complications in childbirth. On the other hand, there is the possibility of an increased risk of SGA infants that could be related to treatment (17,18). The increased incidence of SGA leads to more risk at birth (19) and is associated with late complications related to impaired motor development in children and increased cardiovascular risk in adults.

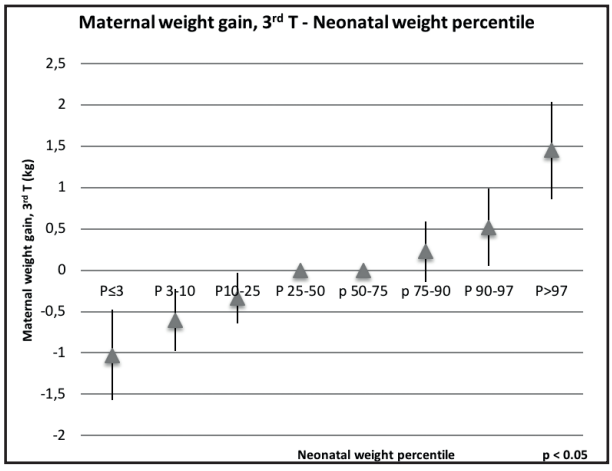

Figure 2.
Difference of maternal weight gain averages in the third trimester for each percentile of neonate weight relative to reference (percentile 26-75), adjusted for maternal BMI, kcal/kg of the prescribed diet, and gestational week at the intervention.

The prevalence of SGA (percentile ≤ 10) in our study was 14.8%; in the general population it is, or should be, 10%. This represents an increase of 48% above expectations. However, the prevalence of macrosomia is 10.1%, similar to the general population (15).

In recent studies, the prevalence of SGA in patients with GD reaches 16% or even 20% in some subgroups of patients. These are studies whose main objective was to evaluate fetal macrosomia, so they do not give an explanation of the findings on SGA (20-22).

Among the factors directly related to neonatal weight we included maternal weight progression and pre-pregnancy BMI.

1. It is known that maternal weight evolution plays a decisive role in fetal growth. In the absence of specific recommendations for gestational diabetes, IOM for general pregnant population recommendations are followed that take into account the pre-pregnancy BMI. The pre-pregnancy BMI in our sample was 26.9 kg/m^2, with a total of 54.2% of patients who have a weight above normal.
   The therapeutic intervention in our sample was at the beginning of the third trimester. Recent guidelines propose a caloric increase in the third trimester, so the prescription diet in our patients was consistent with these recommendations (13). Despite this, maternal weight gain during the third trimester was lower than the recommended level, coinciding with the start of the prescribed treatment.
   There is little scientific evidence about this issue because most studies are directed towards good glycemic control to avoid the risk of macrosomia, not taking into account data on adverse effects such as weight gain or SGA (23).
   Sugiyama et al. (24) found in their observational study of 1,615 patients with GD that the average weight gain during total pregnancy was just over 6 kg, and the prevalence of SGA was 16%. These results are consistent with those found in our work – that poor weight gain and a high percentage of SGA are linked. Surprisingly, they do not explain the possible reasons for the increase in the percentage of SGA.
   Most studies analyze maternal weight gain in total gestation, but Barnes et al. (25) specify the progression of maternal weight during the third trimester. This was designed aiming to establish predictors of LGA ($p > 90$) and SGA ($p \leq 10$) in a population of 1,695 patients with GD. The mean weight gain in this work was 12.3 kg, but since the start of follow-up (average 28.1 weeks of gestation) average weight gain was only 1.7 kg. It is low compared with that recommended by the IOM and consistent with the evidence in our study. On analyzing the subgroup of women with BMI < 20 and weight gain < 10 kg during pregnancy, the percentage of SGA was 17%. In this work, as in our study, it is shown that low maternal weight progression conditions result in inadequate fetal weight gain, thereby increasing the incidence of children with SGA.
   Stotland et al. (26), in their retrospective study on 20,465 non-diabetic patients, showed that a lower maternal weight gain of 7 kg is associated with an increased risk of children with SGA (OR 1.66, 95% CI 1.44-1.92). Other studies

among the Thai population (27), conducted on non-diabetic pregnant patients with normal pre-pregnancy weight, found that those who did not reach the goals of weight gain (less than 10 kg in total gestation) were at increased risk of SGA in the newborn. Several studies evidenced that patients with low weight gain are more likely to have children with SGA ($p < 10$), which is consistent with the findings in our study population with gestational diabetes (11,28-32).

2. On the other hand, our work also shows a relationship between birth weight and maternal pre-pregnancy BMI in patients with gestational diabetes. Women with a lower BMI have children with lower weights, and a higher prevalence of SGA is found.

   A meta-analysis conducted among pregnant women without gestational diabetes concluded that low pre-pregnancy maternal weight (defined by a BMI of less than 20 kg/m^2) is related to newborns with SGA (33).

   Black et al. (34) analyzed the impact of maternal pre-pregnancy BMI and maternal weight gain on fetal growth in a sample of women with and without a diagnosis of gestational diabetes (IADPSG criteria). They concluded that the prevalence of macrosomia is higher in women with higher pre-pregnancy BMI and greater weight gain during pregnancy, both in patients with and without gestational diabetes. It is true that this prevalence is higher in those with gestational diabetes.

   Until now, the treatment of GD has been based on maternal glycemic control with diet and physical activity. In our work, among 1,765 patients with gestational diabetes, we show that maternal weight and BMI before pregnancy are very important on low fetal weight, specifically on the incidence of SGA.

These aspects have not been analyzed in other studies as primary objectives, and for this reason we consider the findings derived from our work to be important.

Although the number of patients included in our study is high, we assume that the fact that it is a retrospective study is a limitation, and therefore new work is necessary to support these conclusions.

Despite this, we consider that the results of our study are applicable to clinical practice. For the therapeutic control of type 2 diabetes mellitus a shift in focus is happening. It is moving from a glycocentric vision to an adipocentric vision. It is not only hyperglycemia causing injury and requiring control as a single target, but also excess weight, and therefore adipose tissue that is central to its development. In view of the results we can apply this approach to patients with gestational diabetes. Thus, not all patients who meet some biochemical diagnostic criteria for gestational diabetes are at the same risk of macrosomia, or benefit from the same therapeutic strategy, and therefore would not be subjected to the same intensity of glycemic control. We consider that if one of the goals of gestational diabetes treatment is to prevent fetal macrosomia and obstetrical adverse events, the intensity of treatment should be determined not only by blood sugar levels but also by maternal pre-pregnancy BMI and weight progression during pregnancy.

Analyzing the potential benefits and risks of treatment for GD, some experts have argued that since the treatment is based on nutritional modifications and blood glucose monitoring exclusively in most cases, it poses little risk of harm to the mother and the fetus because it is a minimally invasive intervention. However, the diagnosis of GD increases the number of prenatal visits and work absences for the mother, besides the inconvenience and costs associated with regular monitoring of blood glucose. The literature suggests that not all patients diagnosed with GD have the same risk of macrosomia and do not therefore receive the same benefit from the prescribed treatment. If the patient has pre-pregnancy obesity, we can induce more limited weight gain (as recommended by the IOM guidelines), aimed at reducing the likelihood of fetal macrosomia, which may be appropriate only in this group of patients. However, those with low pre-pregnancy BMI and/or less weight gain during pregnancy will be those who obtain little benefit from treatment because their risk of macrosomia is already low. They may even experience a detrimental effect by increasing the percentage of SGA (35,36).

In our study, we found that the prevalence of macrosomia in patients with GD is similar to the general population, so we understand that treatment met the goal of reducing the risk of macrosomia effectively. However, maternal weight gain was very scarce and the prevalence of infants with SGA ($p \leq 10$) was higher than expected. This has to do with a therapeutic intervention that, despite being consistent with the recommendations of the IOM, and being considered as "minimally invasive" measures, can have negative consequences. For this reason, and as a consequence of our study, we suggest modulating the intensity of treatment depending not only on glycemic control but also taking into account other factors related to fetal weight such as pre-pregnancy maternal BMI and maternal weight gain.

In conclusion, the dietary treatment for gestational diabetes leads to lower maternal weight gain and has an impact on neonatal weight being a risk factor for the development of SGA neonates. So we should consider other factors besides glycemic control when it comes to intensifying dietary treatment.

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REFERENCES

1. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes – 2019. Diabetes Care 2019;42(Suppl 1):S165-S172.
2. Hosseini E, Janghorbani M. Systematic review and meta-analysis of diagnosing gestational diabetes mellitus with one-step or two-step approaches and associations with adverse pregnancy outcomes. Int J Gynaecol Obstet 2018.
3. Donovan L, Hartling L, Muise M, Guthrie A, Vandermeer B, Dryden DM. Screening tests for gestational diabetes: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med 2013;159(2):115-22.
4. Mitanchez D, Yzydorczyk C, Siddeek B, Boubred F, Benahmed M, Simeoni U. The offspring of the diabetic mother – short- and long-term implications. Best Pract Res Clin Obstet Gynaecol 2015;29(2):256-69.

5. Black MH, Sacks DA, Xiang AH, Lawrence JM. The relative contribution of pre-pregnancy overweight and obesity, gestational weight gain, and IADPSG-defined gestational diabetes mellitus to fetal overgrowth. Diabetes Care 2013;36(1):56-62.
6. Mayo K, Melamed N, Vandenberghe H, Berger H. The impact of adoption of the international association of diabetes in pregnancy study group criteria for the screening and diagnosis of gestational diabetes. Am J Obstet Gynecol 2015;212(2):224.e1-9.
7. Falavigna M, Schmidt MI, Trujillo J, Alves LF, Wendland ER, Torloni MR, et al. Effectiveness of gestational diabetes treatment: a systematic review with quality of evidence assessment. Diabetes Res Clin Pract 2012;98(3):396-405.
8. Horvath K, Koch K, Jeitler K, Matyas E, Bender R, Bastian H, et al. Effects of treatment in women with gestational diabetes mellitus: systematic review and meta-analysis. BMJ 2010;340:c1395.
9. Brown J, Alwan NA, West J, Brown S, McKinlay CJ, Farrar D, et al. Lifestyle interventions for the treatment of women with gestational diabetes. Cochrane Database Syst Rev 2017;5:CD011970.
10. Institute of Medicine. Weight gain during pregnancy: re-examining the guidelines. Washington: National Academic Press 2009.
11. Catalano PM, Mele L, Landon MB, Ramin SM, Reddy UM, Casey B, et al. Inadequate weight gain in overweight and obese pregnant women: what is the effect on fetal growth? Am J Obstet Gynecol 2014;211(2):137.e1-7.117.
12. Hung T-H, Chen S-F, Hsu J-J, Hsieh T-T. Gestational weight gain and risks for adverse perinatal outcomes: A retrospective cohort study based on the 2009 Institute of Medicine guidelines. Taiwan J Obstet Gynecol 2015;54(4):421-5.
13. National Institutes of Health consensus development conference statement: diagnosing gestational diabetes mellitus, March 4-6, 2013. Obstet Gynecol 2013;122(2 Pt 1):358-69.
14. Emond JA, Karagas MR, Baker ER, Gilbert-Diamond D. Better diet quality during pregnancy is associated with a reduced likelihood of an infant born small for gestational age: an analysis of the prospective New Hampshire birth cohort study. J Nutr 2018;148(1):22-30.
15. Carrascosa Lezcano A, Ferrández Longás A, Yeste Fernández D, García-Dihinx Villanova J, Romo Montejo A, Copil Copil A, et al. Estudio transversal español de crecimiento 2008. Parte I: valores de peso y longitud en recién nacidos de 26-42 semanas de edad gestacional. An Pediatr (Barc) 2008 Jun;68(6):544-51.
16. Boulet SL, Alexander GR, Salihu HM, Pass M. Macrosomic births in the United States: determinants, outcomes, and proposed grades of risk. Am J Obstet Gynecol 2003;188(5):1372-8.
17. Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. N Engl J Med 2009;361(14):1339-48.
18. Martis R, Crowther CA, Shepherd E, Alsweiler J, Downie MR, Brown J. Treatments for women with gestational diabetes mellitus: an overview of Cochrane systematic reviews. Cochrane Database Syst Rev 2018;8:CD012327.
19. Gavard JA. Gestational weight gain and maternal and neonatal outcomes in underweight pregnant women: a population-based historical cohort study. Matern Child Health J 2017;21(5):1203-1210.
20. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358(19):1991-2002.
21. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS, et al. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352(24):2477-86.
22. Schaefer-Graf UM, Kjos SL, Fauzan OH, Bühling KJ, Siebert G, Bührer C, et al. A randomized trial evaluating a predominantly fetal growth-based strategy to guide management of gestational diabetes in Caucasian women. Diabetes Care 2004;27(2):297-302.
23. Viana LV, Gross JL, Azevedo MJ. Dietary intervention in patients with gestational diabetes mellitus: a systematic review and meta-analysis of randomized clinical trials on maternal and newborn outcomes. Diabetes Care 2014;37(12):3345-55.
24. Sugiyama T, Nagao K, Metoki H, Nishigori H, Saito M, Tokunaga H, et al. Pregnancy outcomes of gestational diabetes mellitus according to pre-gestational BMI in a retrospective multi-institutional study in Japan. Endocr J 2014;61(4):373-80.
25. Barnes RA, Edghill N, Mackenzie J, Holters G, Ross GP, Jalaludin BB, et al. Predictors of large and small for gestational age birthweight in offspring of women with gestational diabetes mellitus. Diabet Med 2013;30(9):1040-6.
26. Stotland NE, Cheng YW, Hopkins LM, Caughey AB. Gestational weight gain and adverse neonatal outcomes among term infants. Obstet Gynecol 2006;108(3 Pt 1):635-43.
27. Jariyapitaksakul C, Tannirandorn Y. The occurrence of small for gestational age infants and perinatal and maternal outcomes in normal and poor maternal weight gain singleton pregnancies. J Med Assoc Thai 2013;96(3):259-65.
28. Beyerlein A, Schiessl B, Lack N, von Kries R. Associations of gestational weight loss with birth-related outcome: a retrospective cohort study. BJOG 2011;118(1):55-61.
29. Blomberg M. Maternal and neonatal outcomes among obese women with weight gain below the new Institute of Medicine recommendations. Obstet Gynecol 2011;117(5):1065-70.
30. Bogaerts A, Ameye L, Martens E, Devlieger R. Weight loss in obese pregnant women and risk for adverse perinatal outcomes. Obstet Gynecol 2015;126(2):452.
31. Goldstein RF, Abell SK, Ranasinha S, Misso M, Boyle JA, Black MH et al. Association of Gestational Weight Gain With Maternal and Infant Outcomes: A Systematic Review and Meta-analysis. JAMA 2017;317(21):2207-2225.
32. Barquiel B, Herranz L, Meneses D, Moreno O, Hillman N, Burgos MA. Optimal Gestational Weight Gain for Women with Gestational Diabetes and Morbid Obesity. Maternal Child Health J 2018;22(9):1297-305.
33. Yu Z, Han S, Zhu J, Sun X, Ji C, Guo X. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/obesity: a systematic review and meta-analysis. PLoS ONE 2013;8(4):e61627.
34. Black MH, Sacks DA, Xiang AH, Lawrence JM. The relative contribution of pre-pregnancy overweight and obesity, gestational weight gain, and IADPSG-defined gestational diabetes mellitus to fetal overgrowth. Diabetes Care 2013;36(1):56-62.
35. Zhao R, Xu L, Wu mL, Huang SH, Cao XJ. Maternal pre-pregnancy body mass index, gestational weight gain influences birth weight. Women Birth 2018;31(1):e20-e25.
36. Goldstein RF, Abell SK, Ranasinha S, Misso M, Boyle JA, Black MH, et al. Association of gestational weight gain with maternal and infant outcomes: a systematic review and meta-analysis. JAMA 2017;317(21):2207-25.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Nutrición en el anciano

Sarcopenic obesity in community-dwelling older women, determined by different diagnostic methods

Obesidad sarcopénica en mujeres mayores que viven en la comunidad, determinada por diferentes métodos de diagnóstico

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Abstract

Background: sarcopenic obesity (SO) decreases functional capacity, favors loss of autonomy, and is associated with increased mortality in the elderly. The prevalence of sarcopenic obesity differs according to the chosen diagnostic method and/or the population studied.

Objective: to identify sarcopenic obesity in community-dwelling elderly women using different diagnostic methods.

Methods: this is a cross-sectional study involving 138 elderly women enrolled in an Open University of the Third Age. Sarcopenia was defined according to three criteria: a skeletal muscle index (SMI) ≤ 6.42 kg/m²; reduced muscle strength, defined by handgrip strength (HS) < 20 kg/f; and reduced physical performance, determined by a usual gait speed (GS) < 0.8 m/s. Obesity was diagnosed when body mass index (BMI) > 28 kg/m², waist circumference (WC) > 88 cm, total body fat percentage (TBF%) determined by bioelectric impedance analysis (BIA) ≥ 38%, and value for triceps skinfold (TS) ≥ 85th percentile. Sarcopenic obesity is the coexistence of sarcopenia and obesity.

Results: the prevalence of sarcopenia and severe sarcopenia was 14.5% and 3.6%, respectively. The highest prevalence of obesity was found using WC (69.6%) and TBF% (52.9%) ($p < 0.001$). The highest prevalence of sarcopenic obesity was found using TBF% (9.4%) and WC (6.5%) ($p < 0.001$). Sarcopenic obesity according to BMI was only 0.7%.

Conclusion: the prevalence of sarcopenic obesity was high and depended on the diagnostic criteria applied. The association of TBF% with the diagnosis of sarcopenia was the method that identified the highest prevalence of sarcopenic obesity.

Key words:

Sarcopenic obesity.
Body composition.
Elderly.

Resumen

Antecedentes: la obesidad sarcopénica (SO) disminuye la capacidad funcional, favorece la pérdida de autonomía y se asocia a mayor mortalidad en los ancianos. La prevalencia de la obesidad sarcopénica difiere según el método de diagnóstico elegido y/o la población estudiada.

Objetivo: identificar la obesidad sarcopénica en mujeres ancianas que viven en la comunidad utilizando diferentes métodos de diagnóstico.

Métodos: este es un estudio transversal en el que participaron 138 mujeres ancianas inscritas en una Universidad Abierta de la Tercera Edad. La sarcopenia se definió de acuerdo con tres criterios: un índice de músculo esquelético (SMI) ≤ 6.42 kg/m²; fuerza muscular reducida, definida por una fuerza de empuñadura (HS) < 20 kg/f, y rendimiento físico reducido, determinado por una velocidad de marcha habitual (GS) < 0,8 m/s. La obesidad se diagnosticó si: índice de masa corporal (IMC) > 28 kg/m², perímetro de la cintura (WC) > 88 cm, porcentaje de grasa corporal total (TBF%) determinado por análisis de impedancia bioeléctrica (BIA) ≥ 38%, y valor de pliegue cutáneo del tríceps (TS) ≥ percentil 85. La obesidad sarcopénica es la coexistencia de sarcopenia y obesidad.

Resultados: la prevalencia de la sarcopenia y la sarcopenia severa fue del 14,5% y 3,6%, respectivamente. La mayor prevalencia de obesidad se encontró mediante el WC (69,6%) y el porcentaje de TBF (52,9%) ($p < 0,001$). La prevalencia más alta de obesidad sarcopénica se encontró utilizando el % de TBF (9,4%) y el WC (6,5%) ($p < 0,001$). La obesidad sarcopénica según el IMC fue solo del 0,7%.

Conclusión: la prevalencia de la obesidad sarcopénica fue alta y dependió de los criterios diagnósticos aplicados. La asociación del TBF% con el diagnóstico de sarcopenia fue el método que identificó la prevalencia más alta de obesidad sarcopénica.

Palabra clave:

Obesidad sarcopénica.
Composición corporal. Anciano.

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INTRODUCTION

Sarcopenia, when associated with obesity, is called sarcopenic obesity. This condition reduces functional capacity, favors loss of autonomy, and is associated with increased mortality in the elderly (1,2).

The prevalence of sarcopenic obesity differs according to the chosen diagnostic method and/or the population studied, being more frequent in females (3,4). Studies using different diagnostic methods for the diagnosis of sarcopenic obesity show a prevalence between 0 and 41% (5), and in Brazil specifically, prevalence ranges from 3 to 41% (6,7).

Several methods are used to diagnose sarcopenic obesity. For the diagnosis of obesity in the elderly, body mass index (BMI), waist circumference (WC), and BMI–associated with WC and total body fat percentage (TBF %) identified by skinfolds, or by more accurate methods to estimate body composition–have been used (3). For sarcopenia, the most frequent diagnostic methods are skeletal muscle index (SMI), handgrip strength (HS), and usual gait speed (GS) (2).

This study aimed to identify sarcopenic obesity in community-dwelling elderly women using different methods that consider the quantitative assessment of muscle mass, strength, and physical performance, as associated with different diagnostic criteria for obesity.

METHODS

A cross-sectional study with 138 elderly women enrolled in an Open University of the Third Age in Salvador-Bahia was developed by the Center for Studies and Intervention in the Aging Area (CEIAE-CNPq), Nutrition School, Federal University of Bahia. The Research Ethics Committee at the Nutrition School approved the study (assent 1.159.885/2015). All participants signed an informed consent form (TCLE).

A sample size calculation considered a 95% confidence interval (CI) with a sample error estimate of 6%. The initial sample consisted of 147 elderly adults. Four women were excluded from the initial sample because they had a contraindication to bioelectrical impedance analysis (one had a pacemaker and three had metallic prostheses). Five men were excluded from the analysis because they were the only males in the sample. The final sample was 138 elderly women. The trained team, using standardized techniques, performed the data collection and adjustments after conducting a pilot study.

DIAGNOSIS OF SARCOPENIC OBESITY (SO)

The diagnosis of sarcopenia was made according to the three criteria evaluated in the definition by the European Consensus (8).

Muscular mass

This was evaluated by the calculation of skeletal muscular mass (SMM) using the prediction equation proposed by Janssen et al. (9):

$$SMM\ (kg) = [(Height^2 / Resistance) \times 0.401] + (Sex \times 3.825) + (Age \times -0.071) + 5.102$$

where height is measured in cm, resistance in ohms, male = 1, female = 0, and age is measured in years.

The resistance value was obtained by a bioelectrical impedance analysis (BIA) using a Biodynamics® tetrapolar device, model 450. The technique and previous procedures were performed according to Kyle et al. (10).

From the SMM, the skeletal muscle index (SMI) was calculated as (9):

$$SMI = SMM / height^2$$

Women with a SMI ≤ 6.42 kg/m² were classified as pre-sarcopenic or with muscle deficit.

Muscle strength

This was evaluated by the maximal handgrip strength test, measured using a portable Sammons Preston Smedley hand dynamometer (Jamar, Bolingbrook IL, 60440) with a graduation scale of 0-100 kilogram/force (kg/f).

Two attempts to produce a maximal voluntary handgrip force (HS), with 1 min rest between them, were made with each hand (dominant and non-dominant side). The highest value found among the measurements was considered for the analysis. Values below 20 kg/f were considered to show a deficit in muscle strength (11).

Physical performance

This was measured by the usual gait speed (GS) in meters per second (m/s). To perform the test, each elderly woman walked a distance of four meters in a flat and straight environment with their usual gait speed. We measured the time taken to walk the course. A GS < 0.8 m/s was classified as reduced physical performance (11).

CLASSIFICATION OF SARCOPENIA

Pre-sarcopenia was classified by only a reduction in SMI, sarcopenia was classified by reduced SMI associated with reduced HS or GS, and severe sarcopenia was classified by the presence of a reduction in all three criteria (SMI, HS, and GS) (8).

DIAGNOSIS OF OBESITY BY DIFFERENT CRITERIA

Body mass index (BMI)

Women with a BMI > 28 kg/m² were classified as obese according to the criteria described by the Pan American Health Organization (12).

Waist circumference (WC)

This was evaluated by the midpoint measurement between the iliac crest and the last rib edge. Values > 88 cm were classified as central obesity (13).

Total body fat percentage (TBF%)

This was measured by a BIA exam. A TBF% ≥ 38% was considered to indicate obesity, according to Baumgartner (14).

Tricipital skinfold (TS)

This was measured with a Lange skinfold caliper. A value ≥ 85th percentile was classified as an excess of body fat according to specific criteria for the elderly (15).

A diagnosis of sarcopenic obesity was considered as the coexistence of sarcopenia and obesity (Fig. 1). Severe sarcopenic obesity was determined when the diagnosis of obesity was obtained at the same time as the diagnosis of severe sarcopenia.

STATISTICAL ANALYSIS

To test the normal distribution of the data we used the Kolmogorov-Smirnov normality test. Quantitative data were presented as mean and standard deviation, and qualitative variables as relative frequencies. The prevalence of obesity, sarcopenia, and sarcopenic obesity was calculated. We used a chi-square test to examine differences in the prevalence of sarcopenic obesity.

All the analyses were performed using the Statistical Package for the Social Sciences ([SPSS] v.20; IBM Corporation, Armonk, NY). The significance value adopted was a p-value ≤ 0.05.

RESULTS

Of the 138 elderly women evaluated, more than half (60.1%) were between 60 and 69 years old, and the average age was 70 years.

The prevalence of sarcopenia and severe sarcopenia was 14.5% and 3.6%, respectively. Evaluating the defining criteria for sarcopenia separately revealed that 24.6% of the women had pre-sarcopenia, 10.9% had sarcopenia when evaluated by HS, and 7.2% had sarcopenia when assessed by GS.

Considering all the diagnostic criteria for obesity, 79.8% of the women were obese. The highest prevalence of obesity was found using WC (69.6%) and TBF% (Table I).

Figure 2 shows a statistically significant variation in sarcopenic obesity (SO) prevalence according to the obesity diagnostic criteria used. The prevalence of SO, when considering all diagnostic criteria of obesity, was 10.9%. Analyzing the diagnostic criteria of obesity separately revealed that the highest prevalence of SO, 9.4%, was determined by the association of the diagnosis of sarcopenia with the diagnosis of obesity according to TBF%. The lowest prevalence of SO was identified when obesity was diagnosed according to BMI (0.7%). Only 2.2% of the elderly women had severe SO.

Among these obese women, 22.7% were pre-sarcopenic. The reduction in muscle strength and in physical performance of these women was 23.6% and 27.3% ($p < 0.001$), respectively (Fig. 3).

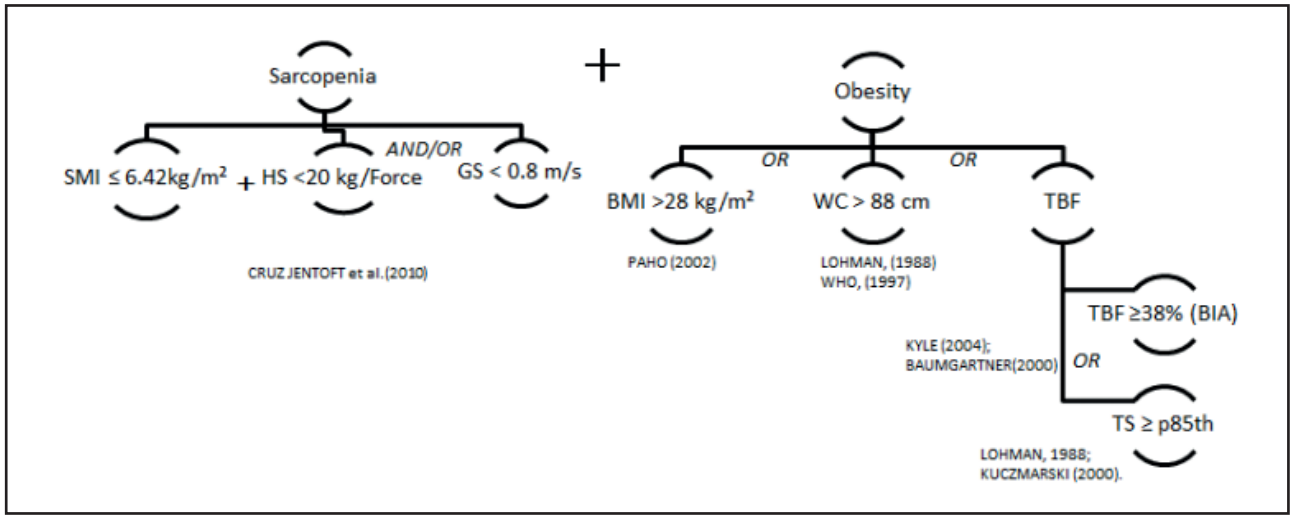

Figure 1.
Selected criteria for the diagnosis of sarcopenic obesity (SMI: skeletal muscle mass; GS: usual gait speed; HS: handgrip strength; BMI: body mass index; WC: waist circumference; TBF%: total body fat percentage by BIA; TS: triceps skinfold).

Table I. Descriptive analysis of the diagnostic criteria for sarcopenia and obesity

Diagnostic criteria for sarcopenia	% (n)	Diagnostic criteria for obesity	% (n)
SMI↓ → Pre-sarcopenia		*Body mass index*	
≤ 6.42 kg/m²	24.6 (34)*	BMI > 28.0 kg/m²	31.9 (44)*
SMI↓ + (GS↓) → Sarcopenia	7.2 (10)*	*Central obesity*	
≤ 6.42 kg/m² + < 0.8 m/s	10.9 (15)*	WC > 88.0 cm	69.6 (96)*
SMI↓ + (HS↓) → Sarcopenia	14.5 (20)*	*Total body fat (TBF)*	
≤ 6.42 kg/m² + < 20 kg/f	3.6 (5)*	TBF% by BIA ≥ 38	52,9 (73)*
SMI↓ + (HS↓) OR (GS↓) → Sarcopenia		TS ≥ p85th	18.1 (19)*
≤ 6.42 kg/m² + < 20 kg/f + < 0.8 m/s		*Obese elderly women*	
SMI↓ + (HS↓) +(GS↓) → Severe sarcopenia		(BMI, WC or TBF)	79.8 (110)*
≤ 6.42 kg/m² + < 20 kg/f + < 0.8 m/s			

X (SD)	SMI (kg/m²)	HS (kg/f)	GS (m/s)	BMI (kg/m²)	WC (cm)	TBF (%)	TS (mm)
	7.1 (1.0)	23.3 (5.2)	0.9 (0.2)	26.2 (4.1)	92.4 (10.4)	37.4 (6.4)	25.7 (7.6)

**p < 0.001; SMI, skeletal muscle mass; GS, usual gait speed; HS, handgrip strength; BMI, body mass index; WC, waist circumference; TBF%, total body fat percentage by BIA; TS, triceps skinfold.*

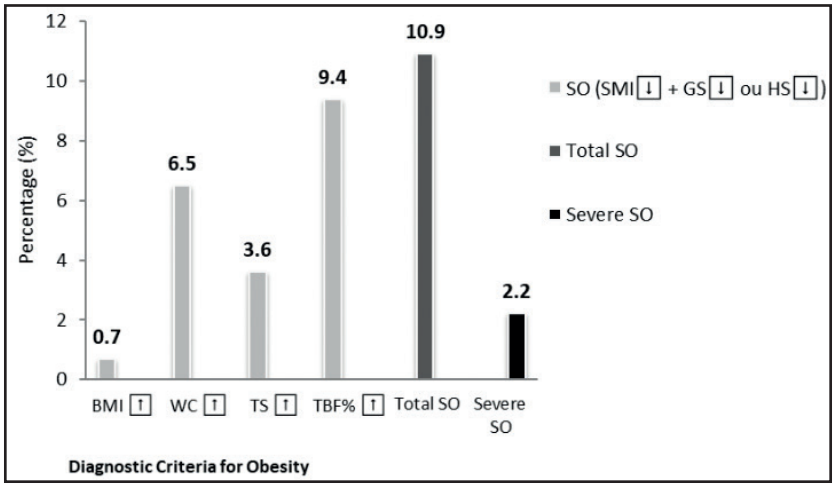

Figure 2.
Prevalence of sarcopenic obesity in community-dwelling older women, determined by different diagnostic methods (SMI: skeletal muscle mass; GS: usual gait speed; HS: handgrip strength; BMI: body mass index; WC: waist circumference; TBF%: total body fat percentage by BIA; TS: triceps skinfold).

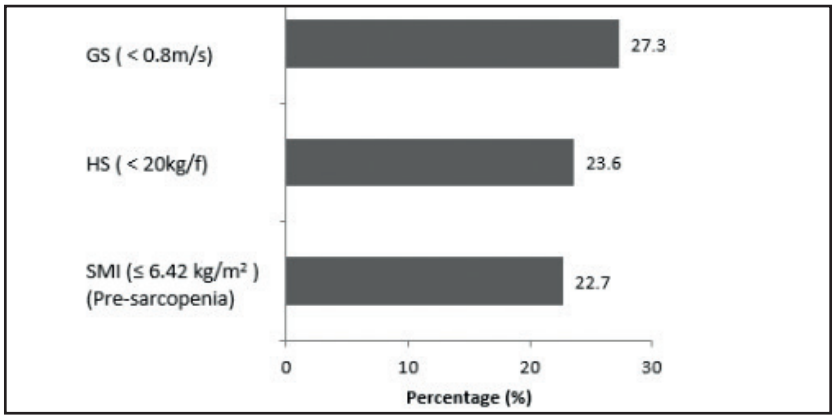

Figure 3.
Muscular and functional changes present in community-dwelling older women with obesity diagnosis (SMI: skeletal muscle mass; GS: usual gait speed; HS: handgrip strength).

DISCUSSION

Sarcopenic obesity, the combination of sarcopenia and obesity, is an important public health problem that limits the human condition and human functionality, and needs to be diagnosed early and accurately. Few studies have evaluated SO according to more than one criterion as we have in the present study (3,4). This is important since the prevalence of SO depends on the definition applied and the attributes of the target population. This study presented differences in the prevalence of SO, with important variations between the diagnostic criteria. There were more elderly women with SO when the diagnosis of sarcopenia was associated with obesity as measured by TBF%, whereas the prevalence was lower when obesity was measured by BMI.

The low prevalence of SO with the use of BMI as diagnostic criterion for obesity demonstrates the limitation of this method for the reliable diagnosis of obesity. This can be due to an excess of body fat combined with a reduction in lean mass, which might result in a BMI within the normal value, thus underdiagnosing SO in the elderly. The use of BMI to evaluate the nutritional status of the elderly is wide; however, it has some limitations, such as the inability to distinguish between differences in body composition and also a lack of consensus regarding cut-off points for the elderly (16,17).

The prevalence of SO according to TS was small, even using specific reference standards for elderly evaluation. However, it is important to consider the limitations of the method in light of the physiological changes of ageing. That is why it should be combined with other indicators that also evaluate body fat (18).

When considering central obesity as a diagnostic criterion for SO in the elderly, attention should be paid to the process of reconfiguration of body fat, characterized by increased adipose tissue in the abdominal region, especially in the visceral region (18). Different criteria for the classification of central adiposity have been applied in the elderly. Some studies use the lower cut-off point (WC ≥ 80 cm), whereas others use the upper cut-off point as a reference [WC ≥ 88 cm (4) or WC ≥ 85 cm (19)]. These differences in classification strongly influence the prevalence of the problem. In our study, the average WC was 92.4 cm. If the lower cutoff point (≥ 80 cm) was used as a reference, 89.2% of the sample would have had a diagnosis of central obesity.

Another method to diagnose obesity in the elderly is the use of the TBF% obtained by BIA. Studies have shown a good correlation of BIA with BMI, TS, and WC, and also with hydrostatic weighing and DEXA, the latter two being reference methods for assessing body composition. However, BIA might present some limitations that compromise the reliability of the method and the interpretation of its results (3,10). Changes inherent to the aging process might interfere with the results, and it is necessary to use validated and tested prediction equations, as well as specific cutoff points, both for fat and fat-free mass evaluation (2,9,14). The application of BIA as a method for SO diagnosis allows the estimation of fat and lean mass, making it possible to diagnose sarcopenia and obesity at the same time (8).

This study also found differences in the prevalence of SO among different defining criteria for sarcopenia. In general, a higher number of elderly women with SO were observed when sarcopenia was defined by low SMI and HS than when sarcopenia was diagnosed by a physical performance evaluation (low SMI and GS). This could be due to the physiological changes in skeletal muscle mass during the aging process, since the loss of muscle mass initially leads to loss of muscle strength and contributes to loss of mobility and functional capacity in elderly people. For this reason, a strategy to minimize its deleterious effects on the quality of life of older adults is to identify early reduction in muscle strength and the mechanisms involved (20,21).

Among the obese women diagnosed by at least one criterion, 22.7% presented a reduced SMI, a condition that can be defined as pre-sarcopenic obesity. Changes in muscle strength and performance were also observed, although there were no changes in SMI. These data become relevant when considering the complications of obesity on muscle tissue. Shimokata et al. (21) highlighted that an excess of body fat intensifies the infiltration of adipocytes into the muscle fibers of older adults, favoring a decrease in muscle strength. In addition, the overload caused by an excess of adipose tissue might decrease the capacity to generate muscular power, thus strongly interfering with the physical performance of the elderly.

In this study, the prevalence of severe sarcopenic obesity was 2.2% and no results were found in the literature to compare these findings to.

Our results suggest the necessity for proper diagnosis of sarcopenic obesity regardless of nutritional state. Thus, it is important to identify elderly people with obesity and muscle changes, mainly with functional and muscular volume impairment (pre-sarcopenia). This will contribute to early intervention (nutritional and physical activity), therefore reducing the chances of progression to SO, since the concurrent increase in the number of elderly people and the prevalence of sarcopenic obesity could increase fragility in this population. For a better accuracy of SO diagnosis, an association of multiple indicators should be considered. Studies with larger samples also containing elderly men are necessary for an evaluation of possible differences between both sexes.

REFERENCES

1. Batsis JA, Villareal DT. Sarcopenic obesity in older adults: aetiology, epidemiology and treatment strategies. Nat Rev Endocrinol 2018;(9):513-37. DOI: 10.1038/s41574-018-0062-9
2. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Age Ageing 2019;48(1):16-31. DOI: 10.1093/ageing/afy169
3. Johnson Stoklossa CA, Sharma AM, Forhan M, Siervo M, Padwal RS, Prado CM. Prevalence of Sarcopenic Obesity in Adults with Class II/III Obesity Using Different Diagnostic Criteria. J Nutr Metab 2017;2017:7307618. DOI: 10.1155/2017/7307618
4. Ethgen O, Beaudart C, Buckinx F, Bruyère O, Reginster JY. The Future Prevalence of Sarcopenia in Europe: A Claim for Public Health Action. Calcified tissue international 2017;100(3):229-34. DOI: 10.1007/s00223-016-0220-9
5. Cauley JA. An Overview of Sarcopenic Obesity. J Clin Densitom 2015;18(4):499-505. DOI: 10.1016/j.jocd.2015.04.013

6. Silva AO, Karnikowski MG, Funghetto SS, Stival MM, Lima RM, de Souza JC, et al. Association of body composition with sarcopenic obesity in elderly women. Int J Gen Med 2013;6:25-9. DOI: 10.2147/IJGM.S36279
7. Gadelha AB, Dutra MT, Oliveira RJ, Safons MP, Lima RM. Associação entre força, sarcopenia e obesidade sarcopénica com o desempenho funcional de idosas/Association among strength, sarcopenia and sarcopenic obesity with functional performance in older women. Motricidade 2014;10(3):31-9. DOI: 10.6063/motricidade.10(3).2775
8. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39(4):412-23. DOI: 10.1093/ageing/afq034
9. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc 2002;50:889-96. DOI: 10.1046/j.1532-5415.2002.50216.x
10. Kyle UG, Bosaeus I, De Lorenzo AD, et al. Composition of the ESPEN Working Group. Bioelectrical impedance analysis–part I: a review of principles and methods. Clinical nutrition 2004;23(5):1226-43. DOI: 10.1016/j.clnu.2004.06.004
11. Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, et al. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol 2003;95:1851-60. DOI: 10.1152/japplphysiol.00246.2003
12. OPAS - ORGANIZACIÓN PANAMERICANA DE LA SALUD. División de Promoción y Protección de la Salud (HPP). XXXVI Reunión del Comité Asesor de Investigaciones en Salud — Encuestra Multicéntrica — Salud Bienestar y Envejecimiento (SABE) en America Latina y el Caribe — Informe preliminar. Washington, D.C. 2001.
13. World Health Organization. Obesity: preventing and managing the total epidemic. Report of a WHO Consultation Group. Geneva: WHO, 1997.
14. Baumgartner R. N. Body composition in healthy aging. Ann NY Acad Sci 2000;904:437-48. DOI: 10.1111/j.1749-6632.2000.tb06498.x
15. Kuczmarski MF, Kuczmarski RJ, Najjar M. Descriptive anthropometric reference data for older Americans. J Am Diet Assoc 2000;100:59-66. DOI: 10.1016/S0002-8223(00)00021-3
16. Chung JY, Kang HT, Lee DC, Lee HR, Lee YJ. Body composition and its association with cardiometabolic risk factors in the elderly: A focus on sarcopenic obesity. Archives of Gerontology and Geriatrics 2013;56(1):270-8. DOI: 10.1016/j.archger.2012.09.007
17. Iozzo P, Rossi G, Michelassi C, Landi P, Carpeggiani C. Interpretation of the "obesity paradox": 30-year study in patients with cardiovascular disease. Int J Cardiol 2013;168:112-6. DOI: 10.1016/j.ijcard.2012.09.061
18. Zamboni M, Mazzali G. Obesity in the elderly: an emerging health issue. International Journal of Obesity 2012;36(9):1151-2. DOI: 10.1038/ijo.2012.120
19. Sanada K, Chen R, Willcox B, Ohara T, Wen A, Takenaka C, et al. Association of sarcopenic obesity predicted by anthropometric measurements and 24-y all-cause mortality in elderly men: The Kuakini Honolulu Heart Program. Nutrition 2018;46:97-102. DOI: 10.1016/j.nut.2017.09.003
20. Shao A, Campbell W, Oliver Chen CY, Mittendorfer B, et al. The emerging global phenomenon of sarcopenic obesity: Role of functional foods; a conference report. Journal of Functional Foods Volume;33:244-50. DOI: 10.1016/j.jff.2017.03.048
21. Shimokata H, Shimada H, Satake S, Endo N, Shibasaki K, et al. Chapter 2 Epidemiology of sarcopenia. Geriatr Gerontol Int 2018;18(Suppl 1):13-22. DOI: 10.1111/ggi.13320

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Nutrición en el anciano

Consistencies and terminologies – the use of the International Dysphagia Diet Standardization Initiative

Consistencias y terminologías: el uso de la Iniciativa Internacional de Estandarización de la Dieta para la Disfagia

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Abstract

Introduction: this study aimed to verify the ability of speech therapists to identify, sort and name the different consistencies used in neurogenic oropharyngeal dysphagia (NOD) management, and to compare the results with the terms proposed by the International Dysphagia Diet Standardization Initiative (IDDSI).

Methods: this research was approved by the ethics committee. Sixty speech therapists who work with NOD patients sorted 5 commercial foods from thinnest to thickest to match IDDSI levels 0 to 4, and then used a term to designate each consistency.

Results: most subjects (76.66%) sorted the foods properly. Terminologies were divergent at all levels. For level 0, practitioners assigned 3 different terms. For level 1, 24 different terms were reported; for level 2 there were 25 terms, 23 terms for level 3, and 18 terms for level 4. Level 0 (IDDSI - thin) was designated by most participants as liquid; level 1 (IDDSI - slightly thick) was referred to as semi-thickened liquid; level 2 (IDDSI - mildly thick) as thickened liquid; level 3 (IDDSI - moderately thick) as honey; and level 4 (IDDSI - extremely thick) as pasty by most subjects. A reduced number of participants used terms in accordance with IDDSI. Level 0 was appropriately named by 5 subjects (8.33%); levels 1, 2 and 4 by 2 practitioners each (3.33%); and level 3 by 1 professional (1.66%). None of the subjects named all 5 IDDSI levels correctly.

Conclusion: most practitioners progressed consistencies properly. There was a diversity of terminologies used for the same consistency at all levels, with no standardization.

Key words:

Deglutition. Deglutition disorders. Terminology. Viscosity. Speech therapy.

Resumen

Introducción: este estudio tuvo como objetivo verificar la capacidad de los logopedas para identificar, clasificar y nombrar las diferentes consistencias utilizadas en el manejo de la disfagia orofaríngea neurogénica (NOD) y comparar los resultados con los términos propuestos por la Iniciativa Internacional de Estandarización de la Dieta para la Disfagia (IDDSI).

Métodos: esta investigación fue aprobada por el comité de ética. Sesenta terapeutas del habla que trabajan con pacientes de NOD clasificaron 5 alimentos comerciales, desde los más finos hasta los más gruesos, coincidiendo con los niveles 0 a 4 de la IDDSI; luego, debían nombrar cada consistencia.

Resultados: la mayoría de los sujetos (76,66%) clasificaron correctamente las consistencias. Las terminologías fueron divergentes en todos los niveles. Para el nivel 0, los participantes asignaron 3 términos diferentes. Para el nivel 1 usaron 24 términos diferentes, 25 términos para el nivel 2, 23 para el nivel 3 y 18 para el nivel 4. La consistencia del nivel 0 (IDDSI: fina) fue nombrada por la mayoría de los participantes como líquida; la del nivel 1 (IDDSI: ligeramente espesa) la denominaron líquida semi-espesada; la del nivel 2 (IDDSI: poco espesa) como líquida espesada; la del nivel 3 (IDDSI: moderadamente espesa) como miel, y la del nivel 4 (IDDSI: extremadamente espesa) como pastosa. Un número reducido de participantes emplearon términos coincidentes con los de la IDDSI. El nivel 0 fue nombrado correctamente por 5 sujetos (8,33%), los niveles 1, 2 y 4 por 2 participantes cada uno (3,33%), y el nivel 3 por 1 profesional (1,66%). Ninguno de los sujetos nombró correctamente los 5 niveles de la IDDSI.

Conclusión: la mayoría de los participantes ordenaron correctamente la progresión de las consistencias. Hubo diversidad en las terminologías utilizadas para una misma consistencia en todos los niveles, sin estandarización alguna.

Palabras clave:

Deglución. Trastornos de la deglución. Terminología. Viscosidad. Terapia del habla.

Author´s contribution: All authors have read, approved and made substantial contributions for the manuscript.

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INTRODUCTION

Swallowing is a complex process that depends on the integrity of various physical structures and aims to transport food from the oral cavity to the stomach without penetration into the airways (1). Any change that hinders swallowing safety and efficiency is classified as dysphagia, recognized by the World Health Organization within the symptoms related to the digestive system (1-3). In the general population, the prevalence of neurogenic oropharyngeal dysphagia (NOD) varies from 2% to 16%, with values above 40% in hospitalized patients (2-4). Although it may occur at any age, the highest prevalence of oropharyngeal dysphagia is found in the elderly, where it may be permanent or transient (4). Risk factors include use of medications, tracheostomy, previous orotracheal intubation, head and neck surgery, and neurological disorders such as Parkinson's disease, Alzheimer's disease, neurodegenerative diseases, and stroke (5,6). Dysphagia, regardless of etiology, leads to severe consequences such as malnutrition, significant weight loss, aspirative pneumonia, and mortality (6,7).

Speech therapy aims to minimize the complications of OD and includes the definition of a safe feeding path (8), as well as the modification of food characteristics such as texture and consistency (9,10). Liquids are associated with laryngeal penetration (11), and to promote safe and efficient swallowing homogeneous and thick diets are recommended (9). Thickened beverages compensate deficits and reduce aspiration risk (2,3,12-16). However, increased viscosity renders oral and pharyngeal transit longer (2,9), increases the risk for food residues (2,10,15), and demands greater tongue pressure when swallowing (2,10,17). Liquids must be thickened to a specific viscosity to improve swallowing safety for each patient, since very thin liquids can be as detrimental as excessively thickened ones (18) and a correct selection depends on evaluation findings (19).

Currently, it is understood that a standardization of terminology to identify consistencies is relevant to guarantee the efficiency of treatment (3,20-22). Internationally, several standardized terminologies are used (23-26), most commonly the National Dysphagia Diet (NDD) (27) and International Dysphagia Diet Standardization Initiative (IDDSI) (28). The NDD was published in 2002 by the American Dietetic Association in order to establish a standard terminology and the practical applications of dietary texture modification for dysphagia; it includes 4 levels for liquid foods (27). The IDDSI was proposed in 2016 with the aim of developing a globally standardized terminology to describe food consistencies as used for individuals with dysphagia. It includes 8 consistency levels and proposes simple methods of measuring consistency using a syringe, fork and spoon (28).

Lack of standardization in consistency nomenclature generates risks to the patient (3,20,29). The viscosity of thickened liquids is often judged subjectively and described using terms such as syrup and honey (29). Prescriptions involving viscosity and texture should allow efficient communication between professionals (3,20,29).

Speech therapists ought to know and use a standard viscosity nomenclature, otherwise their practice may generate risks to their patients. Accordingly, the present study aims to assess the ability of speech therapists to identify, sort, and name the different consistencies used in NOD management, and to compare the results with the terms proposed by the Dysphagia Diet Standardization Initiative (IDDSI).

METHOD

This was a cross-sectional, descriptive and analytical study. It was approved by the institution's Ethics Committee (2.490.627). The sample consisted of speech therapists who work with neurogenic oropharyngeal dysphagia (NOD) patients. These professionals were contacted by e-mail, by phone and in person. A total of 114 participants were contacted and invited, and 65 accepted to take part. As inclusion criteria for this study, the participants had to work with NOD patients. Participants who would not fill out the questionnaire or who later stated that they did not exactly work with NOD patients were excluded.

Data were collected at their workplace. The participants were informed of the study's aims and provided a signed consent to participate. The questionnaire assessed sample characteristics such as age, gender, work with NOD patients or otherwise, timing of professional activity with dysphagia, workplace, and population served.

The sorting and naming tasks were initially explained to each participant, and the 5 foods presented simultaneously in small portions arranged in colored disposable cups, but not in increasing or decreasing order of consistency. The participants were instructed to sort these foods from thinnest to thickest viscosity, and to write in blank spaces the terms they would use to describe the consistencies presented. The materials available to participants were watercolor pens (green, blue, purple, grey, and pink), a 10 mL syringe without needle or plunger, a stopwatch, spoons and forks. Participants were allowed to manipulate the samples if they wanted to. Five levels were considered, from 0 to 4. To ensure consistent presentation of same viscosities, only industrial products were used. These were: mate tea (Chá Mate Leão®) for level 0; mango juice (Summer Fruit®) for level 1; strawberry-flavored yogurt (Itambé®) for level 2; chocolate syrup (Ice Cream®) for level 3; and strawberry-flavored yogurt (Danoninho®) for level 4. Each beverage was previously assigned a level using the IDDSI method with a syringe and stopwatch (30). After completing the questionnaire participants received an IDDSI primer in order to encourage the use of IDDSI standardization in clinical practice.

RESULTS

Sixty-five questionnaires were analyzed to characterize the sample. A total of 5 participants were excluded because they did not work with neurogenic oropharyngeal dysphagia. The sample, therefore, was composed of 60 participants. From this total, 33 (55%) participants reported they worked with NOD patients, and 27 (45%) mentioned they worked with both NOD and mechanic oropharyngeal dysphagia patients. Ages varied from 21 to 54 years, with an average of 33.8 years. They were mostly

female therapists – 56 (93.3%), whereas 4 (6.6%) were male. The duration of their practicing with NOD patients varied from 1 month to 20 years, with an average of 5 years and 4 months. A higher concentration of participants was observed between 3 and 4 years of practice (31.66%). Most of them (48.33%) worked only in one workplace, 45.07% in two workplaces, and 6.60% in three workplaces.

Home care was the main workplace described (61.66%), followed by hospitals (48.33%). The population served varied, but the greatest demand was in the care of elderly individuals (73.33%).

There were no difficulties in identifying the viscosity for level 0. Most speech therapists (76.66%) identified and sorted the consistencies from 0 to 4, from thinnest to thickest, correctly.

Table I shows the viscosity sorting data, from thinnest to thickest. Most participants (49, 81.66%) properly sorted levels 1 and 2. Levels 3 and 4 were sorted properly by 57 (95%). It is important to notice that the number of incorrect sortings decreased as consistency level increased.

Table II lists the terminologies used to describe food viscosity. Concerning the terminology used by speech therapists, there was agreement between 45 participants (75%) on the terminology used to designate level 0. For level 1, 24 different terms were presented; for level 2 there were 25 terms; for level 3 there were 23 terms; and for level 4 the participants used 18 terms. In the analysis, the terminologies used were grouped together based on similarity, as shown in table II. The findings show that different terminologies are used to describe the same viscosity.

Level 0 (IDDSI - thin) was named by most participants as liquid; level 1 (IDDSI - slightly thick) was referred to as semi-thickened liquid; level 2 (IDDSI - mildly thick) was described as thickened liquid; level 3 (IDDSI - moderately thick or liquidized) was named as honey, and level 4 (IDDSI - extremely thick or puréed) was termed pasty by most subjects. A reduced number of participants used terms in accordance to IDDSI – level 0 by 5 subjects (8.33%); levels 1, 2 and 4 by 2 professionals each (3.33%); and level 3 by 1 therapist alone (1.66%). None of the subjects named all 5 IDDSI levels correctly.

Table I. Analysis of the sorting of food consistencies from thinnest to thickest

Levels	Correct n (%)	Incorrect n (%)
0	60 (100)	0 (0)
1	49 (81.66)	11 (18.34)
2	49 (81.66)	11 (18.34)
3	57 (95)	3 (5)
4	57 (95)	3 (5)

DISCUSSION

Regarding the characterization of the sample, the results indicate that most speech therapists (61.66%) worked in home care. Home care was incorporated in Brazil in the 1980s, its guidelines focused on health promotion, conservation and rehabilitation in order to guarantee the health of the population (31). The inclusion of speech-language therapists in home care services is still recent, which explains the shortage of computations aimed at measuring the performance of these professionals (32).

In relation to the population served, the greatest demand for speech therapists is in the care of the elderly (73.33%). Researchers have pointed out that the older the age, the higher the incidence of dysphagia (7). Some studies conclude that it may be associated with anatomical and physiological modifications that promote the risk of disorders in the swallowing process (10). It is important also to consider the increase in this segment of the population, since the number of elderly people is about to exceed the number of people under five years of age (31). As the proportion of elderly people is increasing throughout the country, the high demand of speech therapists for health services is justified (33,34).

When analyzing the ability to sort the presented consistencies, most of the subjects performed the food progression properly, from thinnest to thickest. It was possible to infer that food visualization side by side facilitated sorting the food viscosity. A correct food viscosity identification is extremely relevant as it allows professionals to select the appropriate level to be used in each case (23).

Regarding the terminologies used by the speech therapists, the present study found a great diversity among the participants. Divergence in nomenclature could be seen at all levels, especially at level 2, which collected 25 different terms. The absence of standardization to guide both the preparation and naming of food consistencies results in a variety of nomenclatures in clinical practice (3,20,21,29), whereas a unified terminology provides patient safety and treatment efficiency (3,20,22). It is described in the literature that different consistencies result in crucial changes in the physiology of swallowing, such as reduced risk for aspiration (2,3,12-16). However, they may interfere with oral and pharyngeal transit time (2,9), and may be associated with food stasis (2,9,15) and with changes in the tongue force required for ejection of the bolus (2,10,17).

Diversity in terminology may make it difficult for other professionals, patients, or caregivers to understand and obtain the desired consistence. The extant lack of agreement in nomenclature among professionals, as evidenced by this research, may lead to different interpretations of food consistency prescriptions and to health damage for patients (3,20,29).

The modification of food characteristics such as texture and consistency (9,10) is one of the responsibilities of speech therapists in dysphagia rehabilitation, and a proper use of the available terminology is essential for professionals in this setting. Due to the diversity of terms found in this research, we supposed that most of the professionals participating in the study were unaware of IDDSI.

Table II. Terminologies used for food consistencies

Levels	Number of terms	Terms	Subjects
Level 0	3	Liquid	45
		Thin liquid	5
		Fine liquid	10
Level 1	24	Liquid *(liquid, thin liquid)*	13
		Semi-thickened liquid *(semi-thickened liquid, slightly thickened liquid, thickened liquid, very slightly thickened, slight thickening, slightly thick, thin thickened liquid, lightly thickened liquid, thick liquid, slightly thickened, semi-liquid)*	22
		Thickened liquid *(thickened liquid, coarse liquid, very thickened liquid)*	6
		Nectar *(nectar, thickened liquid nectar, liquid nectar)*	10
		Honey *(honey, almost honey)*	3
		Thin pasty *(thin pasty, pasty liquid, thin pasty liquid)*	6
Level 2	25	Liquid *(liquid, thin liquid)*	7
		Semi-thickened liquid *(semi-thickened liquid, semi-liquid, slightly thick, slightly thick liquid, little condensed liquid, lightly condensed liquid, very lightly thickened)*	9
		Thickened liquid *(thickened liquid, moderately thickened liquid, pasty liquid, extremely thickened liquid, moderately thickened, medium thickened, thickened liquid, coarse liquid, thick)*	22
		Nectar *(nectar, liquid nectar)*	11
		Honey *(honey, thickened liquid honey, liquid honey)*	6
		Thin pasty *(thin pasty, fine pasty)*	5
Level 3	23	Pasty liquefied *(pasty liquefied, liquefied)*	2
		Thickened liquid *(thickened liquid, moderately thickened liquid, thick liquid, coarsened liquid, thick, moderately thickened)*	6
		Nectar *(nectar, liquid nectar, pasty nectar)*	5
		Honey *(honey, liquid honey, pasty like honey, thin pasty honey)*	25
		Pasty *(pasty, thin pasty, semi-pasty, coarse pasty liquid, pasty liquid, medium pasty)*	19
		Pudding *(pudding, thickened liquid pudding)*	3
Level 4	18	Extremely thickened	2
		Pasty *(pasty, coarse pasty, liquid pasty, homogeneous pasty, pasty firm, pasty exclusive, semi-pasty, pasty like yogurt, purée, pasty purée, smooth purée)*	45
		Homogeneous	1
		Pudding *(pudding, liquid pudding, pasty pudding)*	10
		Solid *(solid, pasty solid)*	2

CONCLUSIONS

The professionals who took part in the study were assertive in sorting the progression of food from thinnest to thickest. The research evidenced the diversity of terminologies that speech therapists working with neurologic oropharyngeal dysphagia patients currently use. In clinical practice this fact represents a risk for patients, since it could lead to misunderstandings and errors in communication between professionals, patients and caregivers, to wrong or incomplete prescriptions, and to incorrect management of food consistency. Comparing the nomenclature proposed by IDDSI with those used by our professionals, there was disagreement between them. The study presented limitations due to the reduced number of participants. Therefore, it highlights the need for further research, aiming to check out the use of a unified terminology.

REFERENCES

1. Resende P, Dobelin J, Oliveira I, Luchesi K. Disfagia orofaríngea neurogênica: análise de protocolos de videofluoroscopia brasileiros e norte-americanos. Rev CEFAC 2015;17(5):1610-9. DOI: 10.1590/1982-021620151754315.
2. Newman R, Vilardell N, Speyer R. Effect of bolus viscosity on the safety and efficacy of swallowing and the kinematics of the swallow response in patients with oropharyngeal dysphagia: white paper by the european society for swallowing disorders (ESSD). Dysphagia 2016;31:232-49. DOI: 10.1007/s00455-016-9696-8.
3. Cichero JAY, Steele C, Duivestein J, Clavé P, Kayashita J, Dantas R, et al. The need for international terminology and definitions for texture-modified foods and thickened liquids used in Dysphagia management: Foundations of a Global Initiative. Curr Phys Med Rehabil Reports 2013;1:280-91. DOI: 10.1007/s40141-013-0024-z.
4. Andrade P, Santos C, Firmino H, Rosa C. Importância do rastreamento de disfagia e da avaliação nutricional em pacientes hospitalizados. Inst Isr Ensino e Pesqui Albert Einstein 2018;16(2):1-6.
5. Paiva K, Xavier I, FariaS N. Aging and dysphagia: a public health issue. J Againg Innov [Internet]. 2013; Available from: http://journalofagingandinnovation.org/pt/tag/epidemiologia-da-disfagia/
6. Jotz GP, De Angelis E. Definição de disfagia. Incidência e prevalência – passado, presente e futuro. In: Disfagia: Abordagem clínica e cirúrgica - criança, adulto e idoso. 1st ed. Rio de Janeiro: Elsevier; 2017. p. 1-4.
7. Alves ICF, Andrade CRF de. Mudança funcional no padrão de deglutição por meio da realização de exercícios orofaciais. CoDAS [Internet] 2017;29(3). Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S2317-17822017000300308&lng=pt&tlng=pt. DOI: 10.1590/2317-1782/20172016088.
8. Inaoka C, Albuquerque C. Efetividade da intervenção fonoaudiológica na progressão da alimentação via oral em pacientes com disfagia orofaríngea pós AVE. Rev CEFAC 2014;16(1):187-96. DOI: 10.1590/1982-0216201413112.
9. Silva R, Luchesi K, Furkim A. Programas de intervenção fonoaudiológica para disfagia orofaríngea neurogênica em adultos. In: Manual prático de disfagia diagnostico e tratamento. 1st ed. Rio de Janeiro: Revinter; 2017. p. 279-93.
10. Dornelles S, Jotz GP, Swartz K, Rozenfeld M. Distúrbios da deglutição no adulto e no idoso. In: Disfagia: Abordagem clínica e cirúrgica - criança, adulto e idoso. 1st ed. Rio de Janeiro: Elsevier; 2017. p. 129-58.
11. Pires E, Sassi F, Mangilli L, Limongi S, Andrade C. Alimentos na consistência líquida e deglutição: uma revisão crítica de literatura. Rev Soc Bras Fonoaudiol 2012;17(4):482-8. DOI: 10.1590/S1516-80342012000400020.
12. Queiroz C, Barros S, Borgo H, Marino V, Dutka J. Viscosidade e qualidade da imagem do líquido espessado para videofluoroscopia de deglutição com acréscimo do contraste de bário. Rev CEFAC 2015;17(3):873-89. DOI: 10.1590/1982-021620155614.
13. Choi K, Ryu J, Kim M, Kang J, Yoo S. Kinematic analysis of Dysphagia: significant parameters of aspiration related to bolus viscosity. Dysphagia 2011;26:392-8. DOI: 10.1007/s00455-011-9325-5.
14. Clavé P, Kraa M, Arreola V, Girvent M, Farré R, Palomera E, et al. The effect of bolus viscosity on swallowing function in neurogenic Dysphagia. Aliment Pharmacol Ther 2006;24:1385-94. DOI: 10.1111/j.1365-2036.2006.03118.x.
15. Hind J, Divyak E, Zielinski J, Taylor A, Hartman M, Gangnon R, et al. Comparison of standardized bariums with varying rheological parameters on swallowing kinematics in males. Rehabil Res Dev 2012;49(9):1399-404. DOI: 10.1682/JRRD.2011.09.0180.
16. Leonard R, White C, Mckenzie S, Belafsky P. Effects of bolus rheology on aspiration in patients with dysphagia. J Acad Nutr Diet 2014;114(4):590-4. DOI: 10.1016/j.jand.2013.07.037.
17. Steele CM, Molfenter SM, Péladeau-Pigeon M, Polacco RC, Yee C. Variations in tongue-palate swallowing pressures when swallowing xanthan gum-thickened liquids. Dysphagia [Internet] 2014;29(6):678-84. Available from: http://link.springer.com/10.1007/s00455-014-9561-6. DOI: 10.1007/s00455-014-9561-6.
18. Garcia JM, Chambers E, Matta Z, Clark M. Viscosity measurements of nectar- and honey-thick liquids: product, liquid, and time comparisons. Dysphagia 2005;20:325-35. DOI: 10.1007/s00455-005-0034-9.
19. Garin N, de Pourcq JT, Cardona D, Martín-Venegas R, Gich I, Cardenete J, et al. Cambios en la viscosidad del agua con espesantes por la adición de fármacos altamente prescritos en geriatría. Nutr Hosp [Internet] 2012;27(4):1298-303. Available from: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0212-16112012000400049&lng=es&nrm=iso&tlng=es.
20. Amaral ACF, Rodrigues LA, Furlan RMMM, Vicente LCC, Motta AR. Fonoaudiologia e nutrição em ambiente hospitalar: análise de terminologia de classificação das consistências alimentares. CoDAS [Internet] 2015;27(6):541-9. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S2317-17822015000600541&lng=pt&tlng=pt. DOI: 10.1590/2317-1782/20152015059.
21. Steele CM, Alsanei WA, Ayanikalath S, Barbon CEA, Chen J, Cichero JAY, et al. The Influence of Food Texture and Liquid Consistency Modification on Swallowing Physiology and Function: A Systematic Review. Dysphagia 2015;30(1):2-26. DOI: 10.1007/s00455-014-9578-x.
22. Zargaraan A, Rastmanesh R, Fadavi G, Zayeri F, Mohammadifar MA. Rheological aspects of dysphagia-oriented food products: A mini review. Food Sci Hum Wellness [Internet] 2013;2(3-4):173-8. Available from: http://dx.doi.org/10.1016/j.fshw.2013.11.002. DOI: 10.1016/j.fshw.2013.11.002.
23. Joint T, Group W. National Descriptors for Texture Modification. Br Diet Assoc R Coll Speech Lanuage Ther 2003.
24. Atherton M, Bellis-Smith N, Cichero J, Suter M. Texture-modified foods and thickened fluids as used for individuals whith dysphagia: Australian standardized labels and definitions. Nutr Diet 2007;64(2):53-76.
25. Ministry of Health Labour and Welfare. Food for special dietary uses. Japonese Govrnment. 2009.
26. Institute I& IN and D. Irish consistency descriptors for modified fluids and food. 2009.
27. Mccullough G, Pelletier C, Steele C. The Asha Leader 2003;8:16-27. Available from: https://www.asha.org/SLP/clinical/dysphagia/Dysphagia-Diets/. DOI: 10.1044/leader.FTR3.08202003.16.
28. Martineau C. International Dysphagia Diet Standardisation Initiative: IDDSI Framework. Med des Mal Metab 2015;13(1):101-2.
29. De Sordi M, Mourão L, Silva L. Comportamento reológico e nomenclatura dos alimentos utilizados por fonoaudiólogos de serviços de disfagia. Rev CEFAC 2012;14(5):925-32. DOI: 10.1590/S1516-18462011005000145.
30. Cichero J. IDDSI Framework - Testing Methods 2017;1-12. Available from: www.iddsi.org
31. Fonseca T, Loiola R, Coelho E. Atuação fonoaudiológica no atendimento domiciliar. Rev Tecer 2015;14(8):38-51. DOI: 10.15601/1983-7631/rt.v8n14p38-51.
32. Silva S, Musse R, Nemr K. Assistência domiciliar na cidade de Salvador-BA: possibilidade de atuação fonoaudiológica em motricidade orofacial. Rev CEFAC 2009;11(1):94-101. DOI: 10.1590/S1516-18462009005000001.
33. Goes V, Carpes P, Oliveira L, Hack J, Magro M, Bonini J. Avaliação do risco de disfagia, estado nutricional e ingestão calórica em idosos com Alzheimer. Rev Latino-Am Enferm 2014;22(2):317-24. DOI: 10.1590/0104-1169.3252.2418.
34. Maneira A, De Lima Zanata I. A frequência de disfagia em idosos em um hospital da cidade de Curitiba-PR. Rev Saúde Pública do Paraná [Internet] 2018;1(1):20-6. Available from: http://revista.escoladesaude.pr.gov.br/index.php/rspp/article/view/36. DOI: 10.32811/2595-4482.2018v1n1.36.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Veinticinco años de cruce duodenal. Cómo cambiar al cruce

Twenty-five years of duodenal switch. How to switch to the duodenal switch

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Resumen

Antecedentes: el cruce duodenal (CD) es un procedimiento que combina una gastrectomía vertical (GV) más una derivación biliopancreática (DBP).

Objetivos: informar de nuestra experiencia en 950 CD consecutivos en pacientes con obesidad mórbida (OM) realizados de 1994 a 2011 y con 27 años de seguimiento.

Entorno: mezcla de enseñanza e institución privada en un hospital comarcal de España.

Métodos: revisión retrospectiva de 950 pacientes consecutivos con obesidad mórbida tratados con cirugía de CD.

Resultados: se realizaron 518 CD abiertos (CDA) y 432 CD laparoscópicos (CDL). La mortalidad operatoria fue del 0,84% (1,38% en CDA y 0,38% en CDL). El 4,84% tuvo una fuga, dos tuvieron insuficiencia hepática (0,2%) y la desnutrición estuvo presente en el 3,1%. A los cinco años, el porcentaje de sobrepeso perdido (PSP) de índice de masa corporal (IMC) fue del 80% y el porcentaje de pérdida esperada de IMC fue más del 100%.

Conclusiones: el CD es la técnica bariátrica más agresiva pero con mejor pérdida de peso a largo plazo. Se describen las complicaciones operatorias y pautas de seguimiento a largo plazo.

Palabras clave:

Obesidad mórbida. Cruce duodenal. Cirugía bariátrica. Gastrectomía y desviación pancreática biliar. Pérdida de peso.

Abstract

Background: the duodenal switch (DS) is a procedure that combines a vertical gastrectomy (VG) plus a biliopancreatic diversion (BPD).

Objectives: to report our experience in 950 consecutive DS patients with morbid obesity (MO) performed from 1994 to 2011, with 27 years of follow-up.

Environment: mix of teaching and private institution in a regional hospital in Spain.

Methods: retrospective review of 950 consecutive morbidly obese patients treated with DS surgery.

Results: five hundred and eighteen open DS (ODS) and 432 laparoscopic DS (LDS) were performed. Operative mortality was 0.84% (1.38% in ODS and 0.38% in LDS); 4.84% had one leak, two had liver failure (0.2%) and malnutrition was present in 3.1%. At five years, the body mass index (BMI) percentage of lost overweight (%EWL) was 80% and the percentage of expected BMI loss was more than 100%.

Conclusions: the DS is the most aggressive bariatric technique but with the best long-term weight loss. Operative complications and long-term follow-up guidelines are described.

Key words:

Morbid obesity. Duodenal cross. Bariatric surgery. Gastrectomy and biliary pancreatic diversion. Weight loss.

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INTRODUCCIÓN

La cirugía del cruce duodenal (CD) consta de dos operaciones, gastrectomía vertical (GV) más derivación biliopancreática (DBP). Es la técnica más compleja en cirugía bariátrica por obesidad mórbida (OM). El CD combina la restricción de la ingesta de alimentos y la malabsorción en el intestino delgado. Scopinaro comenzó la DBP en 1976 (1).

Hess (2) describe cómo: a) la GV elimina la curvatura mayor gástrica, reduce el volumen gástrico y la ingesta, y permite un vaciado normal; y b) deriva la ingesta post-píloro desde duodeno a íleon, DBP, para causar malabsorción.

Hess (3) recomienda medir todo el intestino delgado, sin tensión, desde Treitz hasta válvula ileocecal y utiliza el 50% de su longitud proximal como asa biliopancreática (ABP), el 10% distal como asa común (AC) y el 40% intermedio como asa alimentaria (AA).

Marceau (4,5) hacía DBP estándar hasta 1991 y cambió al CD y es el primer autor que publica (6) en 1993 la *gastrectomía parietal más DBP*.

Lagacé (7) informó sobre los primeros buenos resultados del CD en 61 pacientes en 1995 y Marceau comparó en 1998 (8) 252 DBP con gastrectomía distal y 465 CD con una mortalidad operatoria del 1,7%.

Hess (9) y Baltasar (10-17) describen la parte gástrica de la operación como *gastrectomía vertical* (GV) y creación de un *tubo gástrico* (TG). Anthone (18) y Almogy (19) lo llamaron *gastrectomía longitudinal* y Rabkin (20), *gastrectomía de la curvatura mayor*.

El CD (21-26) se estandarizó en los años 90 (Fig. 1). Hess (9) modificó el procedimiento invaginando y suturando la serosa de la GV en los siguientes 188 casos para reducir la incidencia de fugas en la línea de grapas. Ren (27) hizo el *primer CDL completo* en julio de 1999 y Baltasar (28) realizó el *primer CDL en Europa*

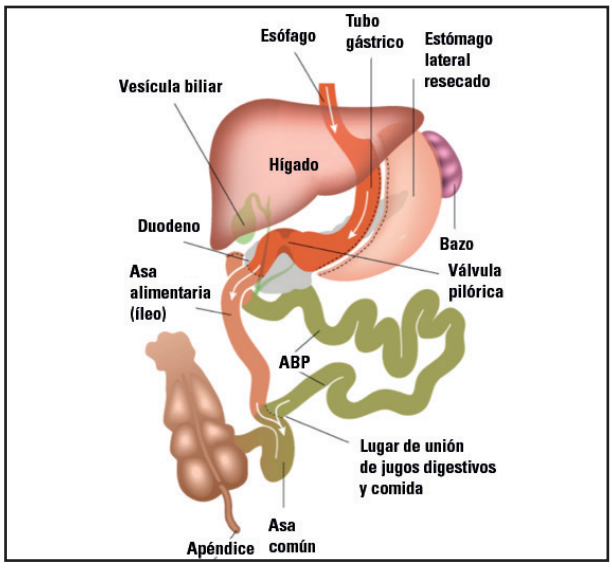

Figura 1.
Cruce duodenal = GV + DBP.

en el año 2000 (29). Paiva (30) en Brasil y Scopinaro (31) en Italia hacen en el año 2000 la *primera DBP laparoscópica* estándar.

Para medir resultados del peso, se usa el índice de masa corporal (IMC = kg/m^2) de Quetelet, pero después de revisar 7.410 pacientes, nuestro matemático desarrolló el concepto de *IMC predictivo* (32) tomando como control un IMC inicial superior a 25 (IMCI; 25 sería el de un peso ideal) y hace el cálculo no desde el IMCI sino desde el *IMCI en exceso* de 25. Los porcentajes de pérdida de sobrepeso perdido (PSP) no son iguales en un sujeto con OM grado 2 que en un sujeto con obesidad triple, y de esta forma solo medimos el IMC en exceso de 25. El porcentaje de pérdida de peso en exceso sería entonces del IMC predictivo = IMCI x 0.4 + 11,75. Este concepto ha sido ya utilizado por otros (33) de forma positiva.

TÉCNICA OPERATORIA

Cruce duodenal abierto (CDA) por laparotomía

El paciente está en posición forzada de Trendelenburg. La operación la realizan tres cirujanos a través de una incisión supraumbilical transversa entre ambos márgenes costales (Fig. 2A y B). Ya en el abdomen, se seccionan los ligamentos redondo y falciforme y se extirpan la vesícula biliar y el apéndice.

Se mide todo el intestino empezando por distal, desde la válvula ileocecal, y se marca con un clip el *asa común* (AC) como 10% del intestino. El *asa alimentaria* (AA) corresponde al 40% del intestino más proximal y se divide con una grapadora lineal. El 50% más proximal es el *asa biliopancreática* (ABP) y empieza en el duodeno proximal, D1. Se empalma el AA distal a la unión ABP y AC por una anastomosis yeyuno-ileal (AYI) con sutura absorbible continua monoplano y se cierra el defecto mesentérico con una sutura no reabsorbible.

Se expone el estómago y se introduce una sonda nasogástrica de 12 mm como guía a la curvatura menor. Se devascularíza *toda* la curvatura mayor gástrica con bisturí ultrasónico desde *3 cm distal al píloro* hasta el ángulo de His. Se divide secuencialmente el estómago con grapadoras desde el píloro hasta la unión esofagogástrica y se extirpa incluyendo la curvatura gástrica mayor. En curvatura menor queda el tubo gástrico (TG), que se refuerza con sutura invaginante continua y que incluye el epiplón separado y ambas paredes gástricas, evitando su torsión y fugas.

Se crea un túnel retroduodenal, distal a la arteria gástrica derecha, y se divide duodeno en D1 con grapadora lineal. Una sutura invertida refuerza el muñón duodenal.

El *AA proximal* pasa retrocólica por la derecha y se realiza una anastomosis duodeno-ileal (ADI) en sutura continua reabsorbible. La operación tiene cuatro líneas de sutura (refuerzo gástrico, ADI, AYR y el muñón duodenal distal). Se colocan dos drenajes, uno al lado del TG y otro en la ADI.

La incisión abdominal se cierra en dos planos con Maxon continuo. Tras perder peso, la longitud de la cicatriz se reduce en un tercio (Fig. 2B) y permite a la abdominoplastia alcanzar el área púbica (Fig. 2C). Iniciamos el CDA el 17 de marzo de 1994 y el tiempo quirúrgico medio fue de 91 minutos.

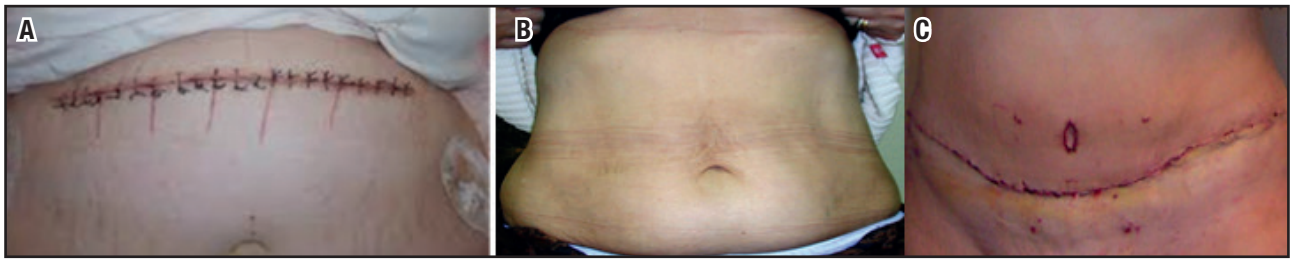

Figura 2.
A. Incisión. B. Cicatriz invisible. C. Dermolipectomía suprapúbica.

Cruce duodenal laparoscópico (CDL)

Se realiza también por un equipo de tres cirujanos. Se usan seis puertos. Un trocar óptico de Ethicon # 12 ingresa al abdomen, bajo visión, en el borde lateral del músculo recto derecho, a tres traveses de dedo y por debajo del margen costal, y es el puerto principal de trabajo. Un puerto supraumbilical de 10 mm se usa para la cámara en la línea media (Fig. 3). El resto de cuatro trocares de 5 mm son tipo Ternamian, que no se deslizan. Colocamos dos subcostales situados a derecha e izquierda, uno en el hipocondrio izquierdo y otro en el epigastrio utilizado para retraer el hígado. El resto del procedimiento es como en la técnica abierta.

Las anastomosis son manuales monocapa, se inician con el punto deslizante autobloqueante de Serra-Baltasar (38,39) y finalizan con el nudo Cuschieri (40). Para evitar lesiones serosas, todo el intestino se mide con pinzas marcadas a 5 cm de distancia. Extraemos el estómago sin bolsa protectora. Una sutura Maxon cierra el puerto de 12 ms. Iniciamos el CDL el 5 de septiembre de 2000 (41). El tiempo operatorio promedio fue de 155' después de los primeros 50 casos.

Al alta, los pacientes recibieron prescripciones con complejo multivitamínico (Centrum Forte), vitamina A 20.000 UI, vitamina D 50.000 UI, carbonato de calcio 1.000 mg y sulfato ferroso 300 mg y vitaminas B1 y B12.

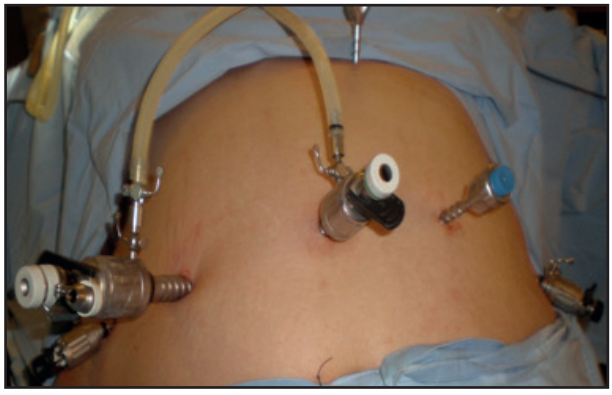

Figura 3.
Posición de los trocares.

MATERIAL Y MÉTODO

Fueron intervenidos 950 pacientes OM consecutivos (518 CDA y 432 CDL) desde 1994 hasta 2011, después de una evaluación preoperatoria multidisciplinaria completa y consentimiento informado legal; 782 eran mujeres (82,3%) y 168 eran hombres (17,7%). La edad promedio fue de 35 años (24-63). Fueron operados 474 ciudadanos extranjeros (376 de Estados Unidos, seis de Canadá, 71 de Noruega y 23 de Inglaterra) por el mismo personal quirúrgico, en la clínica privada.

El IMCI promedio (kg/m^2) era de 49,23 kg/m^2 (mujeres 49,26 y hombres 49,07). Rango de obesidad: a) *obesidad no grave, grado 2* con comorbilidades (IMCI < 40), 110 pacientes (media 37,66); b) *obesos mórbidos* (IMCI 40-50), 464 pacientes (media 45,11); c) *superobesos* (SO) (IMC de 50-60), 272 pacientes (media 54,32); y d) *pacientes con obesidad triple* (OT) e IMCI > 60, 104 pacientes (media > 66,50) y un paciente con IMCI-100.

Con respecto a las comorbilidades, 115 pacientes sufrían diabetes tipo 2 (DMII); 103, hipertensión; cinco, enfermedades cardiacas; 62, dislipidemias; 19, síndrome de la apnea obstructiva del sueño (SAOS); 16, osteoartritis; y uno, un pseudotumor cerebral.

RESULTADOS

PRINCIPALES COMPLICACIONES INTRAOPERATORIAS

Tres pacientes necesitaron traqueotomía por fallo de intubación oral y desaturación severa, sin incidentes.

En tres pacientes, la sonda gástrica de 12 mm no pasó más allá de cardias y el engrapado del estómago se hizo visualmente.

La mortalidad operatoria a 30 días ocurrió en seis CDA pacientes (1,38%). Las causas fueron: a) fuga en ADI: 1; b) fuga AYR, rabdomiólisis y fracaso multiorgánico: 1; c) embolia pulmonar: 2; d) fuga en el muñón duodenal: 1; y e) fuga en su ángulo de His: 1. Dos pacientes con CDL murieron (0,38%) por émbolos pulmonares. La mortalidad promedio de ambos grupos fue del 0,84%.

MORBILIDAD POSTOPERATORIA

Fugas

Hubo 46 fugas para una tasa de fugas total del 4,84%.

1. *Fugas en su ángulo de His:* veintiún casos (2,3% de incidencia). Fueron tratadas con endoprótesis en diez casos, drenaje o laparotomía y derivación en Y-de-Roux en tres casos. Uno de los pacientes murió.
2. *Fuga del muñón duodenal:* un paciente sufrió una fuga en el muñón duodenal que se reparó, pero murió de sepsis. Desde entonces, protegemos todo grapado del muñón duodenal con una sutura invaginante y no ha habido más fugas.
3. *Fugas de ADI:* veinticuatro casos (2,5% de incidencia) y es la anastomosis más difícil. Diecinueve de ellos sufrieron fugas tempranas, que se trataron exitosamente con drenaje o se volvió a realizar la anastomosis. Cinco casos presentaron fugas tardías (hasta 2-14 años después) y necesitaron una nueva operación y rehacer la anastomosis. En un caso, la fuga se produjo tres años después de la intervención, como una fístula gastropleural, y se trató con gastrectomía total.
4. *Fuga en AYR:* a un paciente con divertículo de intestino delgado a 100 cm de la válvula ileocecal se le extirpó y se realizó una AYR abierta en el sitio sin incidentes. Hubo fuga y las pruebas radiológicas de diagnóstico no aclararon la causa. Con diagnóstico tardío, fue reexplorado, sufrió rabdomiólisis y falleció.

Embolia pulmonar

Dos pacientes con BMI-70 y BMI-65 tuvieron embolia a pesar de la terapia profiláctica y murieron. La trombosis venosa profunda en un caso fue tratada con éxito.

Hígado

1. *Trastornos hepáticos:* doce pacientes sufrieron alteraciones tempranas en la función hepática, con elevaciones significativas de bilirrubina (hasta 15 y 29) y resueltas con tratamiento médico.
2. *Fallo hepático:* dos pacientes sufrieron insuficiencia hepática (0,2%). El primero ocurrió en una paciente seis meses después de la cirugía; se incluyó en lista de trasplante hepático urgente pero murió a la falta de donante. La segunda paciente sufrió insuficiencia hepática tres años después de la cirugía y recibió un trasplante de hígado exitoso más reversión de la DBP. Está sana cuatro años después. Un paciente ha fallecido 13 años tras CDA por alcoholismo.

Desnutrición calórica-proteica (DCP)

Treinta y tres pacientes (3,3%) desarrollaron DCP y 24 requirieron alargamiento del AC. Trece de ellos se hicieron abiertos sin complicaciones. En once casos, el AC se alargó laparoscópicamente y en dos de ellos el intestino delgado resultó lesionado por las pinzas de disección, que perforaron fácilmente por debilidad de la pared (Fig. 4). Ambos casos fueron diagnosticados intraoperatoriamente y reparados, pero murieron más tarde debido a fugas. Se encontraron múltiples hernias mucosas en la débil pared muscular entre los vasos del mesenterio. Este tipo de hernias no han sido informadas previamente. Por lo tanto, recomendamos laparotomía para el alargamiento intestinal.

Fístula pancreática-cutánea (Fig. 5): las dos fístulas y las lesiones de la piel sanaron espontáneamente.

Hipoglucemia: dos pacientes tuvieron episodios recurrentes de hipoglucemia que requirieron reversión de la DBP.

Evisceración: se dio en cuatro casos sin consecuencias después de una reparación adecuada.

Obstrucción intestinal tardía: siete casos (incidencia del 0,73%). Tratamos a dos en nuestra unidad y los otros fueron tratados en otras unidades, con resección del intestino delgado.

Beriberi: tres casos presentaron deficiencia de vitamina B1 con síntomas neurológicos, cambios en la marcha y caída espontánea. Todos fueron corregidos con éxito. Esta grave complicación necesita administración urgente de B1 intravenosa.

Fracturas: fueron debidas a la mala absorción de Ca y requirieron vitamina D25 más Ca. Se presentaron dos casos que son asintomáticos después de la atención adecuada.

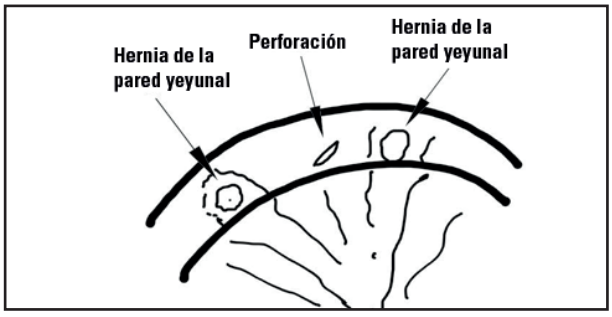

Figura 4.
Hernias en intestino delgado.

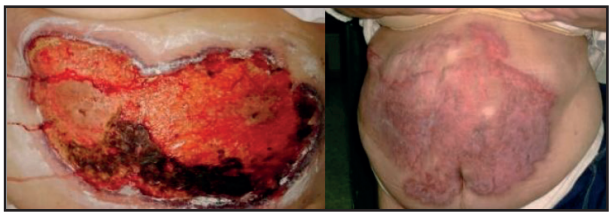

Figura 5.
Quemaduras cutáneas tras dos fístulas pancreáticas.

Megacolon tóxico: debido a colitis pseudomembranosa 16 años después de la cirugía. La paciente requirió una colectomía subtotal a 22 cm del ano, con ileostomía terminal. Más tarde se unió el íleon al recto.

Varios: neumonía (cuatro casos), seroma (cuatro casos), infección de herida (15 casos), hemorragias digestivas (cinco casos, tres de los cuales requieren laparotomía) y sepsis relacionada con el catéter (tres casos).

MORTALIDAD A LARGO PLAZO

Se dieron una apendicitis aguda no diagnosticada a los dos años y una necrosis intestinal por hernia interna a los tres años. Hubo otras causas de muerte no relacionadas con el CD (cáncer, melanoma, infarto de miocardio, etc.).

RESULTADOS DE PÉRDIDA DE PESO

El IMCF se midió en el 60% de 914 pacientes al año y en el 30% a los ocho años. El IMCI medio de 49,3 cayó a un IMCF medio de 30 y el porcentaje de pérdida de IMC (PPIMC) fue del 80% a los 12 meses (Fig. 6).

La figura 6 muestra en azul la caída del promedio del IMC, que bajó alrededor de 30, y en rojo el porcentaje de seguimiento.

La figura 7 muestra, en azul, el *IMC esperado de 30* y en rojo, el porcentaje *de IMC predictivo dependiente del rango del IMC inicial* y que supera el 100% a partir de los 12 meses.

Por lo tanto, el PSP ha sido excelente en la serie y probablemente sea mejor que con cualquier otra operación de obesidad.

Hay que destacar que el CD es tan eficaz en los super/superobesos cuando se mide el *%PIMCEsp,* como se ve en la figura 8.

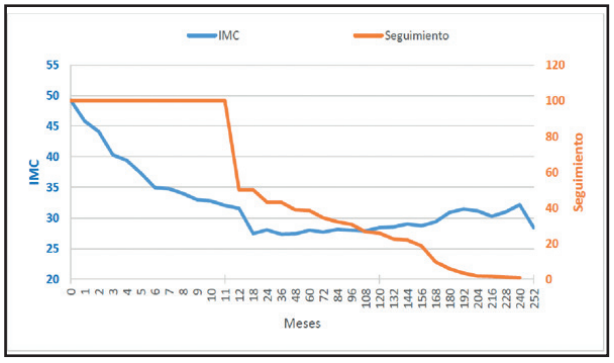

Figura 6.
Caída del IMC y porcentaje de seguimiento.

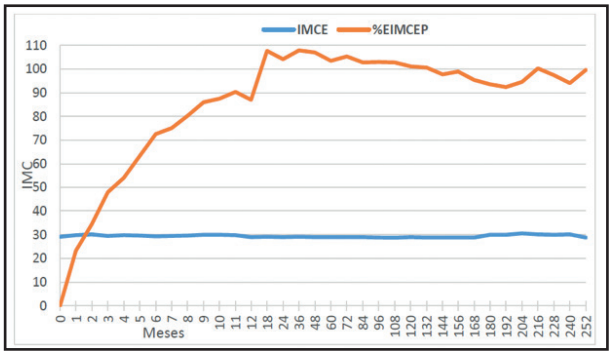

Figura 7.
El IMC esperado es 30. El % del IMC esperado supera el 100%.

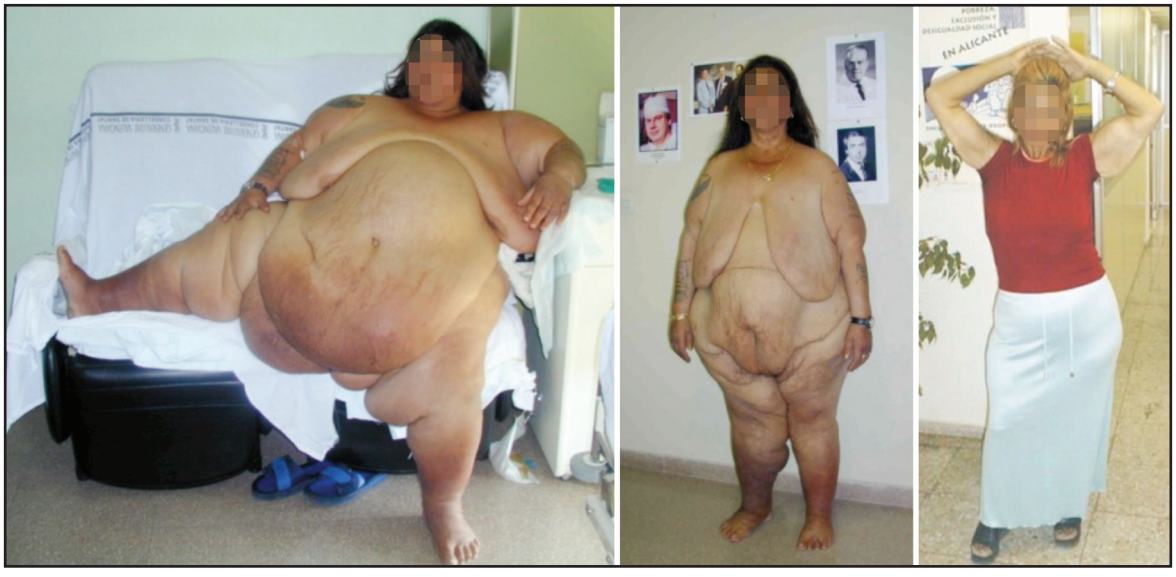

Figura 8.
Una paciente SSO bajó de IMC 100 a 34.

CORRECCIÓN DE COMORBILIDADES

Diabetes tipo II

El CD es una operación muy efectiva para tratar la diabetes. El 98% de nuestros pacientes son normoglucémicos, con una hemoglobina glicosilada normal. Dos pacientes no diabéticos sufrieron hipoglucemia grave y hubo que revertir la DBP. La hipertensión se corrigió en el 73% de los casos y la apnea del sueño, en el 100%.

CALIDAD DE VIDA

Utilizamos la clasificación Horia-Ardelt (41) de la escala BAROS para evaluar los cambios en la calidad de vida de los pacientes. Los cambios después de la cirugía incluyeron: autoestima, actividad física, actividad social, actividad laboral y actividad sexual en una escala de -1 a +1. El puntaje promedio fue de 2,03 de un máximo de tres puntos en 348 pacientes, lo que significa una mejora significativa en su calidad de vida.

Los síntomas gastrointestinales se evaluaron de un mínimo de 1 como excelente a un máximo de 5 como muy malo. En los 558 pacientes evaluados, la ingesta de alimentos de todos los tipos fue de 1,4, vómitos 1,3, apetito 1,96, tipo de deposiciones (de pastosas a líquidas) 2,2, frecuencia (de sin problema a intolerable) 1,8, olor a heces 3,35 e hinchazón abdominal 2,26. Por lo tanto, la suma de todas las medidas fue de 12,14, para una calificación total de 5 (excelente) a 35 (mala). El peor efecto secundario fue el mal olor de las heces, con una media de 3,35.

DISCUSIÓN

El CD nunca fue una terapia popular entre los cirujanos, posiblemente por su complejidad. Hess (6) describe cómo después de ver un vídeo nuestro en Seatle-1996, en la reunión de ASBS, modificó el procedimiento con una sutura de la curvatura mayor y solo tuvo una fuga en 188 casos (17).

Por su dificultad, muy pocos cirujanos siguieron haciendo el CD y, de hecho, se creó una subdivisión en la ASBS denominada "*The Switchers",* con logo propio. Siguió siendo impopular y tuvimos que reunirnos, durante años, fuera de la sede de los congresos como un grupo aparte formado por 25-30 cirujanos.

Figura 9.
Logo de los "switchers" (= cruzadores).

Al contrario, "*los del cruce*" hemos seguido haciendo la intervención y muchos pacientes, incluso extranacionales, supieron de sus ventajas y buscaron esta terapia. No hemos escondido las dificultades de la operación ni, sobre todo, sus complicaciones. Más de 72 cirujanos bariátricos nos visitaron y hemos intervenido en directo en varios congresos nacionales y extranjeros. Nuestro vídeo de CDL fue segundo premio en IFSO 2002 de Sao Paulo (42). Tres pacientes requirieron una traqueotomía de emergencia (43,44).

En el año 2000 usamos *endoprótesis rígida no extraíble* (45) y luego, *endoprótesis extraíbles* (46). Nueve pacientes requirieron gastrectomía total (47). En tres pacientes usamos una derivación Y-de-Roux (48,49) en las fugas y esta es aceptada como la más eficaz (50).

Pueden ocurrir trastornos hepáticos (51,52) e incluso fallos con necesidad de trasplante (53-55), pero también en las DG (56), fístulas bronquiales (57) o pancreáticas (58), desnutrición calórica-proteica (59) y necesidad de alargamientos (60) para corregirlas con posibles fugas (61) por defectos herniarios de la pared intestinal.

En la conferencia de consenso de 2004, Buchwald (62) declaró que en OM, idealmente, la cirugía debe considerarse para pacientes con obesidad superior a clase I (IMC 30-34,9) y con condiciones comórbidas asociadas. Debe tener una baja morbilidad y mortalidad, mientras que proporciona un PSP óptimo y sostenido con efectos secundarios mínimos. Ninguna técnica bariátrica es 100% exitosa o duradera en todos los pacientes, ni existe un único procedimiento estándar, y probablemente nunca lo habrá. Además, la cirugía no puede ser la solución para los 1.700 millones de OM que pueblan la tierra.

Las fugas de la GV son causa de importante morbilidad manifestada en las reuniones específicas de GV de Deitel y Gagner (63). Antes de la década de 1990, esta complicación era rara y los cirujanos del CD (los *"switchers"*) fueron los primeros en comunicarla. La sutura invaginante seroserosa de la línea de grapas con epiplón evita la torsión del TG y las fugas (13).

El CD es un procedimiento largo y difícil que requiere cirujanos expertos y con experiencia. La mortalidad operatoria debería ser < 1% y la morbilidad, < 5%. Nuestra mortalidad del CDL es baja (0,38%). Como los pacientes con CD tienen cuatro líneas de sutura, la detección temprana de fugas es esencial.

Mason (64) llamó la atención sobre la taquicardia como primera señal de advertencia de fugas y ningún paciente debería ser dado de alta con taquicardia.

Duncan (65) ha dado alta precoz en cirugía ambulatoria sin estancia a más de 2.000 pacientes. Nuestra estancia tras CDL es de 2-3 días, instruimos (66) al ingreso a los pacientes para tomar pulso y temperatura de forma digital y nos notifican dichos parámetros cada cuatro horas, durante dos semanas, en una base de datos telemática. Los pacientes con cambio significativo en estos parámetros necesitan una consulta inmediata y urgente.

DeMaria (67) informó que 450 instituciones y 800 cirujanos participaron en el programa 2009 de BSCOE en dos años (2007-2009). A solo el 0,89% de los 57.918 pacientes se les hizo CDL.

English (68) informa en ASMBS-2016 que la obesidad ha aumentado de forma alarmante en las últimas cinco décadas en Estados Unidos, del 13,4% al 36,4% en 2014. Los costos indirectos de la obesidad y el impacto económico general se estiman en 1,42 billones de dólares, el 8,2% del producto interno bruto y más del doble del gasto en defensa. La obesidad es el quinto factor de riesgo más importante de mortalidad en el mundo. En ASMBS-2016 se realizaron 215.666 operaciones en 795 centros acreditados (GV: 58,1%) y aunque se hicieron 1.187 DBP, solo un 0,6% fue CD y el 26%, CDL.

Utilizando datos BOLD de 2007-2010, Nelson (69) identificó 78.951 pacientes sometidos a derivación gástrica (DG) o a CD. De estos pacientes, al 98% se les hizo DG y solo el 2% tenía CD. El CD se asoció con tiempos de operación quirúrgicos más largos, pérdida de sangre y estancias hospitalarias más prolongadas. Las tasas de reintervención temprana fueron más altas en el grupo con CD (3,3% *vs.* 1,5%). La caída del IMC fue significativamente mayor en los casos de CD en todos los intervalos de seguimiento ($p > 0,05$). En los SO (IMC > 50) también hubo mayor caída a los dos años, 79% de CD frente a 67% de DG. La mejora de las comorbilidades (diabetes, hipertensión y apnea del sueño) fue superior con CD (todas $p < 0,05$).

La tasa de reintervención fue del 14%. Las revisiones, incluidas las conversiones, pueden superar en breve el número de procedimientos primarios en bariatría, lo cual sugiere la necesidad de desarrollar mejores algoritmos basados en la evidencia para minimizar el uso de nuevas operaciones. Es evidente que el número de fallos es muy alto y se necesitan operaciones iniciales efectivas.

En 2005, Hess (9) describió 1.150 pacientes con CD e IMCI-50,9. En 15 años hubo ocho reversiones (0,61%) y 37 revisiones (3,7%). La DMII curó en el 98% de los pacientes. Los 19 adolescentes (de 14-18 años) mejoraron, por lo que aboga por CD como la mejor operación en adolescentes. Asimismo, concluyó que el CD es una operación segura y efectiva.

Iannelli (70), en 110 pacientes con IMC > 50, encontró una reducción en la tasa de complicaciones postoperatorias al realizar CD de dos etapas. Al estudiar el procedimiento, solo 39 pacientes (35,5%) requirieron GV y se evitó la DBP en el 74,5% de los pacientes.

Biertho (71) hizo CD en 1.000 pacientes en 2006-2010. La tasa de conversión en el grupo de laparoscopia fue del 2,6%. Hubo una muerte postoperatoria (0,1%) debido a embolia. La estancia hospitalaria media fue más corta con CDL que con CDA. Las complicaciones fueron del 7,5%, sin diferencias significativas.

Biertho (72) trató a 566 pacientes entre 2011-2015 con CDL con IMC-49 y sin mortalidad a los 90 días. La estancia promedio en el hospital fue de 4,5 días. Las complicaciones mayores a los 30 días ocurrieron en el 3,0% de los pacientes y las menores, en el 2,5%. El PSP fue del 81% a los 12 meses, del 88% a los 24 meses y del 83% a los 36 meses. Los pacientes con HbA1C por encima del 6% disminuyeron del 38% al 1,4%. La readmisión fue del 3,5% y solo el 0,5% de los pacientes necesitaron una nueva operación. La tasa de complicaciones a corto y medio plazo del CDL es como en los procedimientos bariátricos mixtos y con excelentes resultados metabólicos.

Biron (73) estudió la calidad de vida de 112 pacientes. El seguimiento fue de 8,8 años y observó mejora de la calidad de vida específica de la enfermedad a corto y largo plazo.

Prachand (74) observó en 152 pacientes con DG y PSP-54%. Y en 198 pacientes con CD y el PSP-68% y así mostró que el CD fue más efectivo.

Para Strain (75), el CD proporciona mejor PSP que la DG en pacientes con obesidad severa. El peso promedio disminuyó un 31,2% después de la DG y un 4,8% tras el CD.

Topart (76,77) realizó 83 CD y 97 DG entre 2002 y 2009, con IMCI-55. Después de tres años de seguimiento, el PSP promedio fue del 63,7% después de la DG y del 84,0% después de CD ($p > 0,0001$). Los resultados fueron significativamente mejores con CD que con DG.

Våge (78) trató a 182 pacientes consecutivos con CD entre 2001-2008 sin mortalidad a los 30 días. Un paciente necesitó cirugía debido a una fuga, tres pacientes debido a sangrado y uno debido a fugas de bilis. Seis pacientes (3,2%) se sometieron a revisión quirúrgica por DCP, lo que refleja datos similares a los nuestros (3,3%).

Søvik (79) mostró mejores PSP después de CD que con DG en pacientes con OM. El promedio de IMC disminuyó un 31,2% después del DG y un 44,8% después del CD.

Angrisani (80) informa que en 2018 se realizaron 685.874 operaciones bariátricas en todo el mundo, el 92,6% fueron intervenciones primarias, un 7,4% de revisión, un 96% quirúrgicas y el 4% endoluminales. Fueron GV el 53,6%, DG el 30,1%, DGUA (derivaciones gástricas de una anastomosis) el 4,8% y solo un 1,3% fueron CDL

En resumen, los pacientes sometidos a CD constantemente reducen el IMC más que los pacientes con DG. Entonces, ¿por qué hay tan pocos pacientes con CD?

Rabkin (81) informa que el CD no está asociado con deficiencias nutricionales extensas. Los estudios anuales de laboratorio, tras cualquier tipo de operación bariátrica, parecen ser suficientes para identificar tendencias desfavorables. En pacientes seleccionados son necesarios suplementos de hierro y calcio adicionales.

Keshishian (82) realizó una biopsia hepática con aguja preoperatoria en 697 pacientes con CD. Hubo empeoramiento transitorio de AST (13% del valor de referencia, $p < 0,02$) y ALT (130-160% de los niveles de referencia, $p < 0,0001$) hasta seis meses después del CD. Asimismo, observó una mejoría progresiva de tres grados en la gravedad de NASH y del 60% en la esteatosis hepática a los tres años tras CD.

DIABETES TIPO II

Buchwald (83) informa que CD y DBP tienen tasas de resolución de diabetes que superan el 90%. En comparación, la tasa de la DG es del 70%, aproximadamente. Tsoli (84) mostró que GV era comparable al DBP en la resolución de la DTII pero menor en la dislipidemia y la presión arterial.

Baltasar (85) trató en 2004 a un paciente con bajo IMC-35 con *CDL sin GV* con excelentes resultados a los diez años.

Våge (86) piensa que el CD es efectivo en DMII, hipertensión e hiperlipidemia y que la duración de la diabetes y la edad son los predictores preoperatorios más importantes.

Según Eisenberg (87), la hipoglucemia hiperinsulinémica refractaria después de la cirugía es muy rara y su fisiopatología aún no se ha dilucidado por completo. La pancreatectomía parcial se asocia con una morbilidad potencial importante y no debe recomendarse. La reversión de la DBP es la terapia más simple y la mejor operación para dichas hipoglucemias, y así lo hicimos a dos de nuestras pacientes.

En el CD por estadios, ¿qué parte de la operación se debe hacer? ¿La DBP o la GV? La mayoría de los cirujanos recomiendan hacer primero la GV.

Marceau (88) trató a 1.762 pacientes de 2001 a 2009, todos programados para CD. Como primera etapa, trató 48 *DBP aisladas sin SG* y 53 casos de *GV aislada*. Los resultados a largo plazo de PSP y resolución de anormalidades metabólicas fueron mejores con *DBP aislada* que con *GV aislad*a. Los PSP con *CD completa* fueron superiores a los realizados en dos etapas. La GV y la DBP contribuyen de forma independiente a los resultados metabólicos beneficiosos.

Moustarah (89) trató a 49 pacientes SO con *DBP sin GV.* El peso inicial fue de 144 kg y el IMCI, de 52,54. La caída en el IMC de 14,5 kg/m^2 fue muy significativa ($p < 0,001$).

La *DBP sin GV* ha sido raramente utilizada como procedimiento único de pérdida de peso, pero en pacientes cuyas indicaciones clínicas justifican la omisión del GV, la DBP aislada tiene mejores resultados de pérdida de peso. En esta serie, PSP a los dos años se compara favorablemente con otras operaciones bariátricas.

La ventaja es que la *DBP sin SG es reversible* y la GV puede agregarse en cualquier momento posterior. Creemos que, con estos resultados en mente, *deberíamos hacer primero la DBP* ya que es un procedimiento totalmente reversible y más fácil que el GV sobre todo en SSO, ya que se realiza en una parte más baja del abdomen. La GV, además, se puede agregar con más facilidad luego si fuese necesaria y en cualquier momento.

No debemos olvidar la extraordinaria participación de cirujanos españoles en desarrollar las técnicas malabsortivas. Larrad y Sánchez desarrollaron una técnica de DBP e hicieron varias publicaciones muy importantes (90,91). Así como Solano y Resa (92), Ballesteros (93) y Hoyuela (94).

La aportación de Sánchez-Pernaute y Torres (95), del Hospital Clínico de Madrid, al hacer una variante del CDL con el CD de una sola anastomosis (CDUA) es muy importante y además se está haciendo popular en todo el mundo.

Un problema mayor del seguimiento del paciente con CD es que otros médicos y/o cirujanos pueden no entender cómo prevenir o tratar sus complicaciones a largo plazo.

El seguimiento de los pacientes con CD es muy importante. Al alta, se proporcionan una explicación técnica detallada de la operación y una extensa hoja explicativa de los análisis de laboratorio necesarios de por vida, de cada una de las posibles complicaciones y de su corrección.

La *determinación de albúmina sérica es el dato más importante* a largo plazo para detectar DCP. Vigilar PTH y vitamina D25 para detectar malabsorción de calcio y prevenir patología. Los déficits de hierro deben tratarse con Fe intravenoso.

Además de las fugas, la complicación más grave a largo plazo de CD es la DCP. La corrección quirúrgica es simple porque emplea la técnica de anastomosis yeyuno-yeyunal denominada "*operación X-en beso*" para alargar el AC, preferiblemente por laparotomía.

Los pacientes OM deberían recibir al alta el DVD de su operación, para que, si es necesaria una nueva operación, el cirujano conozca al detalle la técnica original.

Y también conocer que el apoyo de Endocrinología, Enfermería y Nutrición es esencial en todo el proceso.

UN CAMBIO AL CRUCE DUODENAL

Una llamada de atención para cambiar al CD

Halawani (96) afirma que un tercio (34,9%) de los adultos estadounidenses son obesos. En los años 2011-2015, el número de CDL en Estados Unidos fue inferior al 1%. Hay que añadir el CD a la práctica de los Centros de Excelencia en Obesidad (CEO).

El CD da un PSP superior y tiene una tasa más baja de recuperación de peso. Además, es mejor que la DG, conserva el píloro y produce un vaciamiento gástrico más lento. Con ajustes a la longitud del AC y el tamaño del tubo gástrico, cualquier paciente obeso puede ser candidato a CD.

Los pacientes con IMC < 50 pueden ser también candidatos. El CD es una opción viable debido a su flexibilidad. El cirujano puede ajustar el tamaño del TG y alterar el impacto de la restricción. La longitud de AC puede ser variable.

El CD es bueno en pacientes crónicos, que usen antiinflamatorios no esteroideos y esteroides. La tasa de mortalidad temprana en comparación con la GVL (0,28%) es ligeramente más alta (0,43%), aunque todavía se considera un procedimiento complejo de alto riesgo y los resultados deben analizarse con cautela.

El *CD es muy versátil* y puede ofrecer un manejo integral de la obesidad y sus comorbilidades metabólicas. Con dedicación, capacitación adecuada y una educación integral, el CD se puede implementar en la práctica.

CONCLUSIONES

Las técnicas de CD no son comunes para el manejo de la OM. El CD es la técnica más compleja y su curva de aprendizaje es más larga que en otras operaciones. Para estandarizar la técnica, nos llevó al menos 25 casos en CDA y 50 en CDL. El CD es seguro y el más eficaz en términos de resultados de pérdida de peso a largo plazo.

CONSIDERACIONES ÉTICAS

Todos los procedimientos que involucran participantes humanos se realizaron en los estudios citados en este documento de

acuerdo con los estándares éticos de los comités de investigación nacionales e institucionales y con la Declaración de Helsinki y sus enmiendas.

El consentimiento informado se obtuvo de todos los participantes individuales incluidos en los estudios citados.

BIBLIOGRAFÍA

1. Scopinaro N, Gianetta E, Civalleri D, et al. Two years of clinical experience with biliopancreatic bypass for obesity. Am J Clin Nutr 1980;33:506-14.
2. Hess DS, Hess DW. Biliopancreatic diversion with a duodenal switch. Obes Surg 1998;8:267-82.
3. Hess D. Limb measurements in duodenal switch. Obes Surg 2003;13:966.
4. Marceau P, Biron S, St Georges R, et al. Biliopancreatic diversion with gastrectomy as surgical treatment of morbid obesity. Obes Surg 1991;1:381-7.
5. Marceau S, Biron S, Lagacé M, et al. Biliopancreatic diversion, with distal gastrectomy, 250 cm and 50 cm limbs: long-term results. Obes Surg 1995;5:302-7.
6. Marceau P, Biron S, Bourque RA, et al. Biliopancreatic diversion with a new type of gastrectomy. Obes Surg 1993;3:29-3.
7. Lagacé M, Marceau P, Marceau S, et al. Biliopancreatic diversion with a new type of gastrectomy: some previous conclusions revisited. Obes Surg 1995;5:411-8.
8. Marceau P, Hould FS, Simard S, et al. Biliopancreatic diversion with duodenal switch. World J Surg 1998;22:947-54.
9. Hess DS, Hess DW, Oakley RS. The biliopancreatic diversion with the duodenal switch: results beyond 10 years. Obes Surg 2005;15:408-16.
10. Baltasar A, Bou R, Bengochea M. Hybrid bariatric surgery: duodenal switch and bilio-pancreatic diversion. VCR 1996;12:16-41. Disponible en: www.youtube.com/watch?v=3mNnZte3W_I&feature=youtu.be
11. Baltasar M, Bou R, Cipagauta LA, et al. Hybrid bariatric surgery: bilio-pancreatic diversion and duodenal switch - Preliminary experience. Obes Surg 1995;5:419-23.
12. Baltasar A, Del Río J, Bengochea M, et al. Cirugía híbrida bariátrica: cruce duodenal en la derivación bilio-pancreática. Cir Esp 1996;59:483-6.
13. Baltasar A, Del Río J, Escrivá C, et al. Preliminary results of the duodenal switch. Obes Surg 1998;7:500-4.
14. Baltasar A, Bou R, Miró J, et al. Cruce duodenal por laparoscopia en el tratamiento de la obesidad mórbida: técnica y estudio preliminar. Cir Esp 2001;70:102-4.
15. Baltasar A, Bou R, Bengochea M, et al. Duodenal switch: an effective therapy for morbid obesity-intermediate results. Obes Surg 2001;11:54-8.
16. Baltasar A, Bou R, Bengochea M. Open duodenal switch. Video. BMI 2011;1.5.4(356-9). Disponible en: www.youtube.com/watch?v=h0nTzeUDl5o
17. Baltasar A. Hand-sewn laparoscopic duodenal switch. Surg Obes Relat Dis 2007;3:94-6
18. Anthone G, Lord R, DeMeester T, et al. The duodenal switch operation for the treatment of morbid obesity. Ann Surg 2003;238(4):618-28.
19. Almogy G, Crookes P, Anthone G. Longitudinal gastrectomy as a treatment for the high-risk super-obese patient. Obes Surg 2004;14:492-7.
20. Rabkin RA. Concept. The duodenal switch as an increasing and highly effective operation for morbid obesity. Obes Surg 2004;14:861-5.
21. Baltasar A. Laparoscopic sleeve gastrectomy is a misnomer. Surg Obes Relat Dis 2012;8:127-31.
22. Baltasar A. La Real Academia Nacional de Medicina dice… La "Gastrectomía Vertical" es el término correcto. BMI-Latina 2012;2:2-4. Disponible en: www.bmilatina.com
23. Biron S, Hould FS, Lebel L, et al. Twenty years of biliopancreatic diversion: what is the goal of the surgery? Obes Surg 2004;14:160-4.
24. Marceau P, Biron S, Hould FS. Duodenal switch: long-term results. Obes Surg 2007;17:1421-30.
25. Marceau P, Biron S, Hould FS, et al. Duodenal switch improved standard biliopancreatic diversion: a retrospective study. Surg Obes Relat Dis 2009;5:43-7.
26. Biertho L, Biron S, Hould FS. Is biliopancreatic diversion with duodenal switch indicated for patients with body mass index < 50 kg/m^2? Surg Obes Relat Dis 2010;6:508-15.
27. Ren CJ, Patterson E, Gagner M. Early results of laparoscopic biliopancreatic diversion with duodenal switch: a case series of 40 consecutive patients. Obes Surg 2000;10:514-23.
28. Baltasar A, Bou R, Miró J, et al. Avances en técnica quirúrgica. Cruce duodenal por laparoscopia en el tratamiento de la obesidad mórbida: técnica y estudio preliminar. Cir Esp 2001;70:102-4. Disponible en: www.youtube.com/watch?v=GSfzgYYxZJ8
29. Weiner RA, Blanco-Engert R, Weiner S, et al. Laparoscopic biliopancreatic diversion with duodenal switch: three different duodeno-ileal anastomotic techniques and initial experience. Obes Surg 2004;14:334-40.
30. Paiva D, Bernardes L, Suretti L. Laparoscopic biliopancreatic diversion for the treatment of morbid obesity: initial experience. Obes Surg 2001;11:619-22.
31. Scopinaro N, Marinari G, Camerini G. Laparoscopic standard biliopancreatic diversion: technique and preliminary results. Obes Surg 2002;12:241-4.
32. Baltasar A, Pérez N, Serra C, et al. Weight loss reporting: predicted BMI after bariatric surgery. Obes Surg 2011;21:367-72. DOI: 10.1007/s11695-010-0243-7
33. Molina A, Sabench F, Vives M, et al. Usefulness of Baltasar's expected body mass index as an indicator of bariatric weight loss surgery. Obes Surg 2016;26. DOI: 10.1007/s11695-016-2163-7
34. Baltasar A, Bou R, Miró J, et al. Laparoscopic biliopancreatic diversion with duodenal switch: technique and initial experience. Obes Surg 2002;12:245-8.
35. Baltasar A, Bou R, J Miró M, et al. Laparoscopic duodenal switch: technique and initial experience. Chir Gastroenterol 2003;19:54-6.
36. Baltasar A. Video case report. Hand-sewn laparoscopic duodenal switch. Surg Obes Relat Dis 2007;3:94-6.
37. Baltasar A, Bou R, Bengochea M, et al. Laparoscopic hand-sewn duodenal switch. Video. BMI-Latina 2012;2:11-3.
38. Serra C, Pérez N, Bou R, et al. Sliding self-locking first stitch and Aberdeen knots in suture reinforcement with omentoplasty of the laparoscopic gastric sleeve staple line. Obes Surg 2014;24:1739-40. DOI: 10.1007/s11695-014-1352-5
39. Baltasar A, Bou R, Serra R, et al. Use of self-locking knots in running intestinal bariatric sutures. Glob Surg 2015;2:100-1. DOI: 10.15761/GOS.1000132
40. Cuschieri A, Szabo Z, West D. Tissue approximation in endoscopic surgery: suturing and knotting. Informa Healthcare; 1995. ISBN-13: 9781899066032
41. Oria HE, Moorhead H. Updated bariatric analysis and reporting outcome system (BAROS). Surg Obes Relat Dis 2009;5:60-6.
42. Baltasar A, Bou R, Miró J, et al. Hand sutured laparoscopic duodenal switch V13. V13. Obes Surg 2002;12:483. Disponible en: https://www.youtube.com/watch?v=egoBphA1s90
43. Baltasar A, Bou R, Bengochea M, et al. Emergency tracheotomy in morbid obesity. Sci Forschen. Obes Open Access 2017;3(2). DOI: 10.16966/2380-5528.132
44. Baltasar A, Bou R, Bengochea M, et al. Difficult intubation and emergency tracheotomy in morbid obesity. BMI-Latina 2013;3:4-7.
45. Baltasar A. Wall-stent prosthesis for severe leak and obstruction of the duodenal switch. Obes Surg 2000;10(2):29.
46. Serra C, Baltasar A, Andreo L, et al. Treatment of gastric leaks with coated self-expanding stents after sleeve gastrectomy. Obes Surg 2007;17:866-72.
47. Serra C, Baltasar A, Pérez N, et al. Total gastrectomy for complications of the duodenal switch, with reversal. Obes Surg 2006;16:1082-6.
48. Baltasar A, Bou R, Bengochea M, et al. Use of a Roux limb to correct esophago-gastric junction fistulas after sleeve gastrectomy. Obes Surg 2007;17:1409-10.
49. Baltasar A, Serra C, Bengochea M, et al. Use of Roux limb as remedial surgery for sleeve gastrectomy fistulas. Surg Obes Relat Dis 2008;4:759-63.
50. Mcheimeche H, Dbouk S, Saheli R, et al. Double Baltazar procedure for repair of gastric leakage post-sleeve gastrectomy from two sites: case report of new surgical technique. Obes Surg 2018;28:2092-5.
51. Baltasar A, Serra C, Pérez N, et al. Clinical hepatic impairment after the duodenal switch. Obes Surg 2014;14:77-8.
52. Baltasar A. Liver cirrhosis and bariatric operations. Surg Obes Relat Dis 2006;16:579-81.
53. Baltasar A. Liver failure and transplantation after duodenal switch. Surg Obes Relat Dis 2014;10:c93-6.
54. Castillo J, Fábrega E, Escalante C, et al. Liver transplantation in a case of steatohepatitis and subacute hepatic failure after biliopancreatic obesity surgery diversion for morbid obesity. Obes Surg 2001;11:640-2.
55. Cazzo E, Pareja JC, Chaim EA. Falencia hepática após derivações bilio-pancreáticas: uma revisão narrativa. Sao Paulo Med J 2017;135. E-pub: 10 de noviembre de 2016. DOI: 10.1590/1516-3180.2016.0129220616
56. Ossorio M, Pacheco JM, Pérez D, et al. hepático fulminante a largo plazo en pacientes sometidos a bypass gástrico por obesidad mórbida. Nutr Hosp 2015;32:430-43.

57. Díaz M, Garcés M, Calved J, et al. Gastro-bronchial fistula: long term or very long-term complications after bariatric surgery. BMI-Latina 2011;5:335-7.
58. Bueno J, Pérez N, Serra C, et al. Fistula pancreato-cutánea secundaria a pancreatitis postoperatoria tras cruce duodenal laparoscópico. Cir Esp 2004;76:184-6.
59. Baltasar A, Bou R, Bengochea M, et al. Malnutrición calórico-proteica. Tres tipos de alargamiento de asa común. BMI-Latina 2011;5:96-7.
60. Baltasar A, Serra C. Treatment of complications of duodenal switch and sleeve gastrectomy. En: Deitel M, Gagner M, Dixon JB, et al. (eds.). Handbook of obesity surgery. Toronto: FD Comunicación; 2010. pp. 156-61.
61. Baltasar A, Bou R, Bengochea M. Fatal perforations in laparoscopic bowel lengthening operations for malnutrition. Surg Obes Relat Dis 2010;6:572-4. Disponible en: www.youtube.com/watch?v=Hw_aPYLjGXI
62. Buchwald H. 2004 ASBS. Consensus conference statement bariatric surgery for morbid obesity: health implications for patients, health professionals, and third-party payers. Surg Obes Relat Dis 2005;1:371-81.
63. Dietel M, Gagner M, Erickson AL, et al. Third International Summit. Current status of sleeve gastrectomy. Surg Obes Relat Dis 2011;7:749-59.
64. Mason R. Diagnosis and treatment of rapid pulse. Obes Surg 1995;3:341.
65. Duncan T, Tuggle K, Larry Hobson L, et al. PL-107. Feasibility of laparoscopic gastric bypass performed on an outpatient basis. Surg Obes Relat Dis 2011;7:339-54.
66. Baltasar A. WhatsApp© Assistance in bariatric surgery. J Obes Eating Disord 2017;3(1)28. ISSN: 2471-8203. DOI: 10.21767/2471-8513.100017
67. DeMaria E, Pate V, Warthen M, et al. Baseline data from American Society for Metabolic and Bariatric Surgery - Designated bariatric surgery centers of excellence using the Bariatric Outcomes Longitudinal Database. Surg Obes Relat Dis 2010;6:347-35.
68. English W, DeMaria M, Brethauer SA, et al. American Society for Metabolic and Bariatric Surgery estimation of metabolic and bariatric procedures performed in the United States in 2016. Surg Obes Relat Dis 2018;14:259-63.
69. Nelson D, Blair KS, Martin M. Analysis of obesity-related outcomes and bariatric failure rates with the duodenal switch vs gastric bypass for morbid obesity. Arch Surg 2012;147:847-54.
70. Iannelli A, Schneck AS, Topart P, et al. Laparoscopic sleeve gastrectomy followed by duodenal switch, in selected patients versus single-stage duodenal switch for super-obesity: case-control study. Surg Obes Relat Dis 2013;9:531-8.
71. Biertho L, Lebel S, Marceau S, et al. Perioperative complications in a consecutive series of 1000 duodenal switches. Surg Obes Relat Dis 2013;9:63-8.
72. Biertho L, SimonHould F, Marceau S, et al. Current outcomes of laparoscopic duodenal switch. Ann Surg Innov Res 2016;10:1. DOI: 10.1186/s13022-016-0024-7
73. Biron S, Biertho L, Marceau S. Long-term follow-up of disease-specific quality of life after bariatric surgery. Surg Obes Relat Dis 2018;14(5):658-64. Accepted SOARD 3291.
74. Prachand V, DaVee R, Alberdy JA. Duodenal switch provides superior weight loss in the super-obese (BMI $>$ 50) compared with gastric bypass. Ann Surg 2006;244:611-9.
75. Strain CW, Gagner M, Inabnet WB, et al. Comparison of effects of gastric bypass and biliopancreatic diversion with duodenal switch on weight loss and body composition 1-2 years after surgery. Surg Obes Relat Dis 2007;3:31-6.
76. Topart P, Becouarn G, Salle A. Five-year follow-up after biliopancreatic diversion with duodenal Switch. Surg Obes Relat Dis 2011;7:199-205.
77. Topart P, Becouarn G, Ritz P. Weight loss is more sustained after bilio-pancreatic diversion with duodenal switch than Roux-en-Y gastric bypass in super-obese patients. Surg Obes Relat Dis 2013;9:526-30.
78. Våge V, Gåsdal R, Lakeland C, et al. The biliopancreatic diversion with a duodenal switch (BPDDS): how is it optimally performed? Obes Surg 2011;21:1864-9.
79. Søvik T, Karlsson J, Aasheim E, et al. Gastrointestinal function and eating behavior after gastric bypass and duodenal switch. Surg Obes Relat Dis 2013;9:641-7.
80. Angrisani L, Santonicola A, Iovino P, et al. Bariatric Surgery Worldwide 2013. Obes Surg 2015;25:1822-32. DOI: 10.1007/s11695-015-1657-z
81. Rabkin R, Rabkin JM, Metcalf B, et al. Nutritional markers following duodenal switch for morbid obesity. Obes Surg 2004;14:84-90.
82. Keshishian A, Zahriya K, Willes EB. Duodenal switch has no detrimental effects on hepatic function and improves hepatic steatohepatitis after 6 months. Obes Surg 2005;15:1418-23.
83. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med 2009;122:248-56.e5.
84. Tsoli M, Chronaiou A, Kehagias I. Hormone changes and diabetes resolution after biliopancreatic diversion and laparoscopic sleeve gastrectomy: a comparative prospective study. Surg Obes Relat Dis 2013;9:667-78.
85. Baltasar A. Historical note: first diabetes metabolic operation in Spain. Integr Obes Diabetes 2015;2:180-2. DOI: 10.15761/IOD.1000140
86. Våge V, Roy M, Nilsen M, et al. Predictors for remission of major components of the metabolic syndrome after biliopancreatic diversion with duodenal switch. Obes Surg 2013;23:80-6. DOI: 10.1007/s11695-012-0775
87. Eisenberg D, Azagury D, Ghiassi S, et al. ASMBS statement on postprandial hyper-insulinemic hypoglycemia after bariatric surgery. Surg Obes Relat Dis 2017;371-8.
88. Marceau P, Biron S, Marceau S, et al. Biliopancreatic diversion-duodenal switch: independent contributions of sleeve resection and duodenal exclusion. Obes Surg 2014;24:1843-9.DOI: 10.1007/s11695-014-1284-0
89. Moustarah F, Marceau S, Lebel S, et al. Weight loss after duodenal switch without gastrectomy for the treatment of severe obesity: review of a single institution case series of duodeno-ileal intestinal bypass. Can J Surg 2010;53(4):S51.
90. Larrad A, Moreno B, Camacho A. Resultados a los dos años de la técnica de Scopinaro en el tratamiento de la obesidad mórbida. Cir Esp 1995;58:23-2.
91. Larrad A, Sánchez-Cabezudo C, De Cuadros Borrajo P, et al. Short-, mid- and long-term results of Larrad biliopancreatic diversion. Obes Surg 2007;17:202-10.
92. Solano J, Resa JJ, Fatas JA, et al. Derivación bilio-pancreática laparoscópica para el tratamiento de la obesidad mórbida. Aspectos técnicos y análisis de los resultados preliminares. Cir Esp 2003;74(6):347-50.
93. Ballesteros M, González T, Urioste A. Biliopancreatic diversion for severe obesity: long-term effectiveness and nutritional complications. Obes Surg 2016;26:38-44. DOI: 10.1007/s11695-015-1719-2
94. Hoyuela C, Veloso E, Marco C. Derivación bilio-pancreática con cruce duodenal y su impacto en las complicaciones posoperatorias. Cir Esp 2006;80(Supl 1):1-250 175.
95. Sánchez-Pernaute A, Rubio M, Torres A, et al. Proximal duodenal-ileal end-to-side bypass with sleeve gastrectomy: proposed technique. Obes Surg 2007;17:1614-8. DOI: 10.1007/s11695-007-9287-8
96. Halawani HM, Antanavicius G, Bonanni F. How to switch to the switch: implementation of biliopancreatic diversion with duodenal switch into practice. Obes Surg 2017;27(9):2506-9. DOI: 10.1007/s11695-017-2801-8

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Twenty-five years of duodenal switch. How to switch to the duodenal switch

Veinticinco años de cruce duodenal. Cómo cambiar al cruce

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Abstract

Background: the duodenal switch (DS) is a procedure that combines a vertical gastrectomy (VG) plus a biliopancreatic diversion (BPD).

Objectives: to report our experience in 950 consecutive DS patients with morbid obesity (MO) performed from 1994 to 2011, with 27 years of follow-up.

Environment: mix of teaching and private institution in a regional hospital in Spain.

Methods: retrospective review of 950 consecutive morbidly obese patients treated with DS surgery.

Results: five hundred and eighteen open DS (ODS) and 432 laparoscopic DS (LDS) were performed. Operative mortality was 0.84% (1.38% in ODS and 0.38% in LDS); 4.84% had one leak, two had liver failure (0.2%) and malnutrition was present in 3.1%. At five years, the body mass index (BMI) percentage of lost overweight (%EWL) was 80% and the percentage of expected BMI loss was more than 100%.

Conclusions: the DS is the most aggressive bariatric technique but with the best long-term weight loss. Operative complications and long-term follow-up guidelines are described.

Key words:

Morbid obesity. Duodenal cross. Bariatric surgery. Gastrectomy and biliary pancreatic diversion. Weight loss.

Resumen

Antecedentes: el cruce duodenal (CD) es un procedimiento que combina una gastrectomía vertical (GV) más una derivación biliopancreática (DBP).

Objetivos: informar de nuestra experiencia en 950 CD consecutivos en pacientes con obesidad mórbida (OM) realizados de 1994 a 2011 y con 27 años de seguimiento.

Entorno: mezcla de enseñanza e institución privada en un hospital comarcal de España.

Métodos: revisión retrospectiva de 950 pacientes consecutivos con obesidad mórbida tratados con cirugía de CD.

Resultados: se realizaron 518 CD abiertos (CDA) y 432 CD laparoscópicos (CDL). La mortalidad operatoria fue del 0,84% (1,38% en CDA y 0,38% en CDL). El 4,84% tuvo una fuga, dos tuvieron insuficiencia hepática (0,2%) y la desnutrición estuvo presente en el 3,1%. A los cinco años, el porcentaje de sobrepeso perdido (PSP) de índice de masa corporal (IMC) fue del 80% y el porcentaje de pérdida esperada de IMC fue más del 100%.

Conclusiones: el CD es la técnica bariátrica más agresiva pero con mejor pérdida de peso a largo plazo. Se describen las complicaciones operatorias y pautas de seguimiento a largo plazo.

Palabras clave:

Obesidad mórbida. Cruce duodenal. Cirugía bariátrica. Gastrectomía y desviación pancreática biliar. Pérdida de peso.

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INTRODUCTION

Duodenal switch (DS) surgery consists of two operations, vertical gastrectomy (VG) plus biliopancreatic bypass (BPD). DS is the most complex technique in bariatric surgery for morbid obesity (MO). The DS combines restriction of food intake and malabsorption in the small intestine. Scopinaro started the DBP in 1976 (1).

Hess (2) describes it as: a) VG eliminates major gastric curvature, reduces gastric volume, and intake and allows for normal emptying; and b) derives post-pylorus intake from duodenum to ileum, DBP, to cause malabsorption.

Hess (3) recommends measuring the entire small intestine, without tension, from Treitz to ileocecal valve and uses 50% of its proximal length as a bilio-pancreatic loop (BPL), 10% distal as a common loop (CL) and 40% of the intermediate length as digestive loop (DL).

Marceau (4,5) made standard DBP until 1991 and then switched to DS and is the first author to publish it (6) in 1993 as *parietal gastrectomy* plus DBP.

Lagacé (7) reported the first good results of the DS in 61 patients in 1995 and Marceau in 1998 (8) compared 252 DBP with distal gastrectomy and 465 DS with an operative mortality of 1.7%.

Hess (9) and Baltasar (10-17) describe the gastric part of the operation as *vertical gastrectomy* (VG) and creation of a gastric tube (GT). Anthone (18) and Almogy (19) called it *longitudinal gastrectomy* and Rabkin (20), *gastrectomy of the greater curvature*.

The DS (21-26) became standardized in the 1990s (Fig. 1). Hess (9) modified the procedure by intussusception and suturing the serosa of the VG in the following 188 cases to reduce the incidence of leakage at the staple line. Ren (27) made the *first complete LDS* in July 1999 and Baltasar (28) made the *first LDS in Europe* in 2000 (29). Paiva (30) in Brazil and Scopinaro (31) in Italy made the *first standard laparoscopic* DBP in 2000.

Quetelet reported the use of body mass index (BMI = kg/m^2) to measure weight results, but after reviewing 7,410 patients, our mathematician (32) developed the concept of predictive BMI (PBMI) taking as a control an initial BMI (IBMI) *greater than 25*.

The percentages of lost weight loss (%EWL) are not the same in a subject with MO grade 2 as in a subject with triple obesity (TO), and thus we only measure BMI in excess of 25. %EWL would then be the predictive BMI = BMI x 0:4 + 11.75. This concept has already been used positively by others (33) (Fig. 1).

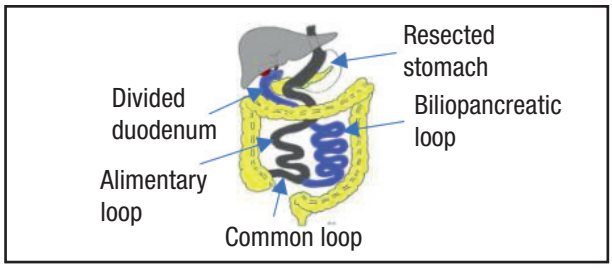

Figure 1.
Duodenal switch = VG + BPD.

OPERATIVE TECHNIQUE

Open duodenal switch (ODS) by laparotomy

The patient is placed in Trendelenburg's forced position. The operation is performed by three surgeons through a transverse supraumbilical incision between both costal margins (Fig. 2A and B). Once in the abdomen, the round and falciform ligaments are severed and the gallbladder and appendix are removed.

The entire intestine is measured starting distally, from the ileocecal valve, and the *common loop* (CL) is marked as 10% of the intestine. The *alimentary loop* (AA) corresponds to 40% of the most proximal bowel and is divided with a linear stapler. The proximal 50% is the *biliopancreatic loop* (BPL) and begins in the proximal duodenum, D1. The AA distal to the junction with BPL and the AC joined by a jejune-ileal anastomosis (JIA) with continuous monoplane absorbable suture, and the mesenteric defect is closed with a non-absorbable suture.

The stomach is exposed, and a 12 mm nasogastric tube is introduced as a guide to the lesser curvature. The major gastric curvature is devascularized with ultrasonic scalpel from 3 cm distal to the pylorus to the angle of His. The entire major gastric curvature is devascularized with ultrasonic scalpel from *3 cm distal to the pylorus* up to the angle of His. The stomach is divided sequentially with staplers from pylorus to the esophagus-gastric junction and removed including the major gastric curvature. In the minor curvature, the gastric tube (GT) remains, which is reinforced with continuous invaginated suture and includes the separate omentum and both gastric walls, to avoid torsion and leakage.

A retro duodenal tunnel is created, distal to the right gastric artery, and the duodenum is divided at D1 with a linear stapler. An inverted suture reinforces the duodenal stump.

The *proximal AA* passes retro colic on the right and a duodenum ileal anastomosis (DIA) is performed with continuous resorbable suture. The operation has four suture lines (gastric reinforcement, ADI, AYR and the distal duodenal stump). Two drains are placed, one next to the GT and the other in the DIA.

The abdominal incision is closed in two layers with continuous Maxon. After weight loss, the scar length is reduced to one third (Fig. 2B) and allows the abdominoplasty edge to reach the pubic area (Fig. 2C). We started the ODS on March 17th, 1994 and the average surgical time was 91 minutes.

Laparoscopic duodenal switch (LDS)

It is also performed by a team of three surgeons. Six ports are used. An Ethicon #12 optical trocar enters the abdomen, under vision, at the lateral edge of the right rectus muscle, through three fingertips and below the costal margin, and is the main working port. A 10 mm supraumbilical port is used for the midline camera (Fig. 3). The remaining four 5 mm trocars are Ternamian type ones that do not slide. We placed two sub-costal on the right and left, one in the left hypochondrium and one in the epigastrium used to retract the liver. The rest of the procedure is as in the open technique.

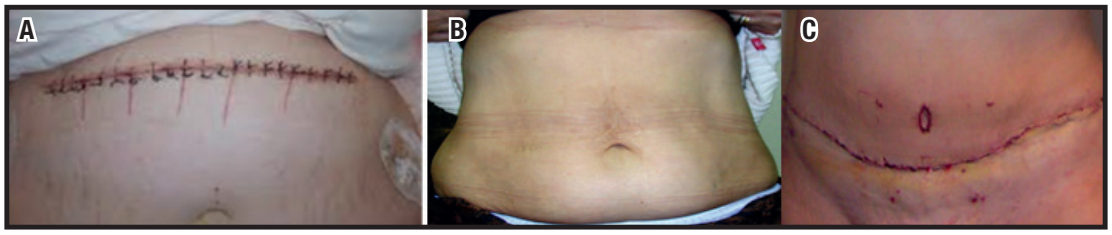

Figure 2.
A. Incision. B. Invisible scar. C. Supra-pubic dermolipectomy.

All anastomosis is manual monolayer, starting with the *self-locking sliding stich* of Serra-Baltasar (38,39) and ending with the *Cuschieri knot* (40). To avoid serous lesions, the entire intestine is measured with forceps marked 5 cm apart. The stomach is removed without a protective bag. A Maxon suture closes the 12 mm port. We started the LDS on September 5th, 2000 (41). The average operating time was 155' after the first 50 cases.

At discharge, patients received prescriptions with multivitamin complex (Centrum Forte), vitamin A - 20,000 IU, vitamin D - 50,000 IU, calcium carbonate 1,000 mg and ferrous sulfate 300 mg vitamins B1 and B12.

MATERIAL AND METHOD

A total of 950 consecutive MO patients (518 ODS and 432 LDS) were operated on from 1994 to 2011, after full multidisciplinary preoperative evaluation and legal informed consent; 782 were women (82.3%) and 168 were men (17.7%). The average age was 35 years (24-63). Four hundred and seventy-four foreign nationals (376 from the United States, six from Canada, 71 from Norway and 23 from England) were operated on by the same surgical staff in the private clinic.

The average IMCI (kg/m^2) was 49.23 (women 49.26 and men 49.07). Obesity range: a) *non-severe obesity*, grade 2 with comorbidities (IMCI < 40), 110 patients (mean 37.66); b) *morbid obese* (IMCI 40-50), 464 patients (mean 45.11); c) *super-obese* (SO) (BMI 50-60), 272 patients (mean 54.32); and d) patients with *triple obesity* (TO) and IMCI > 60, 104 patients (mean > 66.50) and one patient with IMCI-100 (IMCI-100).

Regarding comorbidities, 115 patients suffered from type 2 diabetes (DMII), 103 from hypertension, five from heart disease, 62 from dyslipidemias, 19 from obstructive sleep apnea syndrome (OSAS), 16 from osteoarthritis and one from cerebral pseudotumor.

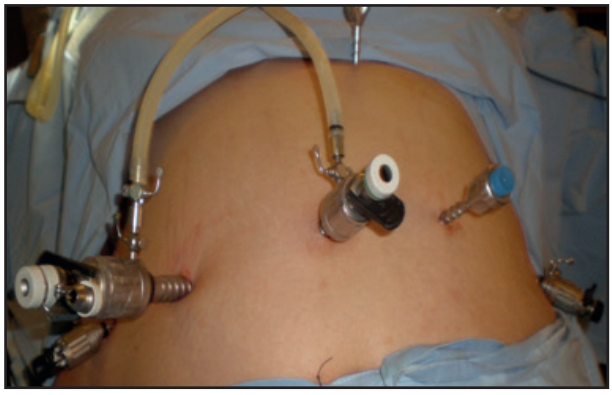

Figure 3.
Position of the trocars.

RESULTS

MAIN INTRAOPERATIVE COMPLICATIONS

Three patients required a tracheotomy for oral intubation failure and severe desaturation, without incidents.

In three patients, the 12 mm gastric tube did not pass beyond the cardias and the stapling of the stomach was done under visual control.

Surgical mortality at 30 days occurred in six ODS patient (1.38%). The causes were: a) leak in DIA: 1; b) leak in AYR, rhabdomyolysis and multiorgan failure: 1; c) pulmonary embolism: 2; d) leak in the duodenal stump: 1; and e) leak in its angle of His: 1. Two LDS patients died (0.38%) by pulmonary emboli. The average mortality of both groups was 0.84%.

POSTOPERATIVE MORBIDITY

Leaks

There were 46 leaks for a total leak rate of 4.84%.

1. *Leaks in the His angle:* twenty-one cases (2.3% incidence). They were treated with stenting in ten cases, drainage or laparotomy and Roux-en-Y shunt in three cases. One of the patients died.
2. *Leakage of the duodenal stump:* a patient suffered a leak in the duodenal stump that was repaired but died of sepsis. Since then, we protect all stapled duodenal stump with an inverting suture and there have been no further leaks.
3. *ADI leaks:* twenty-four cases (2.5% incidence) as it is the most difficult anastomosis. Nineteen of them suffered early leaks, which were successfully treated with drainage or the anastomosis was performed again. Five cases presented *late leaks* (up to 2-14 years later) and required a new operation and redoing

the anastomosis. In one case, the leak occurred three years after surgery, as a gastro pleural fistula, and was treated with total gastrectomy.

4. *RY leakage:* a patient had a small bowel diverticulum 100 cm from the ileocecal valve that was removed, and an open RY was performed at the site without incident. There was a new leakage and diagnostic radiological tests did not clarify the cause. With late diagnosis, he was reoperated, suffered rhabdomyolysis, and died.

Pulmonary embolism

Two patients with IBMI-70 and IBMI-65 had embolism despite prophylactic therapy and died. Deep vein thrombosis in one case was successfully treated.

Liver

1. *Liver disorders:* twelve patients suffered early alterations in liver function, with significant bilirubin elevations (up to 15 and 29) and resolved with medical treatment.
2. *Liver failure:* two patients suffered liver failure (0.2%). The first occurred in a patient six months after surgery; she was included in the liver transplantation *urgent list* but died in the absence of a donor. The second patient suffered liver failure three years after surgery and received a successful liver transplant plus reversal of BPD. She is healthy four years later. One patient has died 13 years after ODS from alcoholism.

Protein-caloric malnutrition (PCM)

Thirty-three patients (3.3%) developed PCM and 24 required CL lengthening. Thirteen of them were open and without complications. In eleven cases, the CL was lengthened laparoscopically and in two of them the small intestine was injured by the dissection forceps, which were easily perforated by weakness of the wall (Fig. 4). Both leaks were diagnosed intraoperatively and repaired but died later due to new leaks. Multiple mucosal hernias were found in the weak muscle wall between the vessels at the mesentery. These types of hernias have not been previously reported. Therefore, we recommend laparotomy for intestinal lengthening.

Pancreatic-cutaneous fistula: both fistulas and skin lesions healed spontaneously (Fig. 5).

Hypoglycemia: two patients had recurrent episodes of hypoglycemia requiring BPD reversal.

Evisceration: four cases without consequences after adequate repair.

Late intestinal obstruction: seven cases (incidence of 0.73%). We treated two in our unit and the others were treated in other units, with resection of the small intestine.

Beriberi: three cases presented vitamin B1 deficiency with neurological symptoms, gait changes and spontaneous fall. All were successfully corrected. This serious complication requires urgent administration of intravenous B-1.

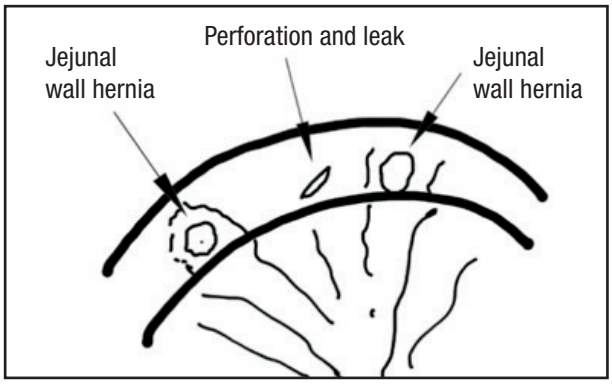

Figure 4.
Small intestine wall hernias.

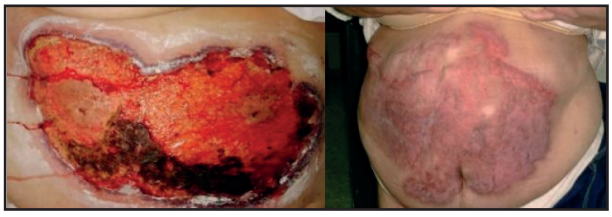

Figure 5.
Skin burns by two pancreatic fistulas.

Fractures: they were due to malabsorption of Ca requiring vitamin D25 plus Ca. Two cases occurred that are asymptomatic after adequate care.

Toxic megacolon: it was due to pseudomembranous colitis 16 years after surgery. The patient required a subtotal colectomy 22 cm from the anus, with terminal ileostomy. Later, the ileum was attached to the rectum.

Miscellaneous: pneumonia (four cases), seroma (four cases), wound infection (15 cases), gastrointestinal bleeding (five cases, three of which require laparotomy) and catheter-related sepsis (three cases).

LONG-TERM MORTALITY

An undiagnosed acute appendicitis occurred at two years and an internal hernia intestinal necrosis at three years. There were other causes of death not related to the DS (cancer, melanoma, myocardial infarction, etc.).

WEIGHT LOSS RESULTS

Final BMI (FBMI) was measured in 60% of 914 patients per year and in 30% at eight years. The mean IMCI of 49.3 fell to an

average BMI of 30 (Fig. 6), and the percentage of BMI loss (PPIMC) was 80% at 12 months (Fig. 6).

Figure 6 shows the fall in the average BMI in blue, which fell by about 30, and the % of follow-up in red.

Figure 7 shows, in blue, the expected BMI of 30 and in red, the percentage of predictive BMI depending on the range of the initial BMI and exceeding 100% from 12 months onwards.

Therefore, the %EWL has been excellent in the series and is probably better than with any other obesity operation.

It should be noted that the DS is as effective in super/supe-robese when the *%PIMC Esp* is measured as shown in figure 8.

CORRECTION OF COMORBIDITIES

Type II diabetes

The DS is a very effective operation to treat diabetes; 98% of our patients are normoglycemic, with normal glycosylated hemoglobin. Two non-diabetic patients suffered severe hypoglycemic phenomena and the BPD had to be reversed. Hypertension was corrected in 73% of cases and sleep apnea in 100%.

QUALITY OF LIFE

We use the Horia-Ardelt classification (41) of the BAROS scale to evaluate changes in patients' quality of life. Changes after surgery included: self-esteem, physical activity, social activity, work activity, and sexual activity on a scale from -1 to +1. The average score was 2.03 out of a maximum of three points in 348 patients, which means a significant improvement in their quality of life.

Gastrointestinal symptoms were rated from a minimum of 1 as *excellent* to a maximum of 5 as *very bad*. In the 558 patients assessed, food intake of all types was 1.4, vomiting 1.3, appetite 1.96, stool type (from pasty to liquid) 2.2, frequency (from unproblematic to intolerable) 1.8, stool odor 3.35 and abdominal swelling 2.26. Therefore, the sum of all measures was 12.14, for a total score of 5 (excellent) to 35 (poor). The worst side effect was the bad smell of the feces, with an average of 3.35.

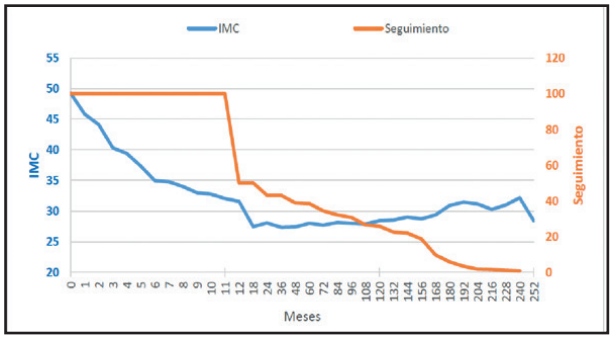

Figure 6.
BMI drop and % follow-up.

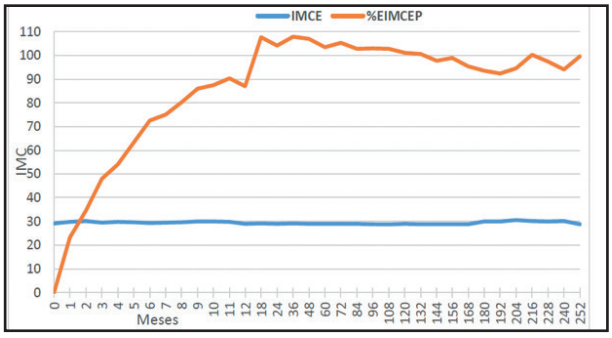

Figure 7.
The expected BMI is 30. The % of the expected BMI exceeds 100%.

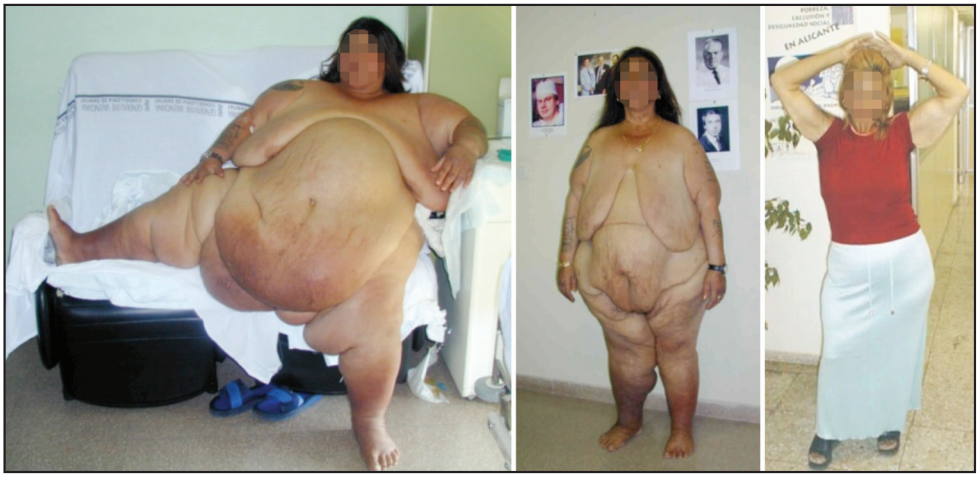

Figure 8.
This IBMI-100 patient as a SSO dropped to BMI 34.

DISCUSSION

The DS has never been a popular therapy among surgeons, possibly because of its complexity. Hess (6) describes how after watching a video of us in Seattle-1996, at the ASBS meeting, he modified the procedure with a major curvature suture and had only one leak in 188 cases (17).

Due to its difficulty, very few surgeons continued to make the DS and, in fact, a subdivision was created in the ASBS called "The Switchers", with its own logo. It remained unpopular and we had to meet, for years, outside the congress venue as a separate group of 25-30 surgeons.

On the contrary, "the switchers" have continued doing the intervention and many patients, even extranational, knew of its advantages and sought this therapy. We have not hidden the difficulties of the operation or, above all, its complications. More than 72 bariatric surgeons visited us and we have intervened live in several national and foreign congresses. Our LDS video was awarded the second prize at IFSO 2002 in Sao Paulo (42). Three patients required an emergency tracheotomy (43,44).

In 2000 we had to use one no removable rigid stent (45) for leaks and then we changed to removable ones (46). Nine patients had required a total gastrectomy (47). In three patients we used a Roux-en-Y diversion shunt (48,49) for the leaks and this is accepted today as the most effective (50).

Liver disorders (51,52) and even failures requiring transplantation (53-55) may occur, but also in gastric bypass (56), bronchial fistulas (57) or pancreatic fistulas (58), calorie-protein malnutrition (59) and the need for lengthening (60) to correct them with possible leaks (61) due to herniated defects of the intestinal wall.

At the 2004 consensus conference, Buchwald (62) stated that in OM, ideally, surgery should be considered for patients with obesity above class I (BMI 30-34.9) and associated comorbid conditions. It should have low morbidity and mortality, while providing an optimal and sustained PSP with minimal side effects. No bariatric technique is 100% successful or durable in all patients, nor is there a single standard procedure, and probably never will be. In addition, surgery cannot be the solution for the 1.7 billion OM that populate the earth.

GV leaks are a cause of significant morbidity manifested in the specific GV meetings of Deitel and Gagner (63). Prior to the 1990s, this complication was rare and CD surgeons (switchers) were the first to communicate it. The serosa inverting suture of the line of staples with omentum prevents GT torsion and leakage (13).

Figure 9.
Logo of "The Switchers".

The DS is a long and difficult procedure that requires expert and experienced surgeons. Operative mortality should be < 1% and morbidity < 5%. Our LDS mortality is low (0.38%). As patients with DS have four suture lines, early detection of leaks is essential.

Mason (64) called attention to tachycardia as the first warning sign of leakage and no patient should be discharged with tachycardia.

Duncan (65) has discharged more than 2,000 patients early in outpatient surgery programmed without a stay. Our stay after LDS is 2-3 days; we instruct (66) patients to take pulse and temperature digitally and we are notified of these parameters every four hours, for two weeks, in a telematic database. Patients with significant changes in these parameters need immediate and urgent consultation.

DeMaria (67) reported that 450 institutions and 800 surgeons participated in the BSCOE two-year (2007-2009) program. Only 0.89% of the 57,918 patients underwent LDS.

English (68) reports in ASMBS-2016 that obesity has increased alarmingly over the past five decades in the United States, from 13.4% to 36.4% in 2014. The indirect costs of obesity and the overall economic impact are estimated at $1.42 trillion, 8.2% of gross domestic product and more than double defense spending. Obesity is the fifth most important risk factor for mortality in the world. In ASMBS-2016, 215,666 operations were performed in 795 accredited centers (GV: 58.1%) and although 1,187 BPDs were made, only 0.6% were CDs and 26% LDSs.

Nelson (69), using 2007-2010 BOLD data, identified 78,951 patients undergoing GBP or CD. Of these patients, 98% had GBP and only 2% had DS. The DS was associated with longer operating times, blood loss and longer hospital stays. Early reintervention rates were higher in the DS group (3.3% *vs* 1.5%). BMI drop was significantly higher in DS cases at all follow-up intervals ($p > 0.05$). In the MO (BMI > 50) there was also a greater fall at two years, 79% DS *versus* 67% GBP. The improvement in comorbidities (diabetes, hypertension and sleep apnea) was superior with DS (all $p < 0.05$).

The reintervention rate was 14%. Reviews, including conversions, may soon exceed the number of primary procedures in bariatrics, suggesting the need to develop better evidence-based algorithms to minimize the use of new operations. It is clear that still the number of failures is very high and more effective initial operations are needed.

In 2005, Hess (9) described 1,150 patients with DS and IMCI-50.9. In 15 years there were eight reversals (0.61%) and 37 revisions (3.7%). DMII cured in 98% of patients. The 19 adolescents (aged 14-18 years) improved, advocating for DS as the best operation in adolescents. He also concluded that the DS is a safe and effective operation.

Iannelli (70), in 110 patients with BMI > 50, found a reduction in the rate of postoperative complications when performing two-stage DS. When studying the procedure, only 39 patients (35.5%) required VG and 74.5% of patients avoided BPD.

Biertho (71) made DS in 1,000 patients in 2006-2010. The conversion rate in the laparoscopy group was 2.6%. There was one postoperative death (0.1%) due to embolism. The mean hospital stay was shorter with LDS than with ODS. Complications were 7.5%, with no significant differences.

Biertho (72) treated 566 patients between 2011 and 2015 with LDS with a mean BMI of 49 and no mortality at 90 days. The average hospital stay was 4.5 days. Mayor complications greater in 30 days occurred in 3.0% of patients and minor complications in 2.5%. The %EWL was 81% at 12 months, 88% at 24 months and 83% at 36 months. Patients with HbA1C above 6% decreased from 38% to 1.4%. Readmission was 3.5% and only 0.5% of patients needed a new operation. The short- and medium-term complication rate of LDS is like in any mixed bariatric procedures with excellent metabolic results.

Biron (73) studied the quality of life of 112 patients and 8.8 years follow-up and observed improvement in the disease-specific quality of life in the short and long term.

Prachand (74) observed 152 patients with GBP with %EWL-54% in 198 patients with DS and %EWL-68% and showed that the DS was more effective.

Strain (75) states the DS provides better %EWL than DS in patients with severe obesity. Average weight decreased 31.2% after DS and 4.8% after GBP.

Topart (76.77) performed 83 DS and 97 GBP between 2002 and 2009, with IMCI-55. After three years of follow-up, the average %EWL was 63.7% after GBP and 84.0% after DS ($p > 0.0001$). Results were significantly better with DS than with GBP.

Våge (78) treated 182 consecutive patients with DS between 2001 and 2008 without 30-day mortality. One patient needed surgery due to one leak, three patients due to bleeding and one due to bile leaks. Six patients (3.2%) underwent surgical BPD revisions, reflecting data similar to ours (3.3%).

Søvik (79) showed better %EWL after DS than with GBP in OM patients. The average BMI decreased 31.2% after GBP and 44.8% after DS.

Angrisani (80) reports in 2018 that 685,874 bariatric operations were performed worldwide; 92.6% were primary interventions, 7.4% were revisions, 96% surgical and 4% endoluminal. They were VG 53.6%, GBP 30.1%, OAGB (single anastomosis gastric bypass) 4.8% and only 1.3% were LDS.

In summary, DS patients consistently reduce BMI more than GBP patients. So why are there so few DS patients?

Rabkin (81) reports that the DS is not associated with extensive nutritional deficiencies. Annual laboratory studies, following any type of bariatric operation, appear to be sufficient to identify unfavorable trends. In selected patients, additional iron and calcium supplements are necessary.

Keshishian (82) performed a preoperative needle liver biopsy on 697 patients with DS. There was transient worsening of AST (13% of baseline, $p < 0.02$) and ALT (130-160% of baseline, $p < 0.0001$) up to six months after DS. And he observed a progressive improvement of three degrees in NASH severity and 60% in hepatic steatosis at three years after DS.

TYPE II DIABETES

Buchwald (83) reports that DS and BPD have diabetes resolution rates in excess of 90%. In comparison, the GBP rate is approximately 70%. Tsoli (84) showed that VG was comparable to BPD in DTII resolution but lower in dyslipidemia and blood pressure.

In 2004, Baltasar (85) treated a patient with low BMI-35 with BPD without VG with excellent results at ten years.

Våge (86) thinks that DS is effective in DMII, hypertension and hyperlipidemia and that duration of diabetes and age are the most important preoperative predictors.

According to Eisenberg (87), refractory hyper insulinemic hypo glycaemia after surgery is very rare and its pathophysiology has not yet been fully elucidated. Partial pancreatectomy is associated with significant potential morbidity and should not be recommended. Reversion of BPD is the simplest therapy and the best operation for such hypoglycemia, and we did so for two of the patient samples.

In the staged DS, what part of the operation should be done first? The BPD or VG? Most surgeons recommend doing VG first.

Marceau (88) treated 1,762 patients from 2001 to 2009, all scheduled for DS. As the first stage he treated 48 isolated BPD without VG and 53 VG isolated cases. Long-term %EWL results and resolution of metabolic abnormalities were better with BPD alone than with isolated VG. Full DS %EWL were superior than the two-stage ones. VG and BPD contribute independently to beneficial metabolic outcomes.

Moustarah (89) treated 49 SO patients with BPD without VG. The initial weight was 144 kg and the IMCI was 52.54 kg. The drop in BMI of 14.5 kg/m^2 was very significant ($p < 0.001$).

BPD without VG has rarely been used as a single weight loss procedure, but in patients whose clinical indications justify omission of VG, isolated BPD has better weight loss results. In this series, %EWL at two years compares favorably with other bariatric operations.

The advantage is that BPD without VG is reversible, and VG can be added at any later time. We believe that, with these results in mind, we should do BPD first since it is a totally reversible procedure and easier than VG especially in SSO as it is performed in a lower part of the abdomen. The VG, in addition, can be added more easily later if necessary and at any time.

We should not forget the extraordinarily high participation of Spanish surgeons in the development of BPD techniques. Larrad and Sánchez (90,91) developed a BPD technique and made several very important publications. Thus, did Solano and Resa (92), Ballesteros (93) and Hoyuela (94).

The contribution of Sánchez-Pernaute and Torres (95) of the Hospital Clinic Hospital in making a variant of the LDS with the single anastomosis (SADI) is very important and is also becoming a popular operation worldwide.

A major problem with DS patient follow-up is that other physicians and/or surgeons may not understand how to prevent or treat their long-term complications. DS patients follow-up is very

important. Upon discharge, a detailed technical explanation of the operation is provided, as well as an extensive explanatory sheet explaining the laboratory analyses needed for life, each of the possible complications and their correction.

The determination of *serum albumin is the most important* long-term data for detecting PCM. Monitor PTH and vitamin D25 to detect calcium malabsorption and prevent pathology. Iron deficits should be treated with intravenous Fe.

In addition to leaks, the most serious long-term complication of DS is PCM. Surgical correction is simple by the jejune-jejunal anastomosis technique called "kiss-operation" to lengthen the AC, preferably by laparotomy.

MO patients should receive the DVD at the time of their operation, so that, if a new operation is necessary, the surgeon knows in detail the original technique.

The support of the Endocrinology, Nursing and Nutrition teams is essential throughout the process.

A SWITCH TO THE DUODENAL SWITCH

A wake-up call to switch to the DS

Halawani (96) states that one-third (34.9%) of United States adults are obese. In 2011-2015, the number of LDS in the United States was less than 1%. The LD should be added to the practice of the Centers of Excellence in Obesity (CEO).

DS gives a superior %EWL and has a lower rate of weight recovery. In addition, it is better than GBP, preserves the pylorus and produces slower gastric emptying. With adjustments to the length of the AC and the size of the gastric tube, any obese patient can be a DS candidate.

Patients with BMI < 50 may also be candidates. The DS is a viable option due to its flexibility. The surgeon can adjust the size of the GT and alter the impact of the restriction. The length of the CL can be variable.

The DS is good in chronic patients, who use nonsteroidal anti-inflammatory drugs and steroids. The early death rate compared with GVL (0.28%) is slightly higher (0.43%), although it is still considered as a complex high-risk procedure and the results should be viewed with caution.

The DS is *very versatile* and may offer comprehensive management of obesity and its metabolic comorbidities. With dedication, adequate training, and comprehensive education, the CD can be implemented in practice.

CONCLUSIONS

DS techniques are not common for OM management. The DS is the most complex technique and its learning curve is longer than in other operations. To standardize the technique, it took us at least 25 cases in ODS and 50 in LDS. The DS is safe and the most effective in terms of long-term weight loss results.

ETHICAL CONSIDERATIONS

All procedures involving human participants were conducted in the studies cited in this document in accordance with the ethical standards of national and institutional research committees and with the Declaration of Helsinki and its amendments.

Informed consent was obtained from all individual participants included in the studies cited.

REFERENCES

1. Scopinaro N, Gianetta E, Civalleri D, et al. Two years of clinical experience with biliopancreatic bypass for obesity. Am J Clin Nutr 1980;33:506-14.
2. Hess DS, Hess DW. Biliopancreatic diversion with a duodenal switch. Obes Surg 1998;8:267-82.
3. Hess D. Limb measurements in duodenal switch. Obes Surg 2003;13:966.
4. Marceau P, Biron S, St Georges R, et al. Biliopancreatic diversion with gastrectomy as surgical treatment of morbid obesity. Obes Surg 1991;1:381-7.
5. Marceau S, Biron S, Lagacé M, et al. Biliopancreatic diversion, with distal gastrectomy, 250 cm and 50 cm limbs: long-term results. Obes Surg 1995;5:302-7.
6. Marceau P, Biron S, Bourque RA, et al. Biliopancreatic diversion with a new type of gastrectomy. Obes Surg 1993;3:29-3.
7. Lagacé M, Marceau P, Marceau S, et al. Biliopancreatic diversion with a new type of gastrectomy: some previous conclusions revisited. Obes Surg 1995;5:411-8.
8. Marceau P, Hould FS, Simard S, et al. Biliopancreatic diversion with duodenal switch. World J Surg 1998;22:947-54.
9. Hess DS, Hess DW, Oakley RS. The biliopancreatic diversion with the duodenal switch: results beyond 10 years. Obes Surg 2005;15:408-16.
10. Baltasar A, Bou R, Bengochea M. Hybrid bariatric surgery: duodenal switch and bilio-pancreatic diversion. VCR 1996;12:16-41. Available from: www.youtube.com/watch?v=3mNnZte3W_I&feature=youtu.be
11. Baltasar M, Bou R, Cipagauta LA, et al. Hybrid bariatric surgery: bilio-pancreatic diversion and duodenal switch - Preliminary experience. Obes Surg 1995;5:419-23.
12. Baltasar A, Del Río J, Bengochea M, et al. Cirugía híbrida bariátrica: cruce duodenal en la derivación bilio-pancreática. Cir Esp 1996;59:483-6.
13. Baltasar A, Del Río J, Escrivá C, et al. Preliminary results of the duodenal switch. Obes Surg 1998;7:500-4.
14. Baltasar A, Bou R, Miró J, et al. Cruce duodenal por laparoscopia en el tratamiento de la obesidad mórbida: técnica y estudio preliminar. Cir Esp 2001;70:102-4.
15. Baltasar A, Bou R, Bengochea M, et al. Duodenal switch: an effective therapy for morbid obesity-intermediate results. Obes Surg 2001;11:54-8.
16. Baltasar A, Bou R, Bengochea M. Open duodenal switch. Video. BMI 2011;1.5.4(356-9). Available from: www.youtube.com/watch?v=h0nTzeUDl5o
17. Baltasar A. Hand-sewn laparoscopic duodenal switch. Surg Obes Relat Dis 2007;3:94-6
18. Anthone G, Lord R, DeMeester T, et al. The duodenal switch operation for the treatment of morbid obesity. Ann Surg 2003;238(4):618-28.
19. Almogy G, Crookes P, Anthone G. Longitudinal gastrectomy as a treatment for the high-risk super-obese patient. Obes Surg 2004;14:492-7.
20. Rabkin RA. Concept. The duodenal switch as an increasing and highly effective operation for morbid obesity. Obes Surg 2004;14:861-5.
21. Baltasar A. Laparoscopic sleeve gastrectomy is a misnomer. Surg Obes Relat Dis 2012;8:127-31.
22. Baltasar A. La Real Academia Nacional de Medicina dice… La "*Gastrectomía Vertical*" es el término correcto. BMI-Latina 2012;2:2-4. Available from: www.bmilatina.com
23. Biron S, Hould FS, Lebel L, et al. Twenty years of biliopancreatic diversion: what is the goal of the surgery? Obes Surg 2004;14:160-4.
24. Marceau P, Biron S, Hould FS. Duodenal switch: long-term results. Obes Surg 2007;17:1421-30.
25. Marceau P, Biron S, Hould FS, et al. Duodenal switch improved standard biliopancreatic diversion: a retrospective study. Surg Obes Relat Dis 2009;5:43-7.
26. Biertho L, Biron S, Hould FS. Is biliopancreatic diversion with duodenal switch indicated for patients with body mass index < 50 kg/m^2? Surg Obes Relat Dis 2010;6:508-15.

27. Ren CJ, Patterson E, Gagner M. Early results of laparoscopic biliopancreatic diversion with duodenal switch: a case series of 40 consecutive patients. Obes Surg 2000;10:514-23.
28. Baltasar A, Bou R, Miró J, et al. Avances en técnica quirúrgica. Cruce duodenal por laparoscopia en el tratamiento de la obesidad mórbida: técnica y estudio preliminar. Cir Esp 2001;70:102-4. Available from: www.youtube.com/watch?v=GSfzgYYxZJ8
29. Weiner RA, Blanco-Engert R, Weiner S, et al. Laparoscopic biliopancreatic diversion with duodenal switch: three different duodeno-ileal anastomotic techniques and initial experience. Obes Surg 2004;14:334-40.
30. Paiva D, Bernardes L, Suretti L. Laparoscopic biliopancreatic diversion for the treatment of morbid obesity: initial experience. Obes Surg 2001;11:619-22.
31. Scopinaro N, Marinari G, Camerini G. Laparoscopic standard biliopancreatic diversion: technique and preliminary results. Obes Surg 2002;12:241-4.
32. Baltasar A, Pérez N, Serra C, et al. Weight loss reporting: predicted BMI after bariatric surgery. Obes Surg 2011;21:367-72. DOI: 10.1007/s11695-010-0243-7
33. Molina A, Sabench F, Vives M, et al. Usefulness of Baltasar's expected body mass index as an indicator of bariatric weight loss surgery. Obes Surg 2016;26. DOI: 10.1007/s11695-016-2163-7
34. Baltasar A, Bou R, Miró J, et al. Laparoscopic biliopancreatic diversion with duodenal switch: technique and initial experience. Obes Surg 2002;12:245-8.
35. Baltasar A, Bou R, J Miró M, et al. Laparoscopic duodenal switch: technique and initial experience. Chir Gastroenterol 2003;19:54-6.
36. Baltasar A. Video case report. Hand-sewn laparoscopic duodenal switch. Surg Obes Relat Dis 2007;3:94-6.
37. Baltasar A, Bou R, Bengochea M, et al. Laparoscopic hand-sewn duodenal switch. Video. BMI-Latina 2012;2:11-3.
38. Serra C, Pérez N, Bou R, et al. Sliding self-locking first stitch and Aberdeen knots in suture reinforcement with omentoplasty of the laparoscopic gastric sleeve staple line. Obes Surg 2014;24:1739-40. DOI: 10.1007/s11695-014-1352-5
39. Baltasar A, Bou R, Serra R, et al. Use of self-locking knots in running intestinal bariatric sutures. Glob Surg 2015;2:100-1. DOI: 10.15761/GOS.1000132
40. Cuschieri A, Szabo Z, West D. Tissue approximation in endoscopic surgery: suturing and knotting. Informa Healthcare; 1995. ISBN-13: 9781899066032
41. Oria HE, Moorhead H. Updated bariatric analysis and reporting outcome system (BAROS). Surg Obes Relat Dis 2009;5:60-6.
42. Baltasar A, Bou R, Miró J, et al. Hand sutured laparoscopic duodenal switch V13. V13. Obes Surg 2002;12:483. Available from: https://www.youtube.com/watch?v=egoBphA1s90
43. Baltasar A, Bou R, Bengochea M, et al. Emergency tracheotomy in morbid obesity. Sci Forschen. Obes Open Access 2017;3(2). DOI: 10.16966/2380-5528.132
44. Baltasar A, Bou R, Bengochea M, et al. Difficult intubation and emergency tracheotomy in morbid obesity. BMI-Latina 2013;3:4-7.
45. Baltasar A. Wall-stent prosthesis for severe leak and obstruction of the duodenal switch. Obes Surg 2000;10(2):29.
46. Serra C, Baltasar A, Andreo L, et al. Treatment of gastric leaks with coated self-expanding stents after sleeve gastrectomy. Obes Surg 2007;17:866-72.
47. Serra C, Baltasar A, Pérez N, et al. Total gastrectomy for complications of the duodenal switch, with reversal. Obes Surg 2006;16:1082-6.
48. Baltasar A, Bou R, Bengochea M, et al. Use of a Roux limb to correct esophago-gastric junction fistulas after sleeve gastrectomy. Obes Surg 2007;17:1409-10.
49. Baltasar A, Serra C, Bengochea M, et al. Use of Roux limb as remedial surgery for sleeve gastrectomy fistulas. Surg Obes Relat Dis 2008;4:759-63.
50. Mcheimeche H, Dbouk S, Saheli R, et al. Double Baltazar procedure for repair of gastric leakage post-sleeve gastrectomy from two sites: case report of new surgical technique. Obes Surg 2018;28:2092-5.
51. Baltasar A, Serra C, Pérez N, et al. Clinical hepatic impairment after the duodenal switch. Obes Surg 2014;14:77-8.
52. Baltasar A. Liver cirrhosis and bariatric operations. Surg Obes Relat Dis 2006;16:579-81.
53. Baltasar A. Liver failure and transplantation after duodenal switch. Surg Obes Relat Dis 2014;10:c93-6.
54. Castillo J, Fábrega E, Escalante C, et al. Liver transplantation in a case of steatohepatitis and subacute hepatic failure after biliopancreatic obesity surgery diversion for morbid obesity. Obes Surg 2001;11:640-2.
55. Cazzo E, Pareja JC, Chaim EA. Falencia hepática após derivações bilio-pancreáticas: uma revisão narrativa. Sao Paulo Med J 2017;135. E-pub: Nov 10th, 2016. DOI: 10.1590/1516-3180.2016.0129220616
56. Ossorio M, Pacheco JM, Pérez D, et al. hepático fulminante a largo plazo en pacientes sometidos a bypass gástrico por obesidad mórbida. Nutr Hosp 2015;32:430-43.
57. Díaz M, Garcés M, Calved J, et al. Gastro-bronchial fistula: long term or very long-term complications after bariatric surgery. BMI-Latina 2011;5:335-7.
58. Bueno J, Pérez N, Serra C, et al. Fistula pancreato-cutánea secundaria a pancreatitis postoperatoria tras cruce duodenal laparoscópico. Cir Esp 2004;76:184-6.
59. Baltasar A, Bou R, Bengochea M, et al. Malnutrición calórico-proteica. Tres tipos de alargamiento de asa común. BMI-Latina 2011;5:96-7.
60. Baltasar A, Serra C. Treatment of complications of duodenal switch and sleeve gastrectomy. In: Deitel M, Gagner M, Dixon JB, et al. (eds.). Handbook of obesity surgery. Toronto: FD Comunicación; 2010. pp. 156-61.
61. Baltasar A, Bou R, Bengochea M. Fatal perforations in laparoscopic bowel lengthening operations for malnutrition. Surg Obes Relat Dis 2010;6:572-4. Available from: www.youtube.com/watch?v=Hw_aPYLjGXI
62. Buchwald H. 2004 ASBS. Consensus conference statement bariatric surgery for morbid obesity: health implications for patients, health professionals, and third-party payers. Surg Obes Relat Dis 2005;1:371-81.
63. Dietel M, Gagner M, Erickson AL, et al. Third International Summit. Current status of sleeve gastrectomy. Surg Obes Relat Dis 2011;7:749-59.
64. Mason R. Diagnosis and treatment of rapid pulse. Obes Surg 1995;3:341.
65. Duncan T, Tuggle K, Larry Hobson L, et al. PL-107. Feasibility of laparoscopic gastric bypass performed on an outpatient basis. Surg Obes Relat Dis 2011;7:339-54.
66. Baltasar A. WhatsApp© Assistance in bariatric surgery. J Obes Eating Disord 2017;3(1)28. ISSN: 2471-8203. DOI: 10.21767/2471-8513.100017
67. DeMaria E, Pate V, Warthen M, et al. Baseline data from American Society for Metabolic and Bariatric Surgery - Designated bariatric surgery centers of excellence using the Bariatric Outcomes Longitudinal Database. Surg Obes Relat Dis 2010;6:347-35.
68. English W, DeMaria M, Brethauer SA, et al. American Society for Metabolic and Bariatric Surgery estimation of metabolic and bariatric procedures performed in the United States in 2016. Surg Obes Relat Dis 2018;14:259-63.
69. Nelson D, Blair KS, Martin M. Analysis of obesity-related outcomes and bariatric failure rates with the duodenal switch vs gastric bypass for morbid obesity. Arch Surg 2012;147:847-54.
70. Iannelli A, Schneck AS, Topart P, et al. Laparoscopic sleeve gastrectomy followed by duodenal switch, in selected patients versus single-stage duodenal switch for super-obesity: case-control study. Surg Obes Relat Dis 2013;9:531-8.
71. Biertho L, Lebel S, Marceau S, et al. Perioperative complications in a consecutive series of 1000 duodenal switches. Surg Obes Relat Dis 2013;9:63-8.
72. Biertho L, SimonHould F, Marceau S, et al. Current outcomes of laparoscopic duodenal switch. Ann Surg Innov Res 2016;10:1. DOI: 10.1186/s13022-016-0024-7
73. Biron S, Biertho L, Marceau S. Long-term follow-up of disease-specific quality of life after bariatric surgery. Surg Obes Relat Dis 2018;14(5):658-64. Accepted SOARD 3291.
74. Prachand V, DaVee R, Alberdy JA. Duodenal switch provides superior weight loss in the super-obese (BMI $>$ 50) compared with gastric bypass. Ann Surg 2006;244:611-9.
75. Strain CW, Gagner M, Inabnet WB, et al. Comparison of effects of gastric bypass and biliopancreatic diversion with duodenal switch on weight loss and body composition 1-2 years after surgery. Surg Obes Relat Dis 2007;3:31-6.
76. Topart P, Becouarn G, Salle A. Five-year follow-up after biliopancreatic diversion with duodenal Switch. Surg Obes Relat Dis 2011;7:199-205.
77. Topart P, Becouarn G, Ritz P. Weight loss is more sustained after bilio-pancreatic diversion with duodenal switch than Roux-en-Y gastric bypass in super-obese patients. Surg Obes Relat Dis 2013;9:526-30.
78. Våge V, Gåsdal R, Lakeland C, et al. The biliopancreatic diversion with a duodenal switch (BPDDS): how is it optimally performed? Obes Surg 2011;21:1864-9.
79. Søvik T, Karlsson J, Aasheim E, et al. Gastrointestinal function and eating behavior after gastric bypass and duodenal switch. Surg Obes Relat Dis 2013;9:641-7.
80. Angrisani L, Santonicola A, Iovino P, et al. Bariatric Surgery Worldwide 2013. Obes Surg 2015;25:1822-32. DOI: 10.1007/s11695-015-1657-z
81. Rabkin R, Rabkin JM, Metcalf B, et al. Nutritional markers following duodenal switch for morbid obesity. Obes Surg 2004;14:84-90.
82. Keshishian A, Zahriya K, Willes EB. Duodenal switch has no detrimental effects on hepatic function and improves hepatic steatohepatitis after 6 months. Obes Surg 2005;15:1418-23.

83. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med 2009;122:248-56.e5.
84. Tsoli M, Chronaiou A, Kehagias I. Hormone changes and diabetes resolution after biliopancreatic diversion and laparoscopic sleeve gastrectomy: a comparative prospective study. Surg Obes Relat Dis 2013;9:667-78.
85. Baltasar A. Historical note: first diabetes metabolic operation in Spain. Integr Obes Diabetes 2015;2:180-2. DOI: 10.15761/IOD.1000140
86. Våge V, Roy M, Nilsen M, et al. Predictors for remission of major components of the metabolic syndrome after biliopancreatic diversion with duodenal switch. Obes Surg 2013;23:80-6. DOI: 10.1007/s11695-012-0775
87. Eisenberg D, Azagury D, Ghiassi S, et al. ASMBS statement on postprandial hyper-insulinemic hypoglycemia after bariatric surgery. Surg Obes Relat Dis 2017;371-8.
88. Marceau P, Biron S, Marceau S, et al. Biliopancreatic diversion-duodenal switch: independent contributions of sleeve resection and duodenal exclusion. Obes Surg 2014;24:1843-9.DOI: 10.1007/s11695-014-1284-0
89. Moustarah F, Marceau S, Lebel S, et al. Weight loss after duodenal switch without gastrectomy for the treatment of severe obesity: review of a single institution case series of duodeno-ileal intestinal bypass. Can J Surg 2010;53(4):S51.-
90. Larrad A, Moreno B, Camacho A. Resultados a los dos años de la técnica de Scopinaro en el tratamiento de la obesidad mórbida. Cir Esp 1995;58:23-2.
91. Larrad A, Sánchez-Cabezudo C, De Cuadros Borrajo P, et al. Short-, mid- and long-term results of Larrad biliopancreatic diversion. Obes Surg 2007;17:202-10.
92. Solano J, Resa JJ, Fatas JA, et al. Derivación bilio-pancreática laparoscópica para el tratamiento de la obesidad mórbida. Aspectos técnicos y análisis de los resultados preliminares. Cir Esp 2003;74(6):347-50.
93. Ballesteros M, González T, Urioste A. Biliopancreatic diversion for severe obesity: long-term effectiveness and nutritional complications. Obes Surg 2016;26:38-44. DOI: 10.1007/s11695-015-1719-2
94. Hoyuela C, Veloso E, Marco C. Derivación bilio-pancreática con cruce duodenal y su impacto en las complicaciones posoperatorias. Cir Esp 2006;80(Supl 1):1-250 175.
95. Sánchez-Pernaute A, Rubio M, Torres A, et al. Proximal duodenal-ileal end-to-side bypass with sleeve gastrectomy: proposed technique. Obes Surg 2007;17:1614-8. DOI: 10.1007/s11695-007-9287-8
96. Halawani HM, Antanavicius G, Bonanni F. How to switch to the switch: implementation of biliopancreatic diversion with duodenal switch into practice. Obes Surg 2017;27(9):2506-9. DOI: 10.1007/s11695-017-2801-8

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Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Influencia de la variante rs670 del gen *APOA1* en la respuesta HDL sérica a una dieta hipocalórica enriquecida con grasas poliinsaturadas frente a una enriquecida con grasas monoinsaturadas

Influence of rs670 variant of APOA1 *gene on serum HDL response to an enriched-polyunsaturated* vs. *an enriched-monounsaturated fat hypocaloric diet*

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Resumen

Antecedentes y objetivos: las variantes genéticas del gen *APOA1* se han relacionado con el perfil lipídico en sujetos obesos. Nuestro objetivo fue analizar los efectos del polimorfismo del gen rs670 *APOA1* sobre el estado metabólico tras la ingesta de dos dietas hipocalóricas enriquecidas con grasas poliinsaturadas o con grasas monoinsaturadas.

Métodos: trescientos sesenta sujetos obesos se asignaron al azar a dos grupos de intervención. Un grupo recibió una dieta enriquecida en grasas poliinsaturadas (dieta P) y el otro grupo una dieta enriquecida en grasas monoinsaturadas (dieta M) durante 12 semanas. Se evaluaron los efectos sobre los biomarcadores relacionados con el metabolismo lipídico y de hidratos de carbono antes y después de la intervención.

Resultados: el índice de masa corporal, el peso, la masa grasa, la circunferencia de la cintura, la presión arterial sistólica, las concentraciones plasmáticas de leptina y la circunferencia de la cintura disminuyeron en todos los pacientes tras ambas dietas. En los portadores del alelo A, después de 12 semanas con la dieta P, los niveles de insulina (delta: -7,3 ± 2,2 UI/l; p = 0,01) y HOMA-IR (delta: -2,8 ± 0,5 unidades; p = 0,02) mejoraron de manera significativa. Tras el tratamiento con la dieta M, los niveles plasmáticos de insulina (delta: -5,9 ± 1,2 UI/l; p = 0,01) y HOMA-IR (delta: -2,1 ± 0,8 unidades; p = 0,02) también mejoraron en los portadores del alelo A. Después de la intervención dietética con la dieta P, el colesterol-LDL (delta: -12,1 ± 4,3 UI/l; p = 0,01) y el colesterol-HDL (delta: 2,6 ± 0,7 unidades; p = 0,01) disminuyeron significativamente en los portadores del alelo A.

Conclusiones: nuestro estudio mostró la asociación del polimorfismo rs670 *ApoA1* con los cambios de resistencia a la insulina inducidos por ambas dietas y aportó evidencia adicional sobre la mejoría del colesterol-HDL y el colesterol-LDL después de una dieta rica en grasas poliinsaturadas en los portadores del alelo A.

Palabras clave:

rs670. Gen *ApoA1*. Perfil lipídico. Dieta hipocalórica. Grasa monoinsaturada. Grasa poliinsaturada.

Abstract

Background and objectives: genetic variants of the *APOA1* gene have been related to lipid profile in obese subjects. Our aim was to analyze the effects of the rs670 *APOA1* gene polymorphism on metabolic changes secondary to an enriched-polyunsaturated fat *vs.* an enriched-monounsaturated fat hypocaloric diet.

Methods: 360 Caucasian obese subjects were randomly allocated to two groups. One group received an enriched-polyunsaturated fat (diet P) and the other an enriched-monounsaturated fat hypocaloric diet (diet M) during 12 weeks. The effects on serum biomarkers related to lipid and carbohydrate metabolism were evaluated before and after the dietary intervention.

Results: after both diets, body mass index, weight, fat mass, waist circumference, systolic blood pressure, plasma leptin concentration, and waist circumference decreased in all patients. After 12 weeks of intervention with diet P, plasma insulin levels and HOMA-IR decreased in A-allele carriers: delta: -7.3 ± 2.2 IU/L (p = 0.01), and delta: -2.8 ± 0.5 units (p = 0.02), respectively. The same changes in delta were observed after diet M in A-allele carriers: insulin delta: -5.9 ± 1.2 IU/L (p = 0.01), and HOMA-IR delta: -2.1 ± 0.8 units (p = 0.02). In A-allele carriers, LDL-cholesterol decreased and HDL-cholesterol increased after the dietary intervention with diet P: delta: -12.1 ± 4.3 mg/dL (p = 0.01), and delta: 2.6 ± 0.7 mg/dL (p = 0.01), respectively. No differences in lipid profile were observed after diet M. These improvements were not observed in non-A-allele carriers after both interventions.

Conclusions: our study showed the association of the rs670 *ApoA1* polymorphism with insulin resistance changes as induced by both diets. An enriched-polyunsaturated fat diet produced an additional improvement of HDL-cholesterol and LDL-cholesterol in A-allele carriers.

Key words:

rs670. *ApoA1* gene. Lipid profile. Hypocaloric diet. Monounsaturated fat. Polyunsaturated fat.

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INTRODUCCIÓN

La interacción entre genes y dieta ha cobrado mucha importancia en el desarrollo de la obesidad y de sus complicaciones metabólicas, aunque el efecto de ambos puede ser muy diferente. Por ejemplo, en un estudio de gemelos se detectó que el colesterol unido a lipoproteínas de alta densidad (C-HDL) estaba significativamente elevado en los gemelos monocigóticos frente a los dicigóticos, mostrando un claro efecto de la genética sobre el perfil lipídico (1). Por otra parte, las recomendaciones dietéticas para controlar el perfil lipídico y reducir el riesgo cardiovascular son un pilar fundamental para tratar a estos pacientes, realizándose modificaciones en el aporte calórico, el aporte de grasas total, el aporte de grasas saturadas y el de colesterol (2). Finalmente, la variabilidad en la respuesta a la dieta tiene un fuerte componente genético (3).

La apolipoproteína ApoA1 es la principal proteína del colesterol-HDL y juega un importante papel en el metabolismo de los lípidos. Las dos principales funciones de la ApoA1 son: activar la enzima lecitina-colesterol-aciltransferasa (4) y ser el principal componente de la vía de transporte del colesterol (5). El gen *ApoA1* se localiza en el brazo largo del cromosoma 11 y es muy polimórfico. Se han descrito 9 polimorfismos de un único nucleótido (SNP, por sus siglas en inglés) relacionados con el metabolismo de los lípidos (6). Algunos trabajos previos han mostrado una reducción del riesgo cardiovascular y un incremento de los niveles de colesterol-HDL secundarios a la sobreexpresión de *APOA1* secundaria a una dieta rica en grasa (7). Se ha descrito una mutación de una adenina (A) a guanina (G) (G/A) en la posición 75bp (rs670) del gen *ApoA1* en la zona de inicio de la transcripción (8). Existe controversia sobre el efecto del alelo A de esta variante genética y, en un estudio, el alelo A se relacionó con niveles elevados de ApoA1 y colesterol-HDL (9). Sin embargo, en otros trabajos no se encontró esa asociación (10,11).

Algunos estudios de intervención nutricional han evaluado el efecto de esta variante genética en las modificaciones de lípidos. En un estudio se ha demostrado que la variante rs670 tiene un efecto directo sobre la respuesta de los niveles de colesterol-LDL a las modificaciones dietéticas de los lípidos (12). Philips y cols. (13) han demostrado que la variante rs670 de *ApoA1* puede influir en el riesgo de síndrome metabólico secundario a la cantidad de grasa de la dieta. Recientemente, nuestro grupo ha demostrado un efecto del alelo A sobre los niveles de colesterol-LDL, insulina y HOMA-IR tras una dieta hipocalórica de patrón mediterráneo (14). Quizás la cantidad de grasas o su calidad (saturadas, monoinsaturadas o poliinsaturadas) podría explicar la variabilidad de la respuesta a la intervención dietética interactuando con esta variante genética.

Nuestro objetivo fue analizar el efecto del polimorfismo rs670 de *APOA1* en los niveles de lípidos y los cambios metabólicos secundarios a dos dietas hipocalóricas, una rica en grasa monoinsaturada y otra en grasa poliinsaturada.

MATERIAL Y MÉTODOS

SUJETOS

En este trabajo reclutamos pacientes de entre 25 y 65 años (360 sujetos de raza blanca), con IMC (índice de masa corporal) ≥ 30 kg/m^2, procedentes de la atención primaria de una área rural y urbana de España. El comité de ensayos clínicos (Hospital Clinico Universitario de Valladolid (HCUVA)) aprobó el protocolo y todos los sujetos firmaron el consentimiento informado antes de su inclusión en el estudio. Este trabajo se realizó teniendo en cuenta las normas de la Declaración de Helsinki.

El reclutamiento de los pacientes obesos se llevó a cabo mediante un método consecutivo y no probabilístico aplicado a los pacientes remitidos desde Atención Primaria con IMC > 30 kg/ m^2 y edad comprendida entre 25 y 65 años, siendo por tanto la edad y el IMC los dos únicos criterios de inclusion. Los criterios de exclusión fueron: historia de cáncer con tratamiento activo, pérdida de peso mayor del 5-10% en los últimos 3 meses, colesterol total ≥ 200 mg/dl, triglicéridos ≥ 150 mg/dl, presión arterial ≥ 140/90 mm Hg y uso de los siguientes tratamientos: metformina, sulfonilureas, inhibidores de la dipeptidil-peptidasa 4, tiazolidinedionas, análogos del receptor de GLP-1, inhibidores del trasportador iSGLT-2, insulina, glucocorticoides, bloqueadores del receptor de angiotensina, inhibidores de la enzima convertidora de angiotensina, medicación psicoactiva, estatinas y otros fármacos hipolipemiantes.

DISEÑO EXPERIMENTAL E INTERVENCIÓN DIETÉTICA

Todos los sujetos fueron aleatorizados mediante un método de aleatorización simple para recibir una de las siguientes dos dietas durante un periodo de 12 semanas: dieta P (dieta hipocalórica rica en grasas poliinsaturadas (PUFA): 45,7% de carbohidratos, 34,4% de lípidos y 19,9% de proteínas) y dieta M (dieta hipocalórica rica en grasas monoinsaturadas: 46,6% de carbohidratos, 34,1% de lípidos y 19,2% de proteínas). Dichas dietas representaban una restricción calórica de alrededor de 500 calorías/día con respecto a la cantidad previa. La distribución de grasa en la dieta P fue: 21,8% de grasa saturada, 55,5% de grasa monoinsaturada y 22,7% de grasa poliinsaturada (7 g/día de ω-6, 2 g/día de ω-3 y una ratio ω-6/ω-3 de 3,5). El patrón de la dieta fue mediterráneo, con 3 porciones cada semana de pescado azul y 30 gramos de nueces diarios. La distribución de grasas en la dieta M fue: 21,7% de grasa saturada, 67,5% de grasa monoinsaturada y 10,8% de grasa poliinsaturada. El patrón de esta dieta fue también mediterráneo, incluyendo el consumo de aceite de oliva virgen de manera libre. Todos los sujetos recibieron dos sesiones individuales (45 minutos de duración y ejemplos de menús) con una dietista al inicio del estudio con el fin de explicar la dieta y resolver las dudas. La dietista evaluó la adherencia a la dieta cada

dos semanas mediante contactos telefónicos. La dietista también efectuó registros de la ingesta de tres días consecutivos (antes y a los 3 meses de la intervención) incluyendo un día de fin de semana; la ingesta se evaluó usando el programa DietSource® (General Software), basándose en tablas nacionales de composición de alimentos (15). El ejercicio físico consistió en actividades aeróbicas al menos 3 veces a la semana (60 minutos). El propio sujeto, usando un autorregistro, recogió su actividad física diaria.

En el momento basal y tras 12 semanas de la intervención dietética, todos los sujetos recibieron las siguientes evaluaciones: exploración física, valoración antropométrica y análisis bioquímico. El análisis antropométrico incluía: peso, talla, IMC, circunferencia de la cintura y masa grasa por impedancia. La presión arterial sistólica y diastólica también se determinó en ambos tiempos.

En el tiempo basal y tras 12 semanas se extrajeron muestras sanguíneas en tubos con EDTA tras 12 horas de ayuno para determinar las concentraciones plasmáticas de insulina, colesterol total, colesterol-LDL, colesterol-HDL, triglicéridos y adipocitoquinas (leptina, adiponectina y resistina). La variante del gen *ApoA1* fue determinada en el momento basal mediante la reacción en cadena de la polimerasa en tiempo real.

DETERMINACIONES ANTROPOMÉTRICAS Y TENSIÓN ARTERIAL

El peso y la talla se determinaron mediante un peso y tallímetro electrónico (Omrom, LA, CA, EE. UU.). El peso se midió por la mañana con los sujetos sin ropa ni zapatos. El IMC se calculó dividiendo el peso en kg entre la talla en metros al cuadrado. La circunferencia de la cintura se midió con una cinta métrica (Type SECA, SECA, Birmingham, Reino Unido). Se efectuó una bioimpedanciometría para determinar la composición corporal con una precisión de 5 g (16) (EFG, Akern, Italia).

GENOTIPADO

Las muestras sanguíneas para el genotipado de los sujetos se obtuvieron al principio del estudio y el ADN se extrajo utilizando un kit al uso de acuerdo con el protocolo habitual (Biorad, LA, CA, EE. UU.). La cantidad y calidad del material extraído se determinaron mediante un espectrofotómetro NanoDrop ND-1000 (Bio-Rad®, San Diego, CA, EE. UU.). Los cebadores (*primers*) que se utilizaron fueron los del Sequenom Assay Design v.4 (SEQUENOM, Inc., San Diego, CA, EE. UU.). El genotipado de la variante rs670 se llevó a cabo mediante la reacción en cadena de la polimerasa. Esta reacción se realizó con 30 ng de ADN genómico, 0.1-0.15 µl de cada cebador de rs670 (*primer forward*: 5′- ACGTTGGATGAAGTTCCACATTGCCAGGAC-3′ y *reverse* 5′- ACGTTGGATGCAGGGCCTATTTATGTCTGC-3′ en un volumen final de 2,5 µl (termociclador Life Tecnologies, LA, CA, EE. UU.). El ADN se desnaturalizó a 85 °C durante 5 min, y se realizaron 45 ciclos a 65 °C durante 15 segundos, con reacción de anillamiento a 58,1 °C durante 45 segundos. El equilibrio de Hardy-Weinberg se calculó mediante la prueba del chi cuadrado y se observó que la variante del gen *ApoA1* estaba en equilibrio (p = 0,37).

DETERMINACIONES BIOQUÍMICAS

Las muestras sanguíneas venosas se recogieron en tubos con EDTA tras 12 horas de ayuno en dos tiempos: basal y a las 12 semanas. Los niveles plasmáticos de glucosa, colesterol total y triglicéridos, y el perfil lipídico (colesterol total y colesterol unido a lipoproteínas de alta densidad (C-HDL)) se determinaron usando un autoanalizador (Hitachi 7060, Tokio, Japón). El colesterol-LDL se calculó usando la fórmula de Friedewald (17). La glucosa se midió con una reacción enzimática colorimétrica (método de la glucosa-oxidasa). La insulina se determinó mediante radioinmunoensayo (RIA) (RIA Diagnostic Corporation, Los Angeles, CA, EE. UU.) con una sensibilidad de 0,5 mUI/l (rango: 0,5-30 mUI/l) (18). La resistencia a la insulina, utilizando el método *Homeostasis model assessment of insulin resistance* (HOMA-IR), se calculó con la siguiente fórmula: HOMA-IR = (insulina x glucosa)/22,5 (19).

Los niveles llamativos de adipocitoquinas se determinaron mediante enzimoinmunoensayo (ELISA). El kit de leptina (Diagnostic Systems Laboratories, Inc., Texas, EE. UU.) (DSL1023100) tiene una sensibilidad de 0,05 ng/ml, un rango de 10-100 ng/ml y un CV% del 3,5% (20). El kit de adiponectina (R&D Systems, Inc., Mineápolis, EE. UU.) (DRP300) tiene una sensibilidad de 0,246 ng/ml, un rango de 8,65-21,43 ng/ml y un CV% del 3,8% (21). El kit de resistina (Biovendor Laboratory, Inc., Brno, República Checa) (RD191016100) tiene una sensibilidad de 0,2 ng/ml, un rango de 4-12 ng/ml (22) y un CV% del 3,2%.

ANÁLISIS ESTADÍSTICO

Los datos se analizaron con el programa SPSS para Windows, versión 19.0 (SPSS Inc., Chicago, IL, EE. UU.). El tamaño de la muestra se calculó para detectar una diferencia de 3,5 mg/dl en los niveles de colesterol-HDL tras la intervención dietética, con un poder del 90% y una significación del 5% (n = 170 en cada grupo). El test de Kolmogorov-Smirnov se usó para determinar la distribución de las variables. Los resultados se expresaron como media ± desviación estándar. Las variables con distribución normal se analizaron con el test de Student. Las variables no paramétricas se analizaron con el test de la U de Mann-Whitney (glucosa, triglicéridos, adiponectina y leptina). Las variables categóricas se analizaron con el chi cuadrado, más la corrección de Yates cuando fue necesario, y el test de Fisher. El análisis estadístico para evaluar la interacción gen-dieta fue un ANCOVA únicamente ajustado según la actividad física, la edad y el sexo. El test del chi cuadrado se usó para evaluar el equilibrio de Hardy-Weinberg. Todos los análisis se realizaron con un modelo dominante con el alelo A como alelo de riesgo (AA + AG *vs.* GG). El valor de $p < 0,05$ se consideró como significativo.

RESULTADOS

Se reclutaron en total 360 sujetos. La edad media fue de 50,1 ± 7,2 años (rango: 28-63) y el IMC medio fue de 36,6 ± 3,2 kg/m^2 (rango: 32,1-39,8). En total, 247 sujetos (68,6%) tenían el genotipo GG, 101 sujetos tenían el GA (29,1%) y 12 sujetos tenían el AA (3,3%). La edad media fue similar en los 3 genotipos (GG: 50,2 ± 9,0 años *vs.* GA: 49,1 ± 8,2 años *vs.* AA: 50,1 ± 8,1 años; no significativo).

Entre los 174 sujetos tratados con la dieta P, 120 (68,9%) tenían el genotipo GG (genotipo salvaje, no portadores del alelo A), 48 (27,5%) sujetos tenían el genotipo GA y 6 (3,6%) sujetos tenían el genotipo AA; los portadores del alelo A (GA + AA) son los que presentan el genotipo mutante. La encuesta nutricional basal mostró una ingesta calórica de 1982,1 ± 612,1 cal/día, siendo los carbohidratos de 201,1 ± 53,9 g/día (43,5% de las calorías), las grasas de 82,0 ± 22,3 g/día (36,2%) y las proteínas de 85,1 ± 30,9 g/día (20,3%). Durante la intervención, estos sujetos alcanzaron las recomendaciones de la dieta P; 1448,1 calorías (45,1% de carbohidratos, 34,3% de grasas y 20,6% de proteínas). La distribución de grasas fue del 20,5% de grasas saturadas, 54,0% de monoinsaturadas y 23,5% de poliinsaturadas (6,9 g por día de ω-6, 1.8 g de ω-3 y una ratio ω-6/ω-3 de 3,7). La actividad física fue similar en ambos genotipos (59,1 ± 21,3 min/semana *vs.* 60,9 ± 19,2 min/semana; p = 0,76).

Entre los 186 sujetos que recibieron la dieta M, 127 (62,8%) presentaban los alelos GG (genotipo salvaje, no portadores del alelo A), otros 53 (28,5%) presentaban el GA y 6 (3,3%) tenían el AA; los portadores del alelo A (GA + AA) son los que presentan el genotipo mutante. La evaluación de la ingesta mostró los siguientes valores: calorías, 2001,9 ± 316,1 cal/día; carbohidratos, 198,1 ± 19,3 g/día (43,2% de las calorías); grasas, 62,3 ± 12,3 g/día (33,7%), y proteínas, 78,0 ± 17,0 g/día (23,1%). Durante la intervención dietética, los sujetos alcanzaron las recomendaciones de la dieta M: 1446,1 calorías (45,2% de carbohidratos, 33,9% de grasas y 20,9% de proteínas). La distribución de grasas fue: 20,3% de grasas saturadas, 67,9% de monoinsaturadas y 11,8% de poliinsaturadas. La actividad física fue similar en los dos genotipos (62,1 ± 14,3 min/semana *vs.* 60,3 ± 17,9 min/semana; p = 0,63).

La tabla I muestra los parámetros antropométricos y los niveles de presión arterial en ambos tiempos (basal y a las 12 semanas). En ambos genotipos (GG *vs.* GA + AA), el peso, el IMC, la masa grasa, la circunferencia de la cintura y la presión arterial sistólica disminuyeron de manera significativa. Tras 12 semanas con la dieta rica en grasas poliinsaturadas (dieta P, GG *vs.* GA + AA), los valores de IMC (delta: -1,6 ± 0,5 kg/m^2 *vs.* -1,3 ± 0,5 kg/ m^2;

Tabla I. Modificaciones en las variables antropométricas (media, DE)

Variables	Rs670									
	Dieta P (n = 174)				p Tiempo Genotipo Genotipo x tiempo	Dieta M (n = 186)				p Tiempo Genotipo Genotipo x tiempo
	GG	GA + AA	GG			GA + AA				
	Basal	3 meses	Basal	3 meses		Basal	3 meses	Basal	3 meses	
IMC	36,7 ± 4,6	35,1 ± 3,0*	36,3 ± 4,9	35,0 ± 4,1*	p = 0,008 p = 0,27 p = 0,03	36,3 ± 4,1	35,0 ± 3,9*	36,4 ± 4,0	35,1 ± 4,1*	p = 0,007 p = 0,41 p = 0,01
Peso (kg)	94,7 ± 13,3	91,2 ± 9,0†	94,0 ± 13,1	91,5 ± 8,1†	p = 0,009 p = 0,31 p = 0,01	92,4 ± 9,1	88,1 ± 7,2†	93,2 ± 8,0	89,0 ± 8,2†	p = 0,009 p = 0,43 p = 0,02
Masa grasa (kg)	41,5 ± 7,1	39,5 ± 7,0‡	39,6 ± 5,1	37,2 ± 4,8‡	p = 0,01 p = 0,46 p = 0,02	39,3 ± 0,1	37,3 ± 6,0‡	39,6 ± 7,2	36,6 ± 6,1‡	p = 0,01 p = 0,43 p = 0,03
CC (cm)	109,3 ± 7,1	106,1 ± 8,0§	107,8 ± 8,0	105,0 ± 6,1§	p = 0,01 p = 0,51 p = 0,02	108,5 ± 8,1	102,5 ± 3,9§	109,3 ± 6,1	105,0 ± 6,3§	p = 0,01 p = 0,54 p = 0,02
TAS (mm Hg)	126,1 ± 11,8	121,8 ± 9,1‖	130,1 ± 9,2	124,7 ± 8,0‖	p = 0,01 p = 0,34 p = 0,03	127,9 ± 4,8	123,9 ± 5,2‖	129,2 ± 3,1	125,1 ± 5,1‖	p = 0,01 p = 0,35 p = 0,02
TAD (mm Hg)	82,1 ± 5,0	80,0 ± 4,2	82,8 ± 4,9	82,1 ± 4,3	p = 0,41 p = 0,54 p = 0,56	82,7 ± 4,0	82,1 ± 3,0	83.7 ± 5,0	83,6 ± 4,1	p = 0,54 p = 0,70 p = 0,46

*IMC: índice de masa corporal; TAS: tensión arterial sistólica; TAD: tensión arterial diastólica; CC: circunferencia de la cintura; diferencias estadísticamente significativas en cada genotipo (*IMC; †peso, ‡masa grasa; §CC; ‖TAS). No hay diferencias estadísticamente significativas entre diferentes genotipos.*

p < 0,05), peso (delta: -3,5 ± 1,0 kg *vs.* -4,0 ± 1,5 kg; p < 0,05), masa grasa (delta: -2,0 ± 0,9 kg *vs.* -2,4 ± 1,1 kg; p < 0.05), circunferencia de la cintura (delta: -3,2 ± 1,0 cm *vs.* -2,9 ± 1,1 cm; p < 0,05) y presión arterial sistólica (delta: -5,3 ± 1,9 mm Hg *vs.* -5,4 ± 1,1 mm Hg; p < 0,05) disminuyeron. Tras la intervención con la dieta rica en grasas monoinsaturadas (dieta M, GG *vs.* GA + AA), los valores de IMC (delta: -1,3 ± 0,5 kg/m^2 vs. -1,3 ± 0,6 kg/m^2; p < 0,05), peso (delta: -4,4 ± 1,1 kg *vs.* -4,2 ± 0,7 kg; p < 0,05), masa grasa (delta: -2,1 ± 0,9 kg *vs.* -3.0 ± 1.4 kg; p < 0,05), circunferencia de la cintura (delta: -6,0 ± 2,9 cm *vs.* -4,4 ± 1,8 cm; p < 0,05) y presión arterial sistólica (delta: -4,0 ± 0,5 mm Hg *vs.* -4,1 ± 1,1 mm Hg; p < 0,05) disminuyeron también. Las mejorías de los parámetros mencionados fueron similares con ambas dietas. Finalmente, las intervenciones durante 12 semanas con ambas dietas produjeron mejorías en los parámetros de adiposidad y presión arterial sistólica, similares en ambos genotipos.

La tabla II muestra los parámetros bioquímicos. Los valores basales y post-intervención del colesterol-HDL fueron superiores en los sujetos portadores del alelo A en ambos grupos dietéticos. En los portadores del alelo A, después de 12 semanas tratados con la dieta P, los niveles de insulina (delta: -7,3 ± 2,2 UI/l; p = 0,01) y HOMA-IR (delta: -2,8 ± 0,5 unidades; p = 0,02) mejoraron de manera significativa. Tras el tratamiento con la dieta M, los niveles plasmáticos de insulina (delta: -5,9 ± 1,2 UI/l; p = 0,01) y HOMA-IR (delta: -2,1 ± 0,8 unidades; p = 0,02) también mejoraron en los portadores del alelo A. Estas mejorías significativas no se observaron en los sujetos no portadores del alelo A.

En los sujetos portadores del alelo A, los niveles de colesterol-LDL disminuyeron y los niveles de colesterol-HDL aumentaron tras la intervención dietética con la dieta P (delta: -12,1 ± 4,3 mg/dl (p = 0,01) y delta: 2,6 ± 0,7 mg/dl (p = 0,01), respectivamente) pero no tras la intervención dietética con la

Tabla II. Parámetros bioquímicos (media, DE)

Variables	rs670									
	Dieta P (n = 174)				p Tiempo Genotipo Genotipo x tiempo	Dieta M (n = 186)				p Tiempo Genotipo Genotipo x tiempo
	GG		GA + AA			GG		GA + AA		
	Basal	3 meses	Basal	3 meses		Basal	3 meses	Basal	3 meses	
Glucosa (mg/dl)	100,1 ± 9,1	98,1 ± 11,9	98,8 ± 7,0	96,5 ± 8,3	p = 0,50 p = 0,69 p = 0,28	101,3 ± 6,8	97,9 ± 9,1	101,9 ± 7,2	100,3 ± 9,1	p = 0,50 p = 0,69 p = 0,21
Colesterol total (mg/dl)	202,5 ± 31,8	197,5 ± 33,1	206,8 ± 11,7	195,3 ± 10,2	p = 0,05 p = 0,34 p = 0,10	199,8 ± 10,7	186,2 ± 13,2	210,6 ± 11,7	200,8 ± 9,2	p = 0,54 p = 0,69 p = 0,18
Colesterol-LDL (mg/dl)	130,8 ± 31,1	125,3 ± 30,1	127,1 ± 9,0	115,0 ± 8,2‖	p = 0,03 p = 0,43 p = 0,02	116,8 ± 9,1	104,8 ± 13,4	133,4 ± 21,1	122,3 ± 9,4	p = 0,51 p = 0,60 p = 0,20
Colesterol-HDL (mg/dl)	49,5 ± 8,1	49,1 ± 7,4	54,5 ± 7,0*	57,1 5,2*§	p = 0,04 p = 0,50 p = 0,03	51,7 ± 11,0	54,8 9,0	55,0 ± 8,0*	59,7 8,2*§	p = 0,03 p = 0,48 p = 0,02
Triglicéridos (mg/dl)	139,1 ± 36,6	126,9 ± 41,1	121,2 ± 38,2	108,8 ± 27,9	p = 0,61 p = 0,80 p = 0,30	111,3 ± 32,9	105,7 ± 34,1	105,2 ± 13,9	107,9 ± 21,1	p = 0,61 p = 0,82 p = 0,.24
PCR (ng/dl)	5,5 ± 3,1	6,0 ± 2,9	5,1 ± 2,0	5,8 ± 1,9	p = 0,40 p = 0,51 p = 0,19	4,9 ± 2,1	4,1 ± 1,8	5,5 ± 1,9	4,3 ± 4,1	p = 0,59 p = 0,71 p = 0,31
Insulina (mUI/l)	18,7 ± 8,1	16,9 ± 7,9	21,7 ± 3,1	14,4 ± 3,9†	p = 0,01 p = 0,28 p = 0,02	15,4 ± 5,8	13,5 ± 4,1	17,2 ± 4,8	11,4 ± 2,1†	p = 0,01 p = 0,30 p = 0,03
HOMA-IR	4,8 ± 3,1	3,9 ± 3,7	5,9 ± 1,0	3,1 ± 1,8‡	p = 0,02 p = 0,34 p = 0,03	4,3 ± 1,7	3,9 ± 1,5	4,6 ± 1,1	2,4 ± 0,9‡	p = 0,03 p = 0,18 p = 0,04

*PCR: proteína C-reactiva. HOMA-IR: homeostasis model assessment; diferencias estadísticamente significativas en cada genotipo (†Insulina; ‡HOMA-IR; §HDL colesterol; ‖LDL colesterol). *Diferencias estadísticamente significativas entre diferentes genotipos.*

dieta M (Tabla II). Esta mejoría no se observó en los sujetos no portadores del alelo A.

La tabla III muestra las concentraciones plasmáticas de adipocitoquinas. No se encontraron diferencias significativas entre los valores basales y post-intervención de resistina, adiponectina y leptina entre ambos genotipos. Tras la pérdida de peso con ambas intervenciones dietéticas, los niveles de leptina disminuyeron. Los niveles de resistina y adiponectina no se modificaron.

DISCUSIÓN

En este estudio aleatorizado de 12 semanas con dos dietas hipocalóricas (una rica en grasas poliinsaturadas y otra rica en grasas monoinsaturadas), observamos un efecto de la variante genética rs670, localizada en el gen *ApoA1*, sobre la modificación de los niveles de colesterol unido a LDL y HDL tras una dieta rica en grasas poliinsaturadas, y sobre la resistencia a la insulina tras ambas dietas hipocalóricas.

En nuestro trabajo, la frecuencia del alelo A de la variante rs670 fue de 0,19, similar a los datos presentes en la literatura en general (23-26) pero inferior a un estudio realizado con población taiwanesa (0,32) (27). Quizás estas diferencias se explican por los diferentes grupos étnicos, siendo nuestro estudio realizado solo con población caucásica. Numerosos trabajos se han diseñado para determinar el efecto del polimorfismo rs670 del gen *ApoA1*, presentando datos contradictorios. En la mayoría de los trabajos se han demostrado niveles elevados de colesterol-HDL en los sujetos portadores del alelo A (28-31), como sucede en nuestro trabajo. Sin embargo, en un único otro trabajo (10) se ha demostrado una relación inversa del alelo A con los niveles de colesterol-HDL. Quizás estos hallazgos contradictorios en la literatura se deban a diferentes factores ambientales como, por ejemplo, otros tratamientos farmacológicos concomitantes, la presencia de obesidad, diferentes ingestas calóricas en las poblaciones evaluadas, el tipo de grasa de la dieta o la presencia de diabetes mellitus en los sujetos reclutados (29-31).

El hallazgo más importante de nuestro trabajo fue la mejoría de los niveles de colesterol-HDL y colesterol-LDL en los sujetos obesos portadores del alelo A tras recibir una dieta hipocalórica rica en grasa poliinsaturada. Los estudios de la literatura que evalúan la relación de una intervención dietética que produce pérdida de peso con el polimorfismo rs670 y los cambios metabólicos secundarios son escasos. Un pequeño trabajo de casos y controles, sobre 50 pacientes (12), demostró que el riesgo de presentar síndrome metabólico se modificaba con la ingesta basal de grasas. Este efecto metabólico deletéreo fue peor en los sujetos no portadores del alelo A con elevada ingesta de grasas. No obstante, los sujetos que consumían bajos niveles de grasas no parecían tener unos niveles de colesterol influenciados por la ingesta lipídica. Como nosotros pudimos observar en nuestro estudio de intervención, los sujetos obesos con el alelo A que recibieron una dieta hipocalórica rica en grasa poliinsaturada presentaron una mejoría de los niveles de colesterol-HDL y colesterol-LDL, y de manera secundaria –por tanto– de la presencia de síndrome metabólico (32), al ser los niveles de colesterol-HDL uno de los componentes de este síndrome. En otro trabajo sin intervención (33), el polimorfismo rs670 del gen *APOA1* se relacionó con los niveles de colesterol-LDL. Quizás la calidad de las grasas, más que la cantidad, es lo que se relaciona con los resultados, ya que en nuestro trabajo nosotros encontrarnos esta respuesta en los niveles de colesterol solo en los sujetos que consumían una dieta hipocalórica rica en grasa poliinsaturada y no en aquellos con dieta hipocalórica rica en grasa monoinsaturada.

Un reciente estudio de intervención con una duración de 10 semanas (34) ha demostrado una relación entre el alelo A y la modificación del peso tras la intervención dietética, sin relación con la modificación de las concentraciones de colesterol. La disminución

Tabla III. Niveles de adipocitoquinas (media, DE)

Variables	Rs670								
	Dieta P (n = 174)				p Tiempo Genotipo Genotipo x tiempo	Dieta M (n = 186)			p Tiempo Genotipo Genotipo x tiempo
	GG		GA + AA			GG		GA + AA	
	Basal	3 meses	Basal	3 meses		Basal	3 meses	Basal	3 meses	
Resistina (ng/dl)	3,8 ± 0,9	3,7 ± 1,0	3,9 ± 1,1	3,8 ± 1,4	p = 0,56 p = 0,70 p = 0,23	3,7 ± 1,9	3,1 ± 1,9	3,9 ± 1,0	3,5 ± 1,9	p = 0,69 p = 0,59 p = 0,21
Adiponectina (ng/dl)	26,9 ± 7,1	25,4 ± 4,5	30,1 ± 12,10	25,9 ± 6,3	p = 0,54 p = 0,81 p = 0,34	40,1 ± 8,0	38,8 ± 4,1	38,6 ± 7,1	39,0 ± 4,8	p = 0,58 p = 0,63 p = 0,20
Leptina (ng/dl)	81,1 ± 26,0	67,9 ± 90,1*	82,1 ± 16,4	67,9 ± 14,3*	p = 0,02 p = 0,18 p = 0,01	95,3 ± 16,1	69,8 ± 100,5*	95,2 ± 7,4	70,9 ± 8,8*	p = 0,01 p = 0,11 p = 0,02

**p < 0,05, diferencias estadísticamente significativas en cada grupo.*

del peso y de otros parámetros adiposos fue superior en los sujetos portadores del alelo A que en los no portadores. En nuestro trabajo no encontramos esta relación de la modificación del peso con la variante genética. Diferencias fenotípicas y genotípicas en las poblaciones evaluadas en estos estudios pueden explicar estos resultados contradictorios; por ejemplo, algunos trabajos han evaluado poblaciones de adolescentes (13), otros poblaciones caucásicas (32); por último, las restricciones calóricas han sido también diferentes en estos trabajos, oscilando entre 500 y 700 calorías al día (34).

Con el objetivo de demostrar el efecto directo del perfil de las grasas de la dieta más allá de la restricción calórica, Mata y cols. (35) observaron que una dieta no hipocalórica rica en grasa poliinsaturada induce un mayor descenso de los niveles de colesterol-LDL en los sujetos portadores del alelo A que en los no portadores, en comparación con una dieta rica en grasa saturada. Este estudio tiene diferencias con el nuestro: por ejemplo, que no fue realizado en sujetos obesos, que la duración de la intervención fue más corta (28-35 días), que no se realizó ninguna restricción calórica y que se aportaron cantidades de grasa diferentes. No obstante, el trabajo demostró una clara relación entre la respuesta del perfil lipídico y el tipo de grasa consumida en relación con la variante genética rs670.

Otro hallazgo de nuestro trabajo es el efecto del alelo A sobre las modificaciones de los niveles de insulina y HOMA-IR tras la pérdida de peso. En este mismo sentido, un estudio de intervención en una muestra de sujetos jóvenes (13) ha demostrado un empeoramiento de la resistencia a la insulina en los sujetos no portadores del alelo A. Por otra parte, otro estudio (36) ha demostrado que el alelo A de la variante genética rs670 parece proteger del deterioro de la sensibilidad a la insulina a los sujetos con mayor ingesta de azúcar en la dieta. La relación en la literatura entre sensibilidad a la insulina, obesidad y adipocitoquinas es compleja. En nuestro estudio parece que las adipocitoquinas no juegan un papel importante en este sentido, ya que solo la leptina vio modificados sus niveles y esta modificación se produjo en ambas intervenciones dietéticas y en ambos genotipos. Quizás la asociación que hemos descrito entre el alelo A y el metabolismo de la glucosa pueda ser explicada porque el gen *APOA1* puede ser estimulado por la insulina a través del elemento de unión SP-1 (37); además, conocemos que la variante rs670 está situada en una secuencia homóloga del sitio que ocupa este factor nuclear SP-1. Finalmente, otras interacciones entre genes relacionados con el transporte inverso de colesterol y su respuesta a factores ambientales podrían explicar estas asociaciones metabólicas, como han demostrado Wang y cols. (38).

Las limitaciones de nuestro trabajo son: primero, la ausencia de determinación de los niveles de ApoA1 y la imposibilidad de analizar los efectos sobre esta apoproteína; segundo, la corta duración de la intervención dietética (12 semanas). Quizás una intervención de mayor duración hubiera arrojado otros resultados. En tercer lugar, los niveles de colesterol séricos son regulados por múltiples factores ambientales y genéticos, así como sus interacciones. Nosotros, en el presente trabajo, solo investigamos la interacción de un único polimorfismo y una modificación dietética (porcentaje de grasas poliinsaturadas y monoinsaturadas). Por último, es necesario demostrar el efecto de estas modificaciones bioquímicas que hemos descrito en el presente trabajo sobre los eventos cardiovasculares. Además, puede que existan otros factores ambientales desconocidos que también estén influyendo (39), como el consumo de alcohol, el tipo de ejercicio y las modificaciones epigenéticas.

Nuestros hallazgos muestran que el polimorfismo rs670 del gen *ApoA1* se asocia a cambios en las concentraciones plasmáticas de colesterol-HDL y colesterol-LDL secundarios a una dieta hipocalórica rica en grasa polinsaturada y, de manera adicional, a una mejoría de la resistencia a la insulina tras ambas dietas hipocalóricas.

BIBLIOGRAFÍA

1. Deng S, Zhu G, Liu F. CYP4F2 gene V433M polymorphism is associated with ischemic stroke in the male Northern Chinese Han population. Pro Neuropsychopharmacol Biol Psychiatry 2010:34;664-8. DOI: 10.1016/j.pnpbp.2010.03.009.
2. Shah M, Adams-Huet B, Franklin B, Phillips M, Mitchell J. The Effects of High-Protein and High-Monounsaturated Fat Meals on Postprandial Lipids, Lipoprotein Particle Numbers, Cytokines, and Leptin Responses in Overweight/Obese Subjects. Metab Syndr Relat Disord 2018;16:150-8. DOI: 10.1089/met.2017.0167.
3. de Luis DA, Mulero I, Primo D, Izaola O, Aller R. Effects of polymorphism rs3123554 in the CBR2 on metabolic and adiposity parameters after weight loss with two hypocalolric diets. Diab Res and Clin Pract 2018;139:339-47. DOI: 10.1016/j.diabres.2018.02.030.
4. Peelman F, Verschelde JL, Vanloo B, Ampe C, Labeur C, Tavernier J, et al. Effects of natural mutations in lecithin:cholesterol acyltransferase on the enzyme structure and activity. J Lipid Res 1999;40:59-69.
5. Ouimet M, Barrett TJ, Fisher EA. HDL and Reverse Cholesterol Transport. Circ Res 2019;124:1505-18. DOI: 10.1161/CIRCRESAHA.119.312617.
6. Li Q, Du Q. Associations between nine candidate genetic polymorphisms with coronary heart disease: A meta-analysis. Herz 2019. DOI: 10.1007/s00059-019-4806-7.
7. Wu BJ, Sun Y, Ong KL, Li Y, Tang S, Barter PJ, Rye KA. Apo (Apolipoprotein) A-I Protects Against Pregnancy-Induced Insulin Resistance in Rats. Arterioscler Thromb Vasc Biol 2019;ATVBAHA118312282. DOI: 10.1161/ATVBAHA.118.312282.
8. Larson IA, Ordovás JM, Barnard JR, Hoffmann MM, Feussner G, Lamon-Fava S, et al. Effects of apolipoprotein A-I genetic variations on plasma apolipoprotein, serum lipoprotein and glucose levels. Clin Genet 2002;61:176-84. DOI: 10.1034/j.1399-0004.2002.610302.x.
9. Wang XL, Badenhop RB, Sim AS, Wilcken DE. The effect on transcription efficiency of the apolipoprotein AI gene of DNA variants at the 5' untranslated region. Int J Clin Lab Res 1998;28:235-41. DOI: 10.1007/s005990050051.
10. Daneshpour MS, Faam B, Mansournia MA, Hedayati M, Halalkhor S, Mesbah-Namin SA, et al. Haplotype analysis of Apo AI-CIII-AIV gene cluster and lipids level: Tehran Lipid and Glucose Study. Endocrine 2012;41:103-10. DOI: 10.1007/s12020-011-9526-6.
11. de Franca E, Alves JG, Hutz MH. APOA1/C3/A4 gene cluster variability and lipid levels in Brazilian children. Braz J Med Biol Res 2005;38:535-41. DOI: 10.1590/S0100-879X2005000400006.
12. López-Miranda J, Espino A, Marin C, Salas J, López-Segura F, Jimenez-Pereperez J, et al. Influence of mutation in human apolipoprotein A-1 gene promoter on plasma LDL cholesterol response to dietary fat. Lancet 1994;343:1246. DOI: 10.1016/S0140-6736(94)92149-0.
13. Phillips CM, Goumidi L, Bertrais S, Field MR, McManus R, Hercberg S, et al. Gene-nutrient interactions and gender may modulate the association between ApoA1 and ApoB gene polymorphisms and metabolic syndrome risk. Atherosclerosis 2011;214:408-14. DOI: 10.1016/j.atherosclerosis.2010.10.029.
14. de Luis DA, Izaola O, Primo D, Aller R. Role of rs670 variant of APOA1 gene on lipid profile, insulin resistance and adipokine levels in obese subjects after weight loss with a dietary intervention. Diab Res and Clin Pract 2018;142:139-45. DOI: 10.1016/j.diabres.2018.05.040.
15. Mataix J, Mañas M. Tablas de composición de alimentos españoles. Ed: University of Granada, 2003.

16. Lukaski H, Johson PE. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am J Clin Nutr 1985;41:810-7. DOI: 10.1093/ajcn/41.4.810.
17. Friedewald WT, Levy RJ, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
18. Duart MJ, Arroyo CO, Moreno JL. Validation of an insulin model for the reactions in RIA. Clin Chem Lab Med 2002;40:1161-7. DOI: 10.1515/cclm.2002.203.
19. Mathews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF. Homeostasis model assessment: insulin resistance and beta cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-4. DOI: 10.1007/BF00280883.
20. Suominen P. Evaluation of an enzyme immunometric assay to measure serum adiponectin concentrations. Clin Chem 2004;50:219-21. DOI: 10.1373/clinchem.2003.025833.
21. Meier U, Gressner M. Endocrine regulation of energy metabolism: review of pathobiochemical and clinical chemical aspects of leptin, Ghrelin, adiponectin, and resistin. Clinical Chemistry 2004;50:1511-25. DOI: 10.1373/clinchem.2004.032482.
22. Pfutzner A, Langefeld M, Kunt T, Lobig M. Evaluation of human resistin assays with serum from patients with type 2 diabetes and different degrees of insulin resistance. Clin Lab 2003;49:571-6.
23. Talmud PJ, Ye S, Humphries SE. Polymorphism in the promoter region of the apolipoprotein AI gene associated with differences in apolipoprotein AI levels: the European Atherosclerosis research study. Genet Epidemiol 1994;11:265-80. DOI: 10.1002/gepi.1370110305.
24. Sigurdsson GJ, Gudnason V, Sigurdsson G, Humphries SE. Interaction between a polymorphism of the ApoA-I promoter region and smoking determines plasma levels of HDL and ApoA-I. Arterioscler Thromb 1992;12:1017-22. DOI: 10.1161/01.ATV.12.9.1017.
25. Coban N, Onat A, Guclu-Geyik F, Komurcu-Bayrak E, Can G, Erginel-Unaltuna N. Gender-specific associations of the APOA1 -75G>A polymorphism with several metabolic syndrome components in Turkish adults. Clin Chim Acta 2014;431:244-9. DOI: 10.1016/j.cca.2014.01.017.
26. Akadam-Teker B, Ozkara G, Kurnaz-Gomleksiz O, Bugra Z, Teker E, Ozturk O, et al. BMP1 5'UTR+104 T/C gene variation: can be a predictive marker for serum HDL and apoprotein A1 levels in male patients with coronary heart disease. Mol Biol Rep 2018;45:1269-76. DOI: 10.1007/s11033-018-4283-8.
27. Wu JH, Kao JT, Wen MS, Lo SK. DNA polymorphisms at the apolipoprotein A1-CIII loci in Taiwanese: correlation of plasma APOCIII with triglyceride level and body mass index. J Formos Med Assoc 2000;99:367-74.
28. Pagani F, Sidoli A, Giudici GA, Barenghi L, Vergani C, Baralle FE. Human apolipoprotein A-I gene promoter polymorphism: association with hyperalphalipoproteinemia. J Lipid Res 1990;31:1371-7.
29. Rai H, Sinha N, Finn J, Agrawal S, Mastana S. Association of serum lipids and coronary artery disease with polymorphisms in the apolipoprotein AI-CIII-AIV gene cluster. Cogent Med 2016;3(1):1266789. DOI: 10.1080/2331205X.2016.1266789.
30. Morcillo S, Cardona F, Rojo-Martínez G, Esteva I, Ruiz-de-Adana MS, Tinahones F, et al. Association between MspI polymorphism of the APO AI gene and type 2 diabetes mellitus. Diabet Med 2005;22:782-8. DOI: 10.1111/j.1464-5491.2005.01514.x.
31. Wang X, He J, Guo H, Mu L, Hu Y, Ma J, et al. Interactions of six SNPs in APOA1 gene and types of obesity on low HDL-C disease in Xinjiang pastoral area of China. Lipids Health Dis 2017;16:187. DOI: 10.1186/s12944-017-0581-8.
32. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: (Adult Treatment Panel III). Jama. 2001;285(19):2486-97. DOI: 10.1001/jama.285.19.2486.
33. Rudkowska I, Dewailly E, Hegele RA, Boiteau V, Dube-Linteau A, Abdous B, et al. Gene-diet interactions on plasma lipid levels in the Inuit population. Br J Nutr 2013;109(5):953-61. DOI: 10.1017/S0007114512002231.
34. Moleres A, Milagro FI, Marcos A, González Zorzano E, Campoy C, Garagorri JM, et al. Common variants in genes related to lipid and energy metabolism are associated with weight loss after an intervention in overweight/obese adolescents. Nutr Hosp 2014;30:75-83.
35. Mata P, López-Miranda J, Pocovi M, Alonso R, Lahoz C, Marín C, et al. Human apolipoprotein A-I gene promoter mutation influences plasma low density lipoprotein cholesterol response to dietary fat saturation. Atherosclerosis 1998;137:367-76. DOI: 10.1016/S0021-9150(97)00265-7.
36. Hosseini-Esfahani F, Mirmiran P, Daneshpour MS, Mottaghi A, Azizi F. The Effect of Interactions of Single Nucleotide Polymorphisms of APOA1/APOC3 with Food Group Intakes on the Risk of Metabolic Syndrome. Avicenna J Med Biotechnol 2017;9:94-103.
37. Samson SL, Wong NC. Role of Sp1 in insulin regulation of gene expression. Journal of Molecular Endocrinology 2002;29:265-79.
38. Wang X, Guo H, Li Y, Wang H, He J, Mu L, et al. Interactions among genes involved in reverse cholesterol transport and in the response to environmental factors in dyslipidemia in subjects from the Xinjiang rural area. PLoS One 201814;13:e0196042. DOI: 10.1371/journal.pone.0196042.
39. Casillas-Muñoz F, Valle Y, Muñoz-Valle JF, Martínez-Fernández DE, Reynoso-Villalpando GL, Flores-Salinas HE, et al. APOA1 and APOB polymorphisms and apolipoprotein concentrations as biomarkers of risk in acute coronary syndrome: Relationship with lipid-lowering therapy effectiveness. Med Clin (Barc) 2017; S0025-7753(17)30654-1. DOI: 10.1016/j.medcle.2018.05.001.

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ARÁN

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Trabajo Original

Obesidad y síndrome metabólico

Incidence and characteristics of metabolic syndrome in patients of the National Cancer Institute of Mexico

Incidencia y características del síndrome metabólico en pacientes del Instituto Nacional de Cancerología de México

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Abstract

Objective: the exact prevalence of obesity in Mexico is not well known and varies between sources, but more than 30% of Mexico's population are obese. Obesity is associated with several diseases such as metabolic syndrome; the latter, along with cancer, have become public health concerns worldwide, and their association has been widely studied in developed countries. The aim of this study was to identify the overall prevalence of metabolic syndrome and to describe its characteristics among first-time cancer patients at a referral center in Mexico.

Methods: a prospective, observational, cohort study of first-time patients of the National Cancer Institute of Mexico in the period of September 2016-2017. We identified 1,165 first-time patients, and 316 patients with known or recently diagnosed metabolic syndrome were included.

Results: median age was 55 years old and most were female (81%). The most frequent tumors were breast, gynecological, and hematological growths. Obesity (class 1-3) and abnormal glucose and/or previous diabetes mellitus diagnosis were mostly observed in patients with skin and soft tissue tumors; dyslipidemia, high triglycerides, and/or low HDL-cholesterol were mostly observed in patients with gastrointestinal tumors.

Conclusion: the prevalence of metabolic syndrome among first-time cancer patients was 27%. As obesity and cancer are of public concern in Mexico, the implementation of preventive strategies for metabolic syndrome patients, focusing on the first level of care during early stages in order to reduce the risk of cancer, is needed.

Key words:

Incidence. Metabolic syndrome. Cancer. Mexico.

Resumen

Objetivo: la prevalencia de la obesidad en México es mayor del 30% de la población total. La obesidad se asocia con diversas enfermedades, entre ellas el síndrome metabólico; este y el cáncer se han convertido en problemas de salud pública a nivel mundial, y su asociación ha sido ampliamente estudiada en países desarrollados. El objetivo de este estudio fue identificar la prevalencia del síndrome metabólico y describir las características entre pacientes oncológicos de primera vez en un hospital de tercer nivel en México.

Métodos: estudio prospectivo, observacional y de cohortes que incluye a pacientes oncológicos atendidos por primera vez en el Instituto Nacional de Cancerología durante el periodo de septiembre 2016 a 2017. Identificamos 1165 pacientes; 316 tenían el diagnóstico de síndrome metabólico y fueron incluidos en el presente estudio.

Resultados: la mediana de edad fue de 55 años y la mayoría de los pacientes eran del sexo femenino (81%). Las neoplasias más frecuentes fueron las de mama, ginecológicas y hematológicas. La obesidad (clase 1-3) y la glucosa anormal y/o un diagnóstico previo de diabetes mellitus se observaron mayormente en pacientes con neoplasias de piel y tejidos blandos; los pacientes con neoplasias gastrointestinales presentaron mayormente dislipidemia, triglicéridos elevados y/o HDL bajo.

Conclusiones: la prevalencia del síndrome metabólico en nuestros pacientes oncológicos fue de 27%. Al ser la obesidad y el cáncer problemas de salud pública en México, la implementación de medidas preventivas para pacientes con síndrome metabólico debe enfocarse en el primer nivel de atención, durante etapas tempranas, para poder reducir el riesgo de cáncer.

Palabras clave:

Incidencia. Síndrome metabólico. Cáncer. México.

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INTRODUCTION

In the last 50 years obesity rates have substantially increased in Mexico, showing a drastic increase in body mass index (BMI) among the population as a result of evolving dietary habits (1). The exact prevalence of obesity in Mexico is not well known and varies among sources, but more than 30% of Mexico's population are obese according to the most recent update of the Organization for Economic Co-operation and Development (OECD) (2). Obesity is associated with several diseases, such as coronary heart disease, high blood pressure, and diabetes (3). The association of obesity and other previously mentioned conditions represents a widely known disorder characterized by the presence of multiple risk factors, and known as metabolic syndrome (4). This disorder is diagnosed when at least three of the following are present: central obesity, hyperglycemia, hypertriglyceridemia, low HDL-cholesterol, and hypertension (5). The last nutritional survey in Mexico (ENSANUT, from its Spanish acronym, 2012) reported that metabolic syndrome had increased to 45% (6) as compared to the report published in 2006 (7).

On the other hand, worldwide leading causes of death according to the World Health Organization (WHO) and the Global Health Observatory include ischemic heart disease, stroke, lower respiratory infection, and chronic obstructive lung disease; however, cancer has also become a leading cause of mortality, causing 1.6 (2.9%) million deaths in 2012. Mortality rates in Mexico are no different, as cancer is the second or third leading cause of death, with approximately 78,000 cancer deaths in 2012 (8). Nonetheless, Mexico does not track morbidity data. Official sources only provide data on the number of hospital discharges from public institutions without identification of patient cases (9).

As both metabolic syndrome and cancer have become public health problems worldwide, and their association has been widely studied mostly in developed countries (10-12), the aim of this study was to identify the overall prevalence of metabolic syndrome and to describe its characteristics among first-time cancer patients at a referral center in Mexico.

PATIENTS AND METHODS

This is a prospective, observational, cohort study of first-time patients of the National Cancer Institute of Mexico (INCan, from its Spanish acronym), from September 2016 to September 2017. The study was approved by the institutional ethics and research committees. All participants provided their written informed consent.

PATIENTS AND DATA

We identified 1,165 first-time patients at the INCan during a 1-year period. We enrolled 316 patients who met the eligibility criteria. Inclusion criteria included: known or recently diagnosed metabolic syndrome, ≥ 18 years of age, and good performance status. Clinical and demographic data, such as gender, age, and type of cancer were collected from the electronic medical records (INCanet). All patients underwent a complete nutritional evaluation to assess the presence of metabolic syndrome.

DEFINITION OF METABOLIC SYNDROME AND MEASUREMENTS

For the diagnosis of metabolic syndrome, the latest harmonized definition (5) was used, which requires the presence of three or more of the following: waist circumference ≥ 80 cm in women and ≥ 94 cm in men; triglycerides ≥ 150 mg/dL; HDL-cholesterol < 50 mg/dL; fasting glucose ≥ 100 mg/dL or diabetes treatment; systolic blood pressure ≥ 130 mm Hg, and diastolic blood pressure ≥ 85 mm Hg or antihypertensive drug treatment.

Blood pressure (BP), weight (kilograms, kg), and height (centimeters, cm) were obtained, and body mass index (BMI) was calculated: weight in kilograms divided by square height in meters (kg/m^2). The waist-hip (W-H) ratio was obtained as waist measurement divided by hip measurement. Any previous history of dyslipidemia and diabetes mellitus (DM) was also recorded. Patients were sent to the laboratory for serum determinations of fasting glucose and a lipid panel.

STATISTICAL ANALYSIS

Continuous variables were described by median and interquartile range values using the frequency analysis. Categorical variables were described by frequencies and percentiles. The SPSS v.21 (IBM, Chicago, IL) was used.

RESULTS

We identified 1,165 patients with cancer, and the incidence of metabolic syndrome according to the underlying cancer was as follows: breast (n = 131/361, 36%), gynecological (n = 75/211, 35%), gastrointestinal (n = 21/208, 10%), hematological (n = 32/126, 25%), urological (n = 29/72, 40%), soft tissue/skin (n = 14/31, 45%), head and neck (n = 9/120, 8%), and lung (n = 2/36, 6%); therefore, out of the 1,165 patients identified at the INCan, the final cohort included 316 patients (27%) with metabolic syndrome. Median age was 55 years (range, 25-91). The majority were women (n = 254, 81%; men, n = 59, 19%). Most frequent tumors included breast, gynecological, and hematological neoplasms: 42%, 24%, and 10%, respectively. Most patients were overweight (n = 130, 42%); median weight and height were 155 cm and 76 kg, respectively. Median BMI and W-H ratio were 31 and 0.92, respectively. Fifty-five percent of patients had diabetes mellitus (n = 172), and 42% had hypertension (n = 132). Before referral to our institution, 237 patients (76%) had already been diagnosed with metabolic syndrome and 76 patients (24%) were diagnosed at admission. Median laboratory parameters were as follows: glucose 121.5 mg/dL, triglycerides

185.5 mg/dL, HDL-cholesterol 41 mg/dL, total cholesterol 181 mg/dL, and LDL-cholesterol 117.6 mg/dL. Obesity (class 1-3) was mostly observed in patients with skin and soft tissue, hematological, and urological tumors: 69%, 63%, and 59%, respectively. Abnormal glucose and/or previous DM diagnosis were mostly observed in patients with skin and soft tissue, gynecological, and gastrointestinal tumors: 86%, 58%, and 57%, respectively. Dyslipidemia, high triglycerides, and/or low HDL-cholesterol were mostly observed in patients with gastrointestinal, skin and soft tissue, and urological tumors: 100%, 76%, and 71%, respectively. Patients with head and neck, gynecological, and breast tumors were those most frequently seen with known or recently diagnosed hypertension: 67%, 44%, and 44%, respectively. The overall characteristics by diagnosis are shown in table I.

Table I. Patient demographics and clinical characteristics by type of cancer

Variable n (%)	Cancer diagnosis							
	Breast	Gynecological	Urological	Gastrointestinal	Skin/Soft tissue	Lung	Head/ Neck	Hematological
Median age (range)	55 (35-91)	58 (32-84)	55 (25-75)	64 (45-75)	57 (44-75)	60 (60-61)	54 (40-72)	50 (25-82)
Gender								
Female	131 (100)	75 (100)	6 (21)	12 (57)	7 (50)	2 (100)	5 (55)	16 (50)
Male	-	-	23 (79)	9 (43)	7 (50)	0	4 (45)	16 (50)
Known metabolic syndrome	99 (76)	54 (72)	23 (79)	19 (90)	11 (79)	2 (100)	6 (67)	23 (72)
Weight (median, kg)	73.7 (51-117)	76.8 (52-119)	81.1 (67-122)	68.8 (56-109)	78.8 (55-103)	70.5 (50-91)	73.7 (69-126)	82.8 (63-130)
Height (median, cm)	153 (140-168)	152 (135-168)	167 (148-189)	160 (140-189)	160 (144-176)	153 (139-167)	161 (142-171)	163 (139-182)
BMI classification								
Overweight	60 (46)	23 (31)	12 (41)	11 (52)	6 (43)	1 (50)	4 (44)	12 (38)
Obesity class 1	36 (27)	25 (33)	14 (48)	8 (38)	6 (43)	1 (50)	0	13 (41)
Obesity class 2	24 (18)	20 (27)	2 (0.7)	2 (10)	2 (14)	0	2 (22)	7 (21)
Obesity class 3	11 (9)	7 (9)	1 (0.3)	0	0	0	3 (34)	0
W-H ratio								
Female								
< 0.86	23 (18)	10 (13)	2 (33)	2 (16)	0	0	0	0
≥ 0.86	108 (82)	65 (87)	4 (66)	10 (81)	7 (100)	2 (100)	5 (100)	16 (100)
Male								
< 0.86	0	0	1 (4)	1 (11)	1 (14)	0	0	0
≥ 0.86	0	0	22 (95)	8 (88)	6 (85)	0	4 (100)	16 (100)
Diabetes *mellitus*	67 (51)	44 (59)	15 (52)	10 (48)	11 (79)	1 (50)	5 (55)	19 (59)
Hypertension	57 (44)	33 (44)	11 (38)	9 (43)	4 (29)	2 (100)	6 (67)	10 (31)
Glucose (median, mg/dL)	117 (60-339)	128 (81-346)	123 (88-500)	127 (103-215)	155.5 (80-390)	126 (113-139)	122 (86-214)	121 (74-574)
Triglycerides (median, mg/dL)	169 (36-587)	210.5 (68-670)	287.5 (61-581)	171.5 (68-599)	173 (116-344)	-	180 (163-228)	151.5 (46-422)
HDL								
Female (median, mg/dL)	42.4 (24-94)	41 (25-60)	-	38.6 (37-57)	39.8 (24-61)	-	41 (32-44)	40 (27-59)
Male	-	-	33.9 (24-54)	40.6 (37-57)	35.2 (24-61)	-	38 (32-44)	45 (27-59)

DISCUSSION

Several studies and meta-analyses (13-15) have demonstrated that common cancers, such as gastrointestinal, breast, pancreatic, and gynecological neoplasms, are associated with metabolic syndrome. However, to date, the mechanisms linking this disorder and cancer are not completely understood, as it is unknown whether the strength of the association between these is greater than the sum of the individual components of metabolic syndrome, which might be driving this association, or whether the metabolic syndrome is a reliable predictor of cancer risk (11). Metabolic syndrome might represent a surrogate marker for other cancer risk factors: sedentary lifestyle, high dietary fat and carbohydrate intake, and oxidative stress (5,10). On the other hand, overweight and obesity are currently very important challenges of public health worldwide, and their negative effect among chronic, non-communicable diseases such as cancer is widely known (18). Mexico has the second highest global prevalence of obesity in the adult population, which implies a major challenge for the health sector (18). Moreover, the most frequent types of cancer in Mexican adults are breast and gastrointestinal tumors in women and men, respectively. Although metabolic syndrome and its association with cancer are topics of interest, data in Mexico and other developing countries where obesity is high remain scarce. A study found a prevalence of MS in 27% of Mexican female survivors of cancer (19); furthermore, a study performed in women with breast cancer reported a prevalence of 50% among obese women (20). Osornio-Sánchez et al. (21) reported a prevalence of 48% among patients with prostate cancer. In this study, we identified a prevalence of metabolic syndrome in 27% of first-time patients of the INCan during a 1-year period. Prior to referral to our Institution, 76% of patients were already diagnosed with metabolic syndrome, which highlights the importance of primary care. Our results showed that breast, gynecological, urological, and soft tissue/skin cancers have the highest prevalence of metabolic syndrome.

Due to the high prevalence of MS and the high incidence of cancer worldwide, it is assumed by some authors that many cases of cancer should be attributed to MS (22). Mexico is no exception, and an implementation of preventive strategies for MS patients, focusing on the first level of care during early stages in order to reduce the risk of cancer, is needed. As we acknowledge the limitations of our study–one center, small cohort due to the 1-year period–we also highlight that this is the first study performed in Mexican patients including all types of cancer and reporting the prevalence of metabolic syndrome among them. More studies in Mexican patients and other developing countries with high incidence of obesity and metabolic syndrome are encouraged for further comparisons.

REFERENCES

1. Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. Nutr Rev 2012;70:3-21. DOI: 10.1111/j.1753-4887.2011.00456.x
2. Obesity Update. Organization for Economic Co-operation and Development website. oecd.org/els/health-systems/Obesity-Update-2014.pdf. Accessed on April 17, 2018.
3. Apovian CM. Obesity: definition, comorbidities, causes, and burden. Am J Manag Care 2016;22(7 Suppl):s176-85.
4. O'Neill S, O'Driscoll L. Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. Obes Rev 2015;16(1):1-12. DOI: 10.1111/obr.12229
5. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640-5. DOI: 10.1161/CIRCULATIONAHA.109.192644
6. Barquera S, Campos-Nonato I, Hernández-Barrera L, Pedroza-Tobías A, Rivera-Dommarco JA. Prevalencia de obesidad en adultos mexicanos, ENSANUT 2012. Salud Pública de México 2013;55(Supl 1):S151-S160. DOI: 10.21149/spm.v55s2.5111
7. Rojas R, Aguilar-Salinas CA, Jiménez-Corona A, Shamah-Levy T, Rauda J, et al. Metabolic syndrome in Mexican adults. Results from the National Health and Nutrition Survey 2006. Salud Pública Mex 2010;52(Supl 1):S11-S18. DOI: 10.1590/S0036-36342010000700004
8. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr. Accessed on April 17, 2018.
9. Mohar-Betancourt A, Reynoso-Noverón N, Armas-Texta D, Gutiérrez-Delgado C, Torres-Domínguez JA. Cancer Trends in Mexico: Essential Data for the Creation and Follow-Up of Public Policies. Journal of Global Oncology 2017;3(6):740-8. DOI: 10.1200/JGO.2016.007476
10. Esposito K, Chiodini P, Colao A, Lenzi A, Giugliano D. Metabolic syndrome and risk of cancer: a systematic review and meta-analysis. Diabetes Care 2012;35:2402-11. DOI: 10.2337/dc12-0336
11. Harding J, Sooriyakumaran M, Anstey KJ, Adams R, Balkau B, Briffa T, et al. The metabolic syndrome and cancer: Is the metabolic syndrome useful for predicting cancer risk above and beyond its individual components? Diabetes Metab 2015;41(6):463-9. DOI: 10.1016/j.diabet.2015.04.006
12. Esposito K, Capuano A, Giugliano D. Metabolic syndrome and cancer: holistic or reductionist? Endocrine 2014;45:362-4. DOI: 10.1007/s12020-013-0056-2
13. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine 2014;45(1):28-36. DOI: 10.1007/s12020-013-9973-3
14. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008;371:569-78. DOI: 10.1016/S0140-6736(08)60269-X
15. Matthews CE, Sui X, LaMonte MJ, Adams SA, Hébert JR, Blair SN. Metabolic syndrome and risk of death from cancers of the digestive system. Metabolism 2010;59:1231-9. DOI: 10.1016/j.metabol.2009.11.019
16. Osaki Y, Taniguchi S, Tahara A, Okamoto M, Kishimoto T. Metabolic syndrome and incidence of liver and breast cancers in Japan. Cancer Epidemiol 2012;36:141-7. DOI: 10.1016/j.canep.2011.03.007
17. Aleksandrova K, Boeing H, Jenab M, Bas Bueno-de-Mesquita H, Jansen E, van Duijnhoven FJ, et al. Metabolic syndrome and risks of colon and rectal cancer: The European prospective investigation into cancer and nutrition study. Cancer Prev Res (Phila) 2011;4:1873-83. DOI: 10.1158/1940-6207.CAPR-11-0218
18. Barrera-Cruz A, Rodríguez-González A, Molina-Ayala MA. Escenario actual de la obesidad en México. Rev Med Inst Mex Seguro Soc 2013;51(3):292-9.
19. Ortiz-Mendoza CM, de la Fuente-Vera TA. Obesity and components of metabolic syndrome in Mexican women survivors of cancer. Rev Med Inst Mex Seguro Soc 2014;52(5):588-93.
20. Ortiz-Mendoza CM, de-la-Fuente-Vera TA, Pérez-Chávez E. Metabolic Syndrome in Mexican Women Survivors of Breast Cancer: A Pilot Study at a General Hospital. Med Arh 2014;68(1):19-21. DOI: 10.5455/medarh.2014.68.19-21
21. Osornio-Sánchez V, Camacho-Castro AJ, García-Salcido F, Muñoz-Ibarra E, Garza-Sainz G, Mayorga-Gómez E, et al. Síndrome metabólico en pacientes con cáncer de próstata en tratamiento con bloqueo androgénico. Rev Mex Urol 2014;74(2):79-83. DOI: 10.1016/S2007-4085(15)30016-1
22. Mendonça FM, de Sousa FR, Barbosa AL, Martins SC, Araújo RL, Soares R, et al. Metabolic syndrome and risk of cancer: Which link? Metabolism 2015;64(2):182-9. DOI: 10.1016/j.metabol.2014.10.008

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Asociación entre el consumo de yerba mate y el perfil lipídico en mujeres con sobrepeso

Association between consumption of yerba mate and lipid profile in overweight women

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Resumen

Introducción: la yerba mate es una bebida tradicional consumida en Sudamérica, producida de hojas tostadas de *Ilex paraguariensis*. Varios estudios han demostrado sus propiedades hipolipemiantes debido a la presencia de polifenoles y saponinas.

Objetivo: analizar el efecto del consumo diario de yerba mate sobre los valores de lípidos séricos y la composición corporal en mujeres con sobrepeso.

Métodos: 119 mujeres con sobrepeso de entre 25 y 50 años fueron divididas en tres grupos: mate y dieta (MD), mate sin dieta (M) y agua y dieta (AD). Durante 12 semanas se suplementaron con mate los grupos M y MD, mientras que los grupos AD y MD, mantuvieron un plan alimentario hipocalórico. Se realizaron mediciones antropométricas y análisis de sangre (colesterol total, colesterol-LDL, colesterol-HDL y triglicéridos) al inicio y la finalización del estudio. El análisis estadístico se realizó mediante la prueba t de Student o la prueba de Wilcoxon para muestras pareadas y ANOVA ($p < 0,05$ en todos los casos).

Resultados: el colesterol total disminuyó en todos los grupos (10,21 mg/dl en MD, 18,29 mg/dl en M y 17,63 mg/dl en AD, sin diferencias entre grupos). El colesterol-LDL disminuyó en ambos grupos tratados con mate (8,07 mg/dl en MD, 16,04 mg/dl en M, sin diferencias entre grupos) mientras que colesterol-HDL decreció en el grupo M (2,09 mg/dl). Por otro lado, los triglicéridos disminuyeron 10,74 mg/dl solo en el grupo MD.

Conclusiones: la ingesta diaria de mate ayuda a reducir el colesterol total y el colesterol-LDL, y reduce los triglicéridos junto a una dieta baja en calorías.

Palabras clave:

Ilex paraguariensis.
Colesterol.
Dislipidemia.

Abstract

Introduction: yerba mate is a traditional drink consumed in South America, produced from toasted leaves of *Ilex paraguariensis*. Several studies have demonstrated its lipid-lowering properties due to the presence of polyphenols and saponins.

Objective: to analyze the effect of daily yerba mate consumption on the values of serum lipids and body composition in overweight women.

Methods: 119 overweight women between 25 and 50 years were divided into three groups: Mate and Diet (MD), Mate without Diet (M), and Water and Diet (AD). For 12 weeks the M and MD groups were supplemented with mate, while the AD and MD groups maintained a hypocaloric food plan. Anthropometric measurements and blood tests (total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides) were taken at the beginning and at the end of the study. The statistical analysis was performed using Student's t-test or Wilcoxon's test for paired samples and ANOVA ($p < 0.05$ was considered significant in all cases).

Results: total cholesterol decreased in all groups (10.21 mg/dL in MD, 18.29 mg/dL in M, and 17.63 mg/dL in AD, without differences between groups). LDL-cholesterol decreased in both groups with mate (8.07 mg/dL in MD, 16.04 mg/dL in M, without differences between groups) while HDL-cholesterol decreased in M (2.09 mg/dL). On the other hand, triglycerides fell 10.74 mg/dL in the MD group.

Conclusions: a daily intake of mate helps reduce total cholesterol and LDL-cholesterol, and provides a reduction of triglycerides along with a low-calorie diet.

Key words:

Ilex paraguariensis.
Cholesterol.
Dyslipidemia.

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INTRODUCCIÓN

La yerba mate (YM) es una infusión muy difundida de consumo cotidiano en países de Sudamérica, entre ellos Argentina, Paraguay, Brasil y Uruguay. En las últimas décadas han tomado relevancia sus propiedades para la salud humana, a pesar de que no están del todo claras pues son muy pocos los estudios realizados en seres humanos.

El árbol de la YM, cuyo nombre científico es *Ilex paraguariensis*, es una especie muy distinguida debido al uso que se hace de sus hojas y tallos, que sometidos a un proceso de secado, triturado y estacionamiento conforman la "yerba mate" utilizada para la preparación de la infusión conocida como "mate" (M). Esta bebida se reconoce por su gran variedad de componentes activos que, en su conjunto, le confieren propiedades especiales. Numerosos fitoquímicos activos se han identificado en la YM, incluidos polifenoles (principalmente ácido clorogénico), xantinas (cafeína y teobromina), alcaloides de purina (ácido cafeico, ácido 3,4-dicafeoilquínico y ácido 3,5-dicafeoilquínico), flavonoides (quercetina, kaempferol y rutina), aminoácidos, minerales (fósforo, hierro y calcio) y vitaminas (ácido ascórbico, tiamina y riboflavina) (1) Estos fitoquímicos son los que le confieren propiedades antioxidantes. Además, contiene saponinas, glucósidos de esteroides solubles en agua a los que se atribuyen propiedades antiinflamatorias e hipocolesterolémicas (2,3).

En los últimos años, el estudio de las propiedades biológicas del M ha tomado mayor interés científico, especialmente en lo referido a su capacidad sobre el control del peso, la pérdida de masa grasa y la reducción de la relación cintura-cadera, mecanismos que aún se siguen investigando. Recientemente, *Ilex paraguariensis* se ha asociado a efectos benéficos en el tratamiento de la obesidad (OB). En un trabajo se reportó que el tratamiento con extracto de *Ilex paraguariensis* (2 g/kg de peso corporal/día) en ratones alimentados con una dieta rica en grasas influyó en la ingesta de alimentos (-20%), resultando en un mayor gasto de energía y pérdida de peso corporal (23%) (1). Por otro lado, se observó que la administración de una solución instantánea de *Ilex paraguariensis* (1 g/kg de peso corporal/día), una vez al día durante 30 días por sonda intragástrica, en ratas obesas cebadas por destete temprano, disminuyó el peso corporal (10%) y la ingesta de alimentos (25%) en comparación con el control (4). De modo que se puede considerar a la YM como una herramienta natural capaz de contribuir al tratamiento de la OB (4).

Debido al crecimiento de la población que se ve afectada por patologías como el sobrepeso (SP) y la OB, surge la necesidad de buscar alternativas que contribuyan a su tratamiento y/o prevención. Una de esas alternativas, que se podría incorporar a una alimentación saludable, es la YM gracias a las propiedades antes mencionadas. Por lo tanto, es necesario describir brevemente el SP y la OB, y cómo inciden en la salud de la población, ya que suponen un factor de riesgo de múltiples patologías metabólicas.

El SP y la OB se definen como una acumulación anormal o excesiva de grasa que puede poner en peligro la salud. Para los adultos, la Organización Mundial de la Salud (OMS) los define de la siguiente manera: el SP es un IMC (índice de masa corporal, cociente entre el peso y la talla al cuadrado) mayor o igual a 25 kg/m^2 y la OB es un IMC mayor o igual a 30 kg/m^2 (5). Estas patologías, especialmente la OB, se consideran un factor de riesgo para la salud, por lo que se las asocia a un incremento de procesos crónicos (diabetes, hipertensión arterial, dislipidemias), a una disminución de la calidad de vida del paciente y a un aumento alarmante de los factores de riesgo cardiovascular (CV). En diversos estudios se ha manifestado la relación entre la OB y la dislipidemia, observándose un patrón dislipidémico en común: aumento de triglicéridos (TG), colesterol-LDL (CLDL) y colesterol total (CT), y colesterol-HDL (CHDL) bajo.

En las investigaciones donde se han estudiado los efectos biológicos de la YM sobre los factores de riesgo CV como la OB y el colesterol, resulta considerable su capacidad de influir en el control del peso corporal y de reducir los niveles de colesterol séricos (6). Esta propiedad se debería en parte a las saponinas que se encuentran en la infusión de YM, que a nivel intestinal forman micelas con la molécula de colesterol, impidiendo así su absorción y favoreciendo su excreción (7-9). En un ensayo clínico realizado por Kim y colaboradores para evaluar los efectos de la YM sobre la salud de los seres humanos se observaron diferencias significativas de IMC y masa grasa corporal entre el grupo tratado con YM y el grupo de control. Sin embargo, no se encontraron diferencias significativas en términos de modificaciones de los niveles del perfil lipídico (10). Este estudio tenía como limitación que el tamaño de la muestra era pequeño (n = 25).

En este marco se planteó el objetivo de analizar el efecto del consumo diario de YM sobre los valores de lípidos séricos y la composición corporal en mujeres con SP.

MÉTODOS

DISEÑO DE ESTUDIO

El presente trabajo se llevó a cabo en la provincia de Mendoza, Argentina, entre septiembre de 2014 y noviembre de 2016. El estudio se realizó en el Laboratorio de Enfermedades Metabólicas de la Universidad Juan Agustín Maza. El diseño del estudio epidemiológico fue longitudinal experimental. La totalidad de las participantes firmaron su consentimiento escrito al protocolo, previamente aprobado por el Comité de Ética de la Universidad Juan Agustín Maza (Mendoza, Argentina).

POBLACIÓN

Se estudiaron 119 mujeres voluntarias de edades comprendidas entre los 25 y 50 años, con IMC entre 25 y 32,5 kg/m^2, y sin alteraciones endocrinas y/o metabólicas conocidas. La inclusión de la muestra fue incidental, basada de los criterios de inclusión y exclusión mencionados en la tabla I, aunque la asignación de grupos fue aleatoria.

También se excluyeron todas aquellas voluntarias que debieron suspender su participación debido a molestias digestivas ocasionadas por el consumo de YM o que reportaron no haberse adherido a las cantidades de YM indicadas o al plan alimenta-

Tabla I. Criterios de inclusión y exclusión

Inclusión	Exclusión
• Edad: entre 25 y 50 años • IMC entre 25 kg/m^2 y 32,5 kg/m^2 • Mujeres sin alteraciones endocrinas y/o metabólicas conocidas	• Presencia de patologías metabólicas o endocrinas no controladas (diabetes mellitus, enfermedades tiroideas) • Obesidad tratada con cirugía • Participación en ensayos clínicos o intervenciones nutricionales en los últimos tres meses • Mujeres posmenopáusicas, embarazadas, puérperas o lactantes • Consumidoras de mate en las últimas seis semanas • Voluntarias tratadas con medicación hipolipemiante u otros medicamentos capaces de alterar el perfil lipídico • Mujeres con consumo elevado de bebidas alcohólicas o drogas, o fumadoras • Pacientes con neoplasias malignas conocidas • IMC menor de 25 kg/m^2 o mayor de 32,5 kg/m^2

IMC: índice de masa corporal.

rio proporcionado. Se asignaron grupos aleatoriamente según el consumo o no de yerba y la presencia o no de intervención nutricional. El grupo MD (mate y dieta) consumió diariamente 100 gramos de YM, preparada con dos litros de agua, distribuidos a lo largo del día, junto a una intervención nutricional (plan alimentario hipocalórico). El grupo M (mate sin dieta) consumió a diario 100 gramos de YM, preparada con dos litros de agua, sin intervención nutricional. Por último, el grupo AD (agua y dieta) solo consumió a diario 2 litros de agua distribuidos a lo largo del día, con intervención nutricional (plan alimentario hipocalórico).

PLAN ALIMENTARIO

A las voluntarias que participaron en la intervención nutricional se les entregó un plan alimentario estandarizado en cuanto a porcentajes de hidratos de carbono, proteínas y grasas, teniendo como base el mismo valor calórico total. Se trató de un plan hipocalórico de 20 kcal por kilo de peso real, con una distribución de macronutrientes estipulada en: 45% de hidratos de carbono, 20% de proteínas y 35% de grasas. La alimentación se distribuyó en seis comidas diarias, para lo que se tuvieron en cuenta los horarios de trabajo y los gustos de las pacientes. Cada grupo recibió instrucciones precisas de cómo proceder durante la participación en el estudio. Además, se instó a las pacientes a no alterar sus hábitos de tabaquismo y actividad física, y se les pidió no consumir suplementos nutricionales. Finalmente, se las citó a concurrir dos semanas después de la entrevista inicial y luego cada catorce días para el control nutricional, con un total de 7 controles nutricionales.

ANÁLISIS DE LABORATORIO

Para establecer el perfil lipídico se realizaron dos extracciones de sangre: al inicio del estudio y a las doce semanas. La evaluación se realizó en muestras de suero, separado dentro de las dos horas de la extracción de sangre venosa. Para tal fin se pidió a las pacientes que acudieran en ayunas de 12 horas después de una cena liviana. Una vez obtenida la muestra se procedió a la cuantificación de CT, CHDL y TG en un analizador químico clínico Mindray BS-300 (Mindray, Shenzhen, China). Se utilizaron kits comerciales proporcionados por Wiener Lab para el CT (colestat enzimático AA®), el CHDL (HDL Colesterol monofase AA plus®) y los TG (TG Color GPO/PAP AA®). EL colesterol-LDL se determinó con la fórmula de Friedewald.

DETERMINACIONES ANTROPOMÉTRICAS

Al inicio del estudio y en cada control nutricional se evaluó la composición corporal por antropometría. El peso corporal se midió en una balanza OMRON (con capacidad de hasta 150 kg) y la estatura se midió en un estadiómetro portátil (MEDNIB) con una escala de 1 a 205 cm y una precisión de 0,5 cm. Se midieron los pliegues cutáneos tricipital, bicipital, suprailíaco y subescapular utilizando un plicómetro (Slim Guide, con una precisión de 0,5 mm). Las circunferencias de cintura (CC) y cadera se midieron con una cinta métrica flexible inelástica dotada de una escala de 10 mm (error de 1 mm, marca Calibres Argentinos, Rosario, Argentina). Con los datos obtenidos se determinaron los siguientes parámetros indirectos: IMC, porcentaje de grasa corporal mediante ecuación de Durnin y Womersley, y relación cintura/cadera.

ANÁLISIS ESTADÍSTICO

Para el análisis estadístico del estudio se utilizó el programa estadístico PASW Statistics® 20 para Windows© (IBM©, Nueva York, EE.UU.). Para la estadística descriptiva se utilizaron la media aritmética como medida de tendencia central y la desviación estándar como medida de dispersión. En lo que respecta a la estadística inferencial, para establecer diferencias entre medias, se utilizó la prueba ANOVA de un solo factor y comparaciones múltiples de Bonferroni, y la prueba t de Student o la de Wilcoxon para muestras pareadas, según la normalidad de las variables establecida mediante el test de Shapiro-Wilk. En todos los casos, se estableció la significación estadística con una $p < 0,05$.

RESULTADOS

Las 119 voluntarias que formaron parte del estudio tenían edades comprendidas entre 25 y 50 años, con una media de 36 ± 8 años y un IMC promedio de 27,52 ± 2,78 kg/m^2. Se puede apreciar que la media de IMC correspondía al rango de SP, es decir, comprendía valores entre 25 y 29,9 kg/m^2.

En la tabla II se detallan las características iniciales de la muestra estudiada en su totalidad: edad, medidas antropométricas y perfil lipídico.

En la tabla III se observa la evolución de las variables antropométricas y del perfil lipídico de los tres grupos tras las doce semanas de intervención. Dentro de las medidas corporales se puede apreciar que el descenso del peso, del IMC y de los valores de CC fue significativo únicamente en los grupos que realizaron la intervención nutricional, no así en el grupo M (Figs. 1-3). Sin embargo, las variables de porcentaje de masa grasa y masa grasa en kilogramos sufrieron un descenso significativo en los tres grupos, sin encontrarse diferencias entre los grupos (Fig. 4).

En cuanto a las variables bioquímicas, se observó que la variación del CT fue significativa en los tres grupos, sin haber diferencia entre los grupos. En cuanto al CLDL y el CHDL, se observó una disminución en los grupos MD y M, no así en el AD. Y en cuanto a los TG, el descenso solo fue estadísticamente significativo en el grupo MD (Tabla IV).

Tabla II. Características iniciales

Características	Media y desviación estándar	IC 95%
Edad (años)	36,09 ± 8,39	33,36-39,06
Peso (kg)	71,46 ± 8,72	68,45-74,44
IMC (kg/m^2)	27,52 ± 2,78	26,64-28,52
Circunferencia de cintura (cm)	85,86 ± 7,96	83,15-88,53
Circunferencia de cadera (cm)	107,73 ± 5,85	105,97-109,79
Relación cintura / cadera	0,80 ± 0,07	0,78-0,82
Porcentaje de masa grasa	37,63 ± 2,88	33,63-38,59
Peso de masa grasa (kg)	26,96 ± 4,40	25,58-28,34
Colesterol total (mg/dl)	180,30 ± 31,81	170,22-191,21
Colesterol-LDL (mg/dl)	110,16 ± 31,81	99,87-122,72
Colesterol-HDL (mg/dl)	49,39 ± 6,28	47,27-51,48
Triglicéridos (mg/dl)	108,15 ± 61,66	90,03-132

IC: intervalo de confianza para la media; IMC: índice de masa corporal; LDL: lipoproteínas de baja densidad; HDL: lipoproteínas de alta densidad.

Tabla III. Evolución de las variables antropométricas

	Grupo MD		Grupo M		Grupo AD		p†
	Inicial	Final	Inicial	Final	Inicial	Final	
Peso (kg)	69,01± 11,20	67,04 ± 10,81	64,77 ± 11,16	65,7 ± 11,53	70,23 ± 7,55	67,91 ± 7,41	< 0,001
Variación	1,96 (2,84%)*		-0,92 (-1,42%)		2,32 (3,30%)*		
IMC (kg/m^2)	26,99 ± 4,10	26,24 ± 3,95	25,34 ± 3,97	25,70 ± 4,12	27,10 ± 1,99	26,15 ± 2,01	< 0,001
Variación	0,76 (2,81%)*		-0,36 (-1,42%)		0,95 (3,50%)*		
Circunferencia de cintura (cm)	87,68 ± 10,06	84,84 ± 9,12	86,57 ± 12,13	87,70 ± 12,53	84,27 ± 7,11	80,00 ± 6,91	0,05
Variación	2,84 (3,24%)*		-1,13 (-1,30%)		4,27 (5,07%)*		
Circunferencia de cadera (cm)	105,59 ± 1,2	102,85 ± 1,085	101,44 ± 12,36	101,40 ± 11,7	108,05 ± 6,39	105,47 ± 5,76	0,11
Variación	2,74 (2,59%)*		0,034 (0,033%)		2,59 (2,40%)*		
Relación cintura/cadera	0,84 ± 0,11	0,82 ± 0,08	0,86 ± 0,14	0,87 ± 0,13	0,78 ± 0,07	0,76 ± 0,05	0,11
Variación	0,02 (2,38%)		-0,0098 (1,14%)		0,021 (2,69%)*		
Porcentaje masa grasa (%)	37,29 ± 5,29	31,05 ± 5,87	35,34 ± 6,29	28,14 ± 5,85	37,97 ± 3,14	36,30 ± 3,54	0,23
Variación	6,13 (16,48%)*		7,19 (20,34%)*		1,67 (4,40%)*		
Kilogramos de masa grasa (kg)	26,23 ± 7,02	21,60 ± 6,43	23,31 ± 7,31	18,65 ± 6,45	26,83 ± 3,99	24,86 ± 4,22	0,20
Variación	4,63 (17,65%)*		4,66 (19,99%)*		1,97 (7,34%)*		

**Diferencias intragrupo significativas para la prueba de Wilcoxon. †Significación de las diferencias entre grupos para la prueba de ANOVA. MD: grupo con mate y dieta; M: grupo con mate; AD: grupo con agua y dieta; IMC: índice de masa corporal.*

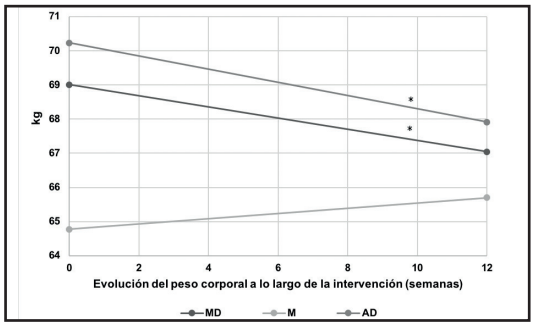

Figura 1.
Evolución del peso corporal según el grupo de estudio (*diferencias intragrupo significativas para la prueba de Wilcoxon).

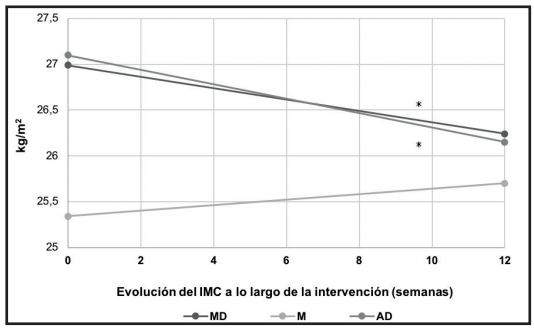

Figura 2.
Evolución del IMC según el grupo de estudio (*diferencias intragrupo significativas para la prueba de Wilcoxon).

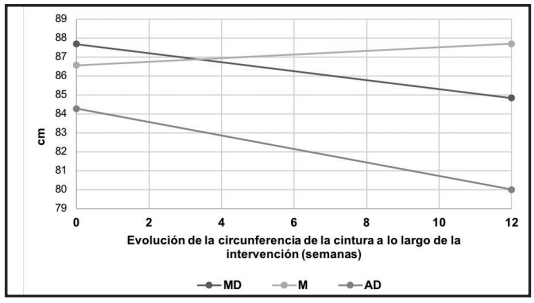

Figura 3.
Evolución de la circunferencia de la cintura según el grupo de estudio (*diferencias intragrupo significativas para la prueba de Wilcoxon).

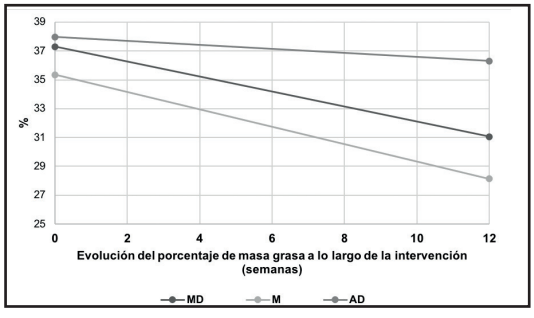

Figura 4.
Evolución del porcentaje de masa grasa según el grupo de estudio (*diferencias intragrupo significativas para la prueba de Wilcoxon).

Tabla IV. Evolución del perfil lipídico

	Grupo MD		Grupo M		Grupo AD		p†
	Inicial	Final	Inicial	Final	Inicial	Final	
Colesterol total (mg/dl)	194,35 ± 38,04	184,14 ± 39,12	204,53 ± 35,05	186,24 ± 39,54	184,69 ± 25,85	167,06 ± 24,80	0,20
Variación	10,21 (5,25%)*		18,29 (8,94%)*		17,62 (9,54%)*		
Colesterol-LDL (mg/dl)	124,33 ± 35,83	116,26 ± 34,24	131,97 ± 30,94	115,93 ± 33,58	112,44 ± 28,27	100,5 ± 22,18	0,36
Variación	8,06 (6,48%)*		16,04 (12,15%)*		11,94 (10,62%)		
Colesterol-HDL (mg/dl)	47,14 ± 4,98	46,61 ± 4,33	47,91 ± 4,85	45,82 ± 4,88	50,56 ± 6,73	48,19 ± 5,59	0,14
Variación	0,53 (1,12%)*		2,09 (4,36%)*		2,37 (4,69%)		
Triglicéridos (mg/dl)	117,00 ± 60,37	106,25 ± 61,41	123,00 ± 69,85	122,67 ± 101,54	107,75 ± 35,89	92,56 ± 45,69	0,48
Variación	10,74 (9,18%)*		0,31 (0,25%)		15,19 (14,10%)		

**Diferencias intragrupo significativas para la prueba de Wilcoxon. †Significación de las diferencias entre grupos para la prueba de ANOVA. MD: grupo con mate y dieta; M: grupo con mate; AD: grupo con agua y dieta; IMC: índice de masa corporal.*

En la figura 5 se observa el descenso absoluto de las variables bioquímicas, siendo más marcado en los grupos que consumieron la infusión y aun más en el grupo MD en el caso de los TG.

DISCUSIÓN

Partiendo de lo observado en un estudio previo llevado a cabo por nuestro equipo en años anteriores, se pensó evaluar si la combinación de un régimen alimentario hipocalórico con el consumo de YM en mujeres con exceso de peso ocasionaba mejoras tanto de las variables antropométricas como de las concentraciones de lípidos séricos. Este trabajo mostró que el consumo diario de la bebida produce una disminución, dependiente del tiempo, del CT y sus fracciones en los individuos dislipidémicos. Se pudo observar que, al finalizar las doce semanas de consumo de YM, el CT descendió un 9,49%, el CLDL un 11,95% y el CHDL un

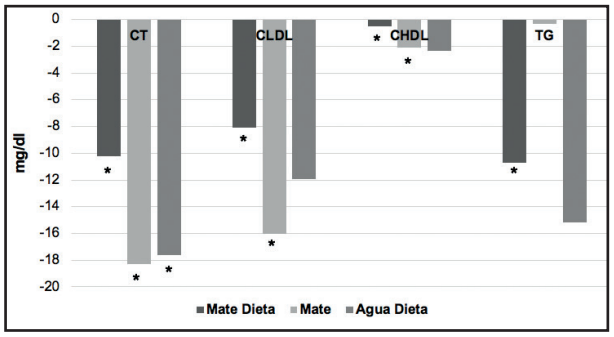

Figura 5.
Descenso absoluto del perfil lipídico según el grupo de estudio (*diferencias intragrupo significativas para la prueba de Wilcoxon).

3,34%, con una $p < 0,001$ para todos los casos, sin diferencias entre los grupos. Pero en cuanto a los TG, solamente se observó una disminución del 7,02% (10,74 mg/dl, $p = 0,029$) en los consumidores de 50 g de YM, sin cambios significativos en las variables antropométricas (11).

En otras investigaciones que han llevado a cabo diversos autores se han logrado demostrar los efectos positivos de la YM sobre uno o más de los criterios que contribuyen al diagnóstico del síndrome metabólico, como la reducción del colesterol, los triglicéridos plasmáticos y las concentraciones sanguíneas de glucosa.

Una reciente investigación *in vitro*, realizada sobre mioblastos murinos C2C12, demostró que el agregado de extracto de YM estimula la biosíntesis de mitocondrias, lo que conduce a un mayor gasto energético (12). Por otra parte, en ratones alimentados con una dieta alta en grasas, la ingesta de YM durante ocho semanas produjo un importante descenso del peso sin reducir la cantidad de comida ingerida, además de una menor acumulación de grasa corporal, frente a aquellos que no consumieron la bebida (12). Además, el grupo tratado con YM mostró una mejoría en la termogénesis, un mayor número de mitocondrias en el tejido muscular, una mayor oxidación de ácidos grasos y una menor acumulación de lípidos en el hígado (12). En un estudio publicado en 2012 se informó de que el tratamiento con extractos de YM en ratones obesos disminuyó alrededor de un 27% las concentraciones de glucosa sanguínea y un 10% las de CT (1). En ratones alimentados con una dieta alta en grasas y suplementados con YM durante 16 semanas se observó un mayor gasto energético junto a una menor expresión de ácido graso-sintasa en el tejido adiposo blanco. Esto sería el factor responsable de la disminución del peso corporal (13).

Por otra parte, se observó que el consumo prolongado de un extracto de YM en gusanos *C. elegans* aumentó la expresión de una lipasa de los adipocitos, junto a una reducción de la acumulación de lípidos y un aumento del gasto energético (14).

Un ensayo clínico realizado para evaluar los efectos de la YM sobre la salud, efectuado con seres humanos, obtuvo diferencias significativas en los cambios del IMC y la masa grasa corporal entre el grupo tratado con YM y el de control. Sin embargo, no se encontraron diferencias significativas en cuanto a modificaciones en los niveles del perfil lipídico. Este estudio tenía como limitación que la muestra tomada era pequeña ($n = 25$) (10). Por otra parte, la suplementación con YM disminuyó la masa grasa corporal, el porcentaje de grasa corporal y la CC. Estos resultados sugirieron que la suplementación con YM puede ser efectiva como tratamiento de individuos obesos (10).

Como se puede observar, la mayoría de los estudios encontrados sobre esta temática están basados en experimentos con animales o *in vitro* y son muy pocos los llevados a cabo con seres humanos.

La YM, por lo que se lleva estudiado hasta la actualidad, se ha descubierto que tiene la capacidad de disminuir la diferenciación de los preadipocitos y de reducir la acumulación de lípidos en los adipocitos, lo que contribuye a la disminución del crecimiento del tejido adiposo (10).

En resumen, los datos presentados aquí mostraron que el uso de YM podría ser útil en el tratamiento de la OB, mejorando los parámetros de lípidos tanto en los seres humanos como en los modelos animales. Además, la YM modula la expresión de los genes que se modifican en el estado obeso y los restaura a niveles de expresión más normales. Al hacerlo, aborda varios de los factores anormales y causantes de enfermedades que se asocian a la OB. También se observaron efectos protectores y de mejora sobre la resistencia a la insulina. Por lo tanto, como conclusión general, parece que las bebidas y suplementos de YM podrían ser útiles en la lucha contra la OB (15). Aun así, los mecanismos de acción por los que se llevan a cabo estos efectos sobre el perfil lipídico no están totalmente claros.

De este modo se podría incluir el consumo de YM como medida auxiliar en el contexto de una alimentación adecuada para la prevención y el tratamiento de las patologías metabólicas relacionadas con la presencia de SP u OB.

Un punto a destacar respecto a nuestra investigación es su aplicación en modelos de alimentación hipocalórica, ya que otras investigaciones solamente han trabajado sin intervención nutricional o bien en modelos de dietas altas en grasas o hipercalóricas. Además, el hecho de haberse empleado la YM al estilo tradicional y en cantidades habituales, es decir, de la manera en que la población realmente la consume, otorga una aproximación bastante realista a la magnitud esperable de los efectos del consumo de esta infusión en la población general. Finalmente, el hecho de tratarse de un ensayo realizado solamente en mujeres con exceso de peso puede considerarse una limitación de este estudio.

En conclusión, la ingesta diaria de YM ayuda a reducir el CT y el CLDL, y proporciona una reducción de los triglicéridos junto a una dieta baja en calorías.

BIBLIOGRAFÍA

1. Kang YR, Lee HY, Kim JH, Moon DI, Seo MY, Park SH, et al. Anti-obesity and anti-diabetic effects of Yerba Mate (Ilex paraguariensis) in C57BL/6J mice fed a high-fat diet. Lab Anim Res 2012;28(1):23-9. DOI: 10.5625/lar.2012.28.1.23
2. Ferreira F, Vázquez A, Güntner C, Moyna P. Inhibition of the passive diffusion of cholic acid by the Ilex paraguariensis St. Hil. saponins. Phytotherapy Res 1997;11:79-81. DOI: 10.1002/(SICI)1099-1573(199702)11:1<79::AID-PTR34>3.0.CO;2-R

3. Gnoatto SCB, Schenkel EP, Bassani VL. HPLC method to assay total saponins in Ilex paraguariensis aqueous extract. J Braz Chem Soc 2005;16:723-6. DOI: 10.1590/S0103-50532005000500007
4. Lima Nda S, Franco JG, Peixoto-Silva N, Maia LA, Kaezer A, Felzenszwalb I, de Oliveira E, de Moura EG, Lisboa PC. Ilex paraguariensis (yerba mate) improves endocrine and metabolic disorders in obese rats primed by early weaning. Eur J Nutr 2014;53(1):73-82. DOI: 10.1007/s00394-013-0500-3
5. http://www.who.int/mediacentre/factsheets/fs311/en/. Hoja informativa n° 311. 2015.
6. Dickel mL, Rates SM, Ritter MR. Plants popularly used for losing weight purposes in Porto Alegre, South Brazil. J Ethnopharmacol 2007;109:60-71. DOI: 10.1016/j.jep.2006.07.003
7. Bracesco N, Sanchez AG, Contreras V, Menini T, Gugliucci A. Recent advances on Ilex paraguariensis research: Minireview. J Ethnopharmacol 2011;136(3):378–84. DOI: 10.1016/j.jep.2010.06.032
8. De Morais EC, Stefanuto A, Klein GA, Boaventura BC, de Andrade F, Wazlawik E et al. Consumption of yerba mate (Ilex paraguariensis) improves serum lipid parameters in healthy dyslipidemic subjects and provides an additional LDL-cholesterol reduction in individuals on statin therapy. J Agric Food Chem 2009;57(18):8316-24. DOI: 10.1021/jf901660g
9. De Resende PE, Verza SG, Kaiser S, Ferreira Gomez L, Kucharski LC, González Ortega G. The activity of mate saponins (Ilex paraguariensis) in intra-abdominal and epididymal fat, and glucose oxidation in male Wistar rats. J Ethnopharmacol 2012;144:735-40. DOI: 10.1016/j.jep.2012.10.023
10. Kim SY, Oh MR, Kim MG, Chae HJ, Chae SW. Anti-obesity effects of Yerba Mate (Ilex Paraguariensis): a randomized, double-blind, placebo-controlled clinical trial. BMC Complement Altern Med 2015;15:338. DOI: 10.1186/s12906-015-0859-1
11. Messina, D; Soto, C; Méndez, A; Corte, C; Kemnitz, M; Avena, V; Del Balzo, D; Perez Elizalde, R. Efecto hipolipemiante del consumo de mate en individuos dislipidémicos. Nutr Hosp 2015;(5):2131-9.
12. Dos Santos TW, Miranda J, Teixeira L, Aiastui A, Matheu A, Gambero A, Portillo MP, Ribeiro mL. Yerba Mate Stimulates Mitochondrial Biogenesis and Thermogenesis in High-Fat-Diet-Induced Obese Mice. Mol Nutr Food Res. 2018;62(15):1800142-172. DOI: 10.1002/mnfr.201800142
13. Choi MS, Park HJ, Kim SR, Kim DY, Jung UJ. Long-Term Dietary Supplementation with Yerba Mate Ameliorates Diet-Induced Obesity and Metabolic Disorders in Mice by Regulating Energy Expenditure and Lipid Metabolism. J Med Food 2017(12):1168-75. DOI: 10.1089/jmf.2017.3995
14. Machado mL, Arantes LP, Gubert P, Zamberlan DC, da Silva TC, da Silveira TL, Boligon A, Soares FAA. Ilex paraguariensis modulates fat metabolism in Caenorhabditis elegans through purinergic system (ADOR-1) and nuclear hormone receptor (NHR-49) pathways. PLoS One 2018;13(9):e0204023. DOI: 10.1371/journal.pone.0204023
15. Gambero A y Ribeiro mL. The positive effects of Yerba Mate (Ilex Paraguariensis) in obesity. Nutrients 2015;7(2):730-50. DOI: 10.3390/nu7020730

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Measurement of body composition in cancer patients using CT planning scan at the third lumbar vertebra

Medición de la composición corporal en pacientes oncológicos mediante la TC de planificación a nivel de la tercera vértebra lumbar

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Abstract

Objective: the main objective was to assess body composition in terms of skeletal muscle index (SMI), myosteatosis, visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and intermuscular adipose tissue (IMAT) as an adjunct of information provided by radiotherapy CT planning scan.

Material and methods: a sample of 49 patients with lung and digestive cancers underwent a CT scan for radiotherapy treatment, which included measurements at the L3 region. Images were analyzed with a radiotherapy contouring software, using different Hounsfield Unit (HU) settings. Cross-sectional areas (cm^2) were automatically computed by summing tissue pixels and multiplying by pixel surface area. Low SMI (cm^2/m^2) and muscle density (HU) were determined according to the recently established cut-off points.

Results: the prevalence of low SMI was detected in 46.94% of patients, being present in 8 women, 4 men with BMI < 25 kg/m^2, and 11 men with BMI ≥ 25 kg/m^2. The average mean skeletal attenuation of total skeletal muscle area was 29.02 (± 8.66) HU, and myosteatosis was present in 13 women (81.25%) and 31 men (93.94%). Mean SAT was 131.92 (± 76.80) cm^2, mean VAT was 133.19 (± 85.28) cm^2, and mean IMAT was 11.29 (± 12.86) cm^2.

Conclusion: skeletal muscle abnormalities are frequently present in cancer patients and a low SMI may also exist even in the presence of overweight. As CT scans are an important tool at any radiation oncology department, they could also be used to offer highly sensitive and specific information about body composition, as well as to detect early malnutrition before starting radiotherapy treatment.

Key words:

Cancer. Radiotherapy. CT scan. Body composition.

Resumen

Objetivo: evaluar la composición corporal mediante el índice de músculo esquelético (IME), el tejido adiposo visceral (TAV), el tejido adiposo subcutáneo (TAS) y el tejido adiposo intermuscular (TAIM) o la densidad muscular (DM) en pacientes oncológicos antes de iniciar el tratamiento con radioterapia mediante cortes de TAC.

Materiales y métodos: se estudiaron 49 pacientes con cáncer de pulmón y del aparato digestivo sometidos a tomografía computarizada con cortes en L3 para la determinación del tratamiento con radioterapia. El tejido adiposo y muscular se cuantificó mediante distintas Unidades Hounsfield (UH) (-29 a +150 para masa muscular, -190 a -30 para TAIM/TAS y -150 a -50 para TAV).

Resultados: la prevalencia de un IME bajo se detectó en el 46,94% de los pacientes, estando presente en 8 mujeres, 6 de ellas con un IMC ≥ 25 kg/m^2. Según la distribución masculina, se identificaron 4 hombres con IMC < 25 kg/m^2 y 11 hombres con ≥ 25 kg/m^2. La DM media fue de 29,02 (± 8,66) UH y la mioesteatosis estuvo presente en 13 mujeres (81,25%) y 31 hombres (93,94%). La media del TAS fue de 131,92 (± 76,80) cm^2, la del TAV de 133,19 (± 85,28) cm^2 y la del TAIM de 11,29 (± 12,86) cm^2.

Conclusión: las anormalidades del músculo esquelético y la masa grasa son muy frecuentes en los pacientes con cáncer, pudiendo existir un bajo IME incluso en presencia de sobrepeso u obesidad. Teniendo en cuenta que la TAC es una herramienta importante en cualquier departamento de radioterapia, también podría utilizarse para ofrecer información sensible y específica sobre la composición corporal, así como para detectar la malnutrición precoz.

Palabras clave:

Cáncer. Radioterapia. Tomografía computarizada. Sarcopenia. Composición corporal.

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INTRODUCTION

Patients with cancer often have important nutritional deficiencies that significantly affect their quality of life, and the incidence of malnutrition increases as the disease progresses, until it affects 80% of patients (1). Sarcopenia is the loss of skeletal muscle mass with an increase in functional impairment and physical disability (2). According to an international group gathered to define sarcopenia in cancer patients, it is a fundamental part of cancer cachexia and an important part of the cancer patient evaluation (3). On the other hand, it is known that decreased muscle mass (MM) in cancer patients, also called pre-sarcopenia, increases the toxicity levels of treatment and therefore leads to treatment interruptions, dose reductions, and a higher risk of mortality (2,3,4).

In addition, muscle depletion is characterized by a reduction in muscle size and an increased proportion of intermuscular and intramuscular fat, denominated "myosteatosis" (5). This pathological problem has been relatively recently characterized; however, interest has been raised by its relationship to insulin resistance, poor physical function, and more recently poor survival (5,6).

On the other hand, sarcopenia is not restricted to people who are thin or cachectic (6,7). The condition called sarcopenic obesity has been reported to have higher rates of complications and hospital costs when compared to patients with normal weight, an observation in accord with the obesity paradox (8). Moreover, cancer patients with sarcopenic obesity had the poorest prognosis (9). Historically, bioelectrical impedance analysis (BIA), body mass index (BMI), triceps skin fold, and serum albumin or prealbumin levels have been used as indicators for detecting malnutrition (10). However, anthropometric quantification methods have a significant inter- and intra-observer variability, and this may limit sensitivity for detecting muscle changes and sarcopenic obesity (2,10,11).

However, considering that we are in an age of technology based on imaging techniques, computed tomography (CT) scans, which have long been used for the diagnosis of cancer, are becoming forefront strategies for nutritional assessment and intervention (12).

Nowadays, it is known that the cross-sectional areas of tissue in a single image at the third lumbar vertebra appear to be strongly correlated to whole-body adipose tissue and lean tissue mass (13). Due to these findings, body composition as skeletal muscle mass (SMM) and area of visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and intermuscular adipose tissue (IMAT) can be accurately estimated using this approach (12).

As muscularity and adiposity were associated with their own risk for poor health outcomes in cancer patients, our main goal in this study was to detect pre-sarcopenia and myosteatosis, as well as to assess the presence of VAT, SAT, and IMAT using the powerful information provided by CT planning scans in cancer patients evaluated for radiation treatment.

MATERIAL AND METHODS

PATIENTS

A sample of 49 patients referred for radiation oncology treatment with lung cancer and tumors affecting the digestive system (esophagus, stomach, pancreas, gallbladder, rectum, and anus) were retrospectively analyzed between 2015 and 2017. All patients underwent virtual tomography with a SIEMENS Somaton Sensation Open CT planning scan (120 KV) for radiotherapy treatment preparation, with measurements at the level of the L3 area. Patients without clinical data or without suitable CT examinations were excluded from the study.

The following clinical characteristics at the time of the CT scan were recorded: age (> 18 years), tumor stage, secondary pathologies, weight, height, surgery, dose of radiation, type of chemotherapy, and surgical outcome. Body mass index (BMI) in kg/m^2 was calculated according to weight and height, and there were applied different categories to classify patients: < 18.45, underweight; 18.5 kg/m^2 to 24.9 kg/m^2, normal weight; 25.0 kg/m^2 to 29.9 kg/m^2, overweight; and ≥ 30.0 kg/m^2, obese.

SKELETAL MUSCLE AND ADIPOSE TISSUE AREA MEASUREMENTS

The cross-sectional area of the skeletal muscle mass area, subcutaneous adipose tissue area, visceral adipose tissue area, and intermuscular adipose tissue, including skeletal attenuation of the skeletal muscle area, were measured using CT scans at the level of the third lumbar vertebra (L3) (Fig. 1). This region contains different muscles including the psoas and paraspinal muscles, transversus abdominis, external and internal obliques of the abdomen, and rectus abdominis, as well as visceral, subcutaneous and intermuscular adipose tissue. All images for the study were used for the measurements and planning of the radiotherapy treatment (without extra patient radiation).

Images were analyzed with a radiotherapy contouring software (MIM® 6.7 Inc., Cleveland, OH, USA) using different Hounsfield Unit (HU) thresholds, these being -29 to +150 for SMM, -190 to -30 for SAT and intermuscular adipose tissue (IMAT), and -150 to - 50 for VAT (13,14).

Cross-sectional areas (cm^2) were automatically computed by summing tissue pixels and multiplying the result by their surface area (slice thickness range: between 1.5 mm and 3 mm). The data obtained were normalized by height (cm^2/m^2). The skeletal muscle index (SMI) (cm^2/m^2) was determined according to the currently established cut-off points, these being ≤ 41 cm^2/m^2 for women, ≤ 53 cm^2/m^2 for men with BMI ≥ 25, and ≤ 43 cm^2/m^2 for men with BMI < 25 kg/m^2 (15). Low muscle density (myosteatosis) was detected according to HU, and was < 33 for women and < 41 for men (5,16).

Examples of how the different tissue areas were measured with the MIM® software are shown in figure 2.

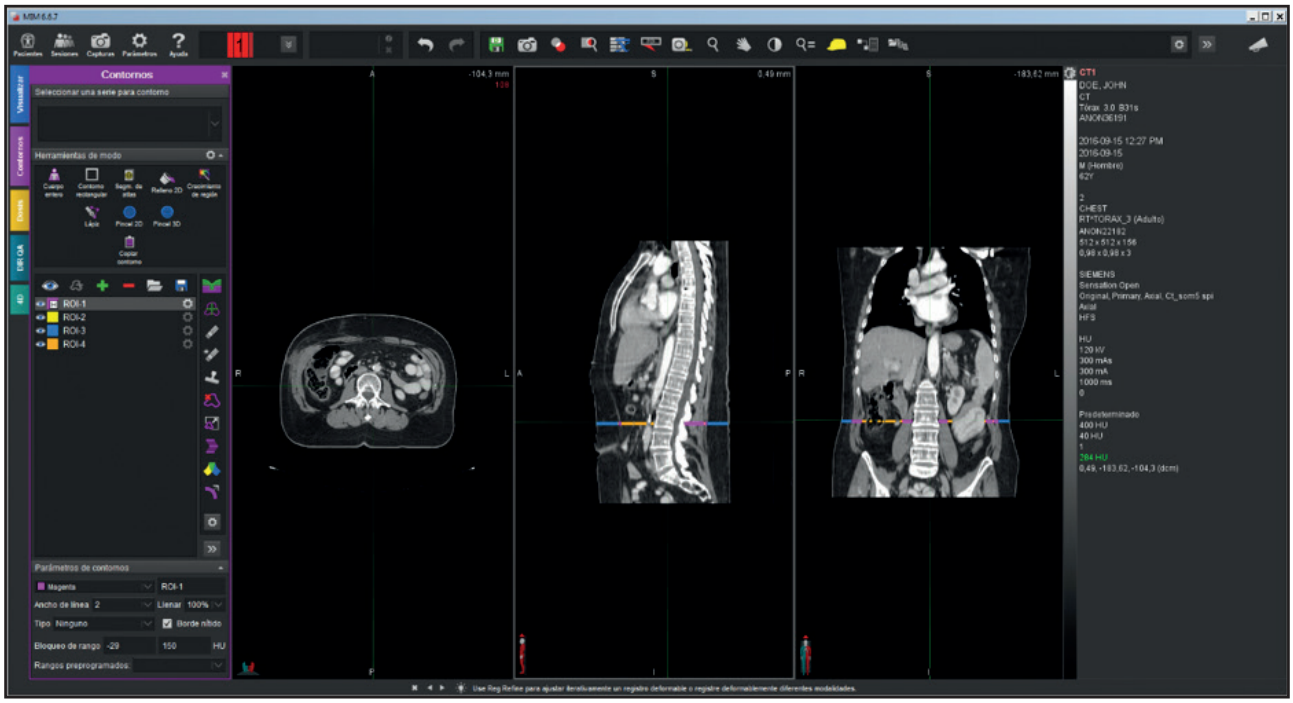

Figure 1.
Determination of the third lumbar vertebra (L3). An isolated CT image from the third lumbar vertebra (L3) was used for the body measurements. The chosen image was the one with both transverse processes clearly visible, right in the middle of L3. All abdominal images were ordered for radiotherapy tumor treatment. All images were analyzed using the anonymous mode. Poor-quality and unsuitable CT scans were not included for the body analysis.

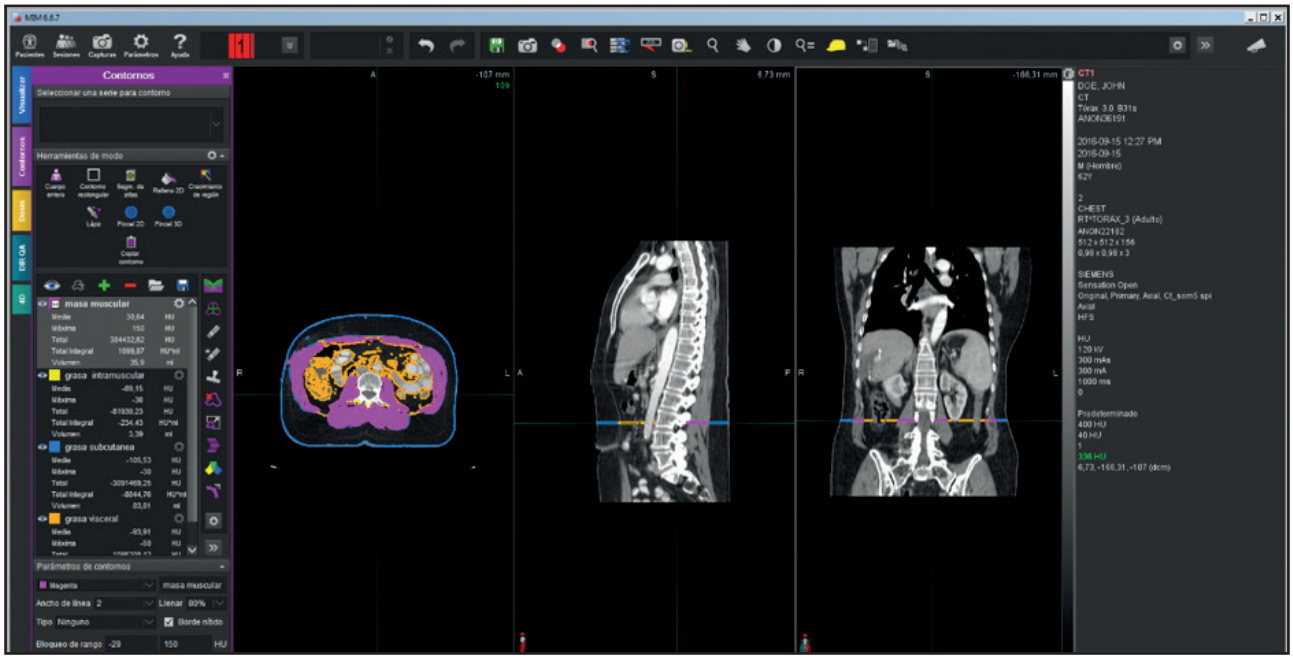

Figure 2.
Body composition analysis. The CT analysis was made by contouring every tissue of interest on the L3 image. Different tissue densities were measured in Hounsfield Units (HU), these being -29 to +150 for SMM (pink color), -190 to -30 for SAT (blue color) and IMAT (green color), and -150 to -50 for VAT (orange color). As fat is more infiltrated inside muscles, its density (HU) decreases, so muscle density may also be measured according to the HU obtained for skeletal muscle mass. After the tagging process, the cross-sectional areas of tissues (cm^2) were automatically computed by summing tissue pixels and multiplying by pixel surface area.

For the assessment of cross-sectional areas an automatic, software-driven identification and delineation method was used, manually corrected after automatic coloring, instead of free hand delineation, which may overestimate the results.

STATISTICAL ANALYSIS

The different variables contained in the study were analyzed with descriptive statistics, and the continuous variables were represented by mean, median, standard deviation and percentiles. The adjustments of variables to normality were done with the Shaphiro-Wilk test. The statistical program STATA 14 was used for the analysis.

ETHICAL CONSIDERATIONS

All CT images were used for the measurements and planning of the radiotherapy treatment (without extra radiation). Our retrospective study was approved by the Ethics Committee; however, because all images were used in an anonymized mode and cancer patients have a high risk of morbidity, the informed consent was not necessary according to the Law and 'Best Practice' guidelines.

RESULTS

A sample of 49 patients (16 women, 33 men) were enrolled in this retrospective study. Patients had different cancer locations – lung (28.57%), esophagus (20.41%), stomach (18.37%), pancreas (12.24%), gallbladder (6.12%), rectum (10.20%), and anus (4.08%).

The clinical and demographic characteristics of the patients, including cancer stage, classification of malignant tumors (TNM) according to the American Joint Committee on Cancer Staging manual (7th edition), secondary pathologies, type of treatment, and surgery outcomes are shown in table I.

Table I. Clinical and demographic characteristics of patients

Clinical feature of variable		Number of cases (%)
Median age (range)	65.10 (32-84)	
Sex	Female 16	(32.65%)
	Male 33	(67.35%)
Tumor stage	EI 3	(6.12%)
	EII 10	(20.41%)
	EIII 32	(65.31%)
	EIV 4	(8.16%)
Tumor location	Lung 14	(28.57%)
	Esophagus 10	(20.41%)
	Stomach 9	(18.37%)
	Pancreas 6	(12.24%)
	Gallbladder 3	(6.12%)
	Rectum 5	(10.20%)
	Anus 2	(4.08%)
Diabetes *mellitus*	9	(18.37%)
Hypertension	16	(32.65%)
Dyslipidemia	10	(20.41%)
Hypothyroidism	2	(4.08%)
COPD	4	(8.16%)
Barrett's esophagus	2	(4.08%)
TB	1	(2.04%)
Osteoporosis	2	(4.08%)
Parkinson	1	(2.04%)
Gastritis	1	(2.04%)
HIV	1	(2.04%)
HCV	1	(2.04%)
Type of treatment	*Curative*	(95.92%)
	Neoadjuvant chemo-RT	(18.37%)
	Adjuvant chemo-RT	(30.61%)
	Concomitant chemo-RT	(40.82%)
	Radical	(6.12%)
	Palliative	(4.08%)

COPD: chronic obstructive pulmonary disease; TB: tuberculosis; HIV: human immunodeficiency virus; HCV: hepatitis C virus; Chemo-RT: chemoradiotherapy.

The mean age of patients was 65 years (range, 32-84 years), mean weight was 66.75 (± 11.25) kg, and mean BMI was 24.66 (± 3.98) kg/m^2. In terms of muscle and fat composition of these cancer patients before radiotherapy, mean SMM was 123.81 (± 34.01) cm^2, mean SAT was 131.92 (± 76.80) cm^2, mean VAT was 133.19 (± 85.28) cm^2, and mean IMAT was 11.29 (± 12.86) cm^2 (Table II). Considering the distribution by gender, mean female weight was 60.9 (± 10.09) kg and most of the women were within the normal BMI range, with an average of 24.23 (± 4.24) kg/m^2 according to their BMI. As per males, mean weight was 69.98 (± 10.44) kg, also with a normal average according to their BMI – 24.83 (± 3.90) kg/m^2 (Table III).

On the other hand, skeletal muscle abnormalities were frequently present in cancer patients before radiotherapy. The prevalence of low SMI was detected in 46.94% of the sample – 8 women (50%) and 15 men (45.45%). Amongst the women with low SMI, 6 (37.50%) had a BMI ≥ 25 kg/m^2, and were considered sarcopenic obese. Amongst men, 4 (12.12%) had a BMI < 25 kg/m^2 and 11 (33.33%) had a BMI ≥ 25 kg/m^2, these being sarcopenic obese as well (Fig. 3). Mean average SMI was 45.51 (10.33) cm/m^2. The mean skeletal attenuation of total skeletal muscle area was 29.02 (± 8.66) HU. This fact shows that myosteatosis was present in 89.79% of patients. Of these, 26.53% (13 patients) were women, and 63.26% (31 patients) were men (Fig. 4).

Figure 5 illustrates two different body compositions of cancer patients before starting radiotherapy.

DISCUSSION

Cancer induces muscle wasting and oncologic patients are at higher risk of malnutrition not only due to the physical and metabolic effects of cancer but also because of anticancer therapies, as occurs after oncological surgery or during radiochemotherapy (3,17,18). On the other hand, it is known that the nutritional side effects of radiation depend on tumor location, total dose, and the effects of combined radiochemotherapy, with head and neck, digestive system, and lung cancer patients being most affected (19,20).

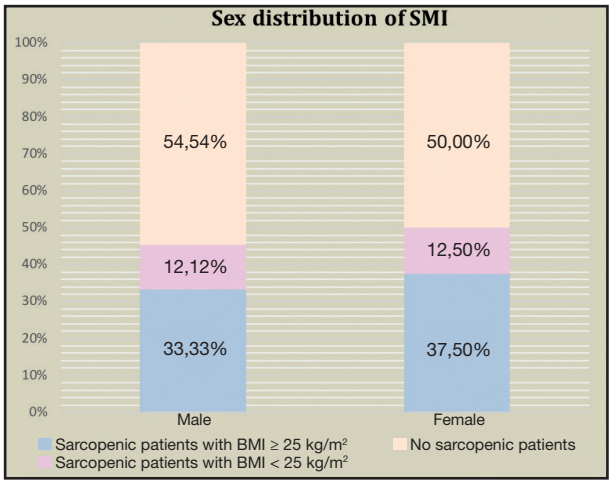

Figure 3.
Sex distribution of the skeletal muscle index (cm^2/m^2) as analyzed by CT scans. Amongst women with low SMI, 37.50% had a BMI ≥ 25 kg/m^2, and were considered sarcopenic obese, and 12.50% had a BMI < 25 kg/m^2. Amongst males, 12.12% had a BMI < 25 kg/m^2 and 33.33% had a BMI ≥ 25 kg/m^2, and were also considered sarcopenic obese. On the other hand, 50% of women and 54.54% of men were not considered to be sarcopenic.

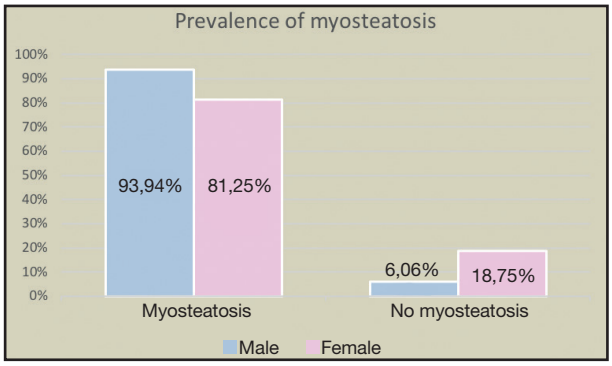

Figure 4.
Prevalence of myosteatosis (HU) as analyzed by CT scans. Myosteatosis (low muscle density) was present in 89.79% of the sample. According to sex distribution, myosteatosis was present in 93.94% of males and 81.25% of females. On the other hand, 6.06% of males and 18.75% of females had normal muscle density.

Table II. Body composition using CT measurements at L3 vertebra

	Age (years)	Weight (kg)	BMI (kg/m^2)	SMM (cm^2)	SMI (cm^2/m^2)	SAT (cm^2)	VAT (cm^2)	IMAT (cm^2)	Muscle density (HU)
Mean	65.10	66.75	24.63	123.82	45.51	131.92	133.19	11.29	29.02
SD	11.62	11.25	3.98	34.01	10.33	76.80	85.28	12.86	8.66
Median	66	66	24.83	121.17	45.37	114.17	109.00	6.90	29.32
IQ25 range	56.50	59.40	22.34	100.72	40.38	75.03	74.29	3.55	22.78
IQ75 range	73.50	75.50	26.26	145.87	52.00	180.77	184.37	13.90	34.43

BMI: body mass index (kg/m^2); SMM: skeletal muscle surface area at L3 = Sum of spinal vertebrae, transverse abdominis, external/internal oblique, and rectus abdominis muscles divided by CT slice thickness (cm^2); SMI: lumbar skeletal muscle index = (SMM at L3/stature)^2 (cm^2/m^2); SAT: subcutaneous adipose tissue surface area at L3 = The adipose tissue between the muscle and the skin (HU -190 to -30), divided by CT slice thickness (cm^2); VAT: visceral adipose tissue surface area at L3 = Fat surrounding organs (HU -150 to –50), divided by CT slice thickness (cm^2); IMAT: intermuscular adipose tissue surface area at L3 = Fat between and within the muscle groups (HU -190 to -30), divided by CT slice thickness (cm^2).

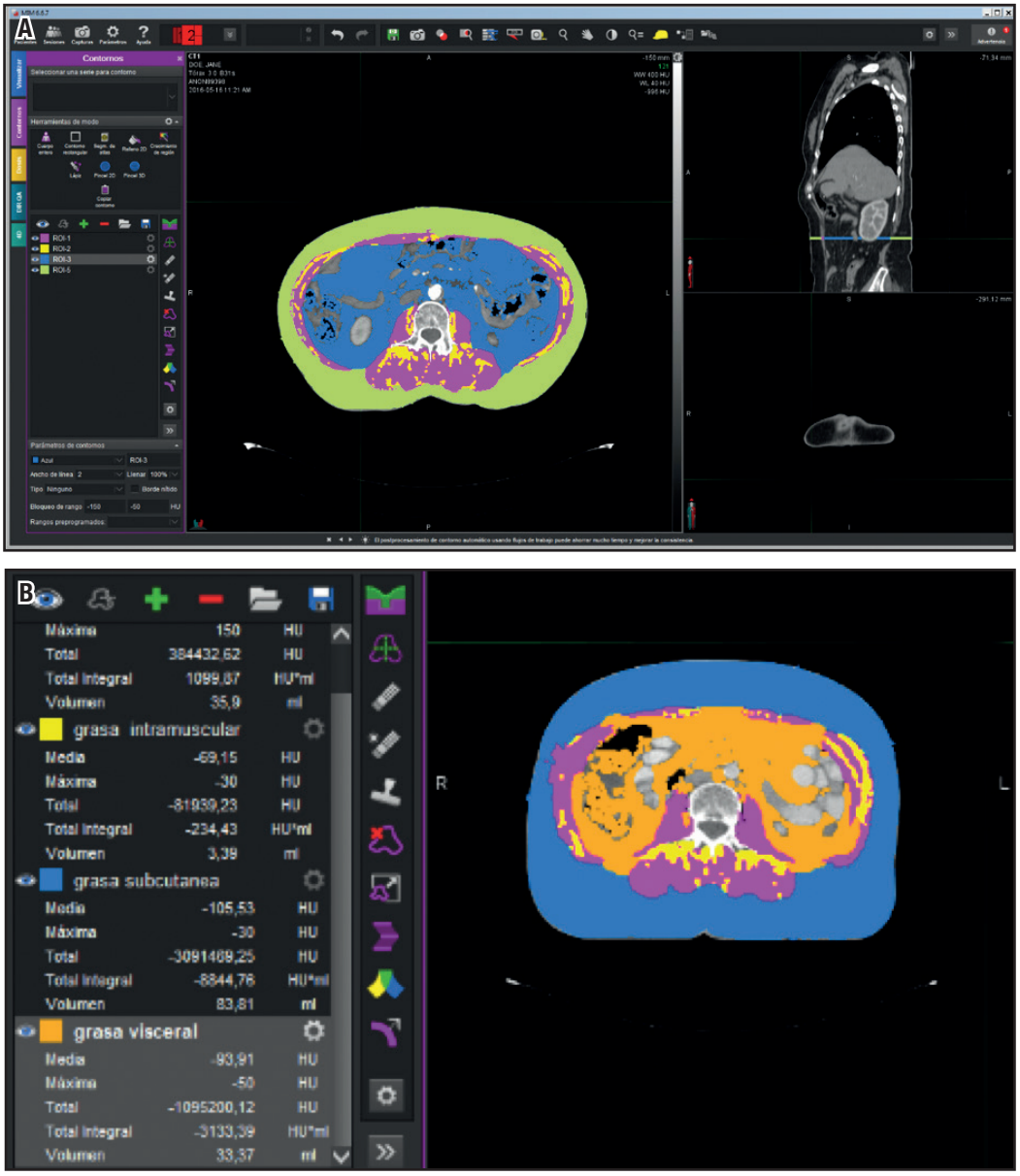

Figure 5.
Variation of SMI, VAT, SAT, and IMAT in cancer patients before starting radiotherapy. Comparison of two cancer patients with different body composition using CT planning scans (A and B). A. Patient with visceral obesity, myosteatosis and low muscle mass. ■ : skeletal muscle; ■ : visceral adipose tissue; ■ : subcutaneous adipose tissue; ■ : intramuscular adipose tissue. B. Patient with subcutaneous obesity, myosteatosis and low muscle mass. ■ : skeletal muscle; ■ : visceral adipose tissue; ■ : subcutaneous adipose tissue; ■ : intramuscular adipose tissue.

To date many studies have reported that malnutrition is frequently found between 30% and 85% of patients with progressive cancer disease (3,21). In terms of health outcomes, this fact is associated with muscle and weight loss, reduced immune competence, and higher risk of infection, psychosocial stress, lower quality of life, higher toxicity from antineoplastic treatments, poorer survival, longer hospital stays, and increased hospital costs (2,3,22,23). Consequently, monitoring body composition before cancer treatment could be very useful to provide nutritional and medical interventions in order to optimize treatment and reduce toxicity levels (24,25).

Nowadays, many studies show that the third lumbar vertebra (L3) is strongly correlated with total body tissue areas, and cross-sectional imaging provides an intuitive and highly differentiated analysis of human body composition with discrimination of specific organs and tissue types (13,14). Routine use of CT imaging in the general population has been limited by cost and the necessary exposure to high-dose radiation; however, some specialties, such as oncology,

rely heavily on imaging techniques for diagnosis and treatment, for the care and radiotherapy of their patients. As body composition phenotypes in cancer patients have recently been associated with their risk for poor health outcomes, computerized tomography scans have emerged as a readily accessible method of assessing adipose tissues and muscle mass (26,27,28), all of them being available at any radiotherapy department and offering important and singular images about body composition.

Lean body mass in the form of skeletal muscle is the predominant source of protein in the body, and a major predictor of functional capacity, as over 99% of metabolic processes take place in this surface area (29). Moreover, muscle protein depletion is a hallmark of cancer cachexia, a multifactorial wasting syndrome characterized by involuntary weight loss with ongoing loss of SMM with or without loss of fat (3,30). Cachexia's wasting consequences cannot frequently be reversed by conventional nutrition care, and its presence may lead to functional impairment (3,31). Sarcopenia is a major feature of cancer cachexia and is related with reduced quality of life and survival in cancer patients (2,32,33). A meta-analysis of 38 studies found that a low skeletal muscle index in cancer was associated with worse survival in patients with solid tumors (26). On the other hand, another study shows that decreased muscle mass had a harmful effect against grade 3-4 neutropenia and all grade 3-4 toxicities (4). Our study indicates that skeletal muscle abnormalities are frequently present in cancer patients, and according to our patients' body composition, mean SMM was 123.81 (± 34.01) cm^2, and low SMI was present in almost half of the sample (46.94%) – 8 women (50%) and 15 men (45.45%). This is a very important fact, taking into account the mounting of scientific evidence to suggest that LBM may be a better predictor of drug administration and cancer therapies than either total bodyweight or body surface area (34,35). Currently there are about fourteen studies that have related CT-based body composition to the prevalence of dose limiting toxicity (DLT) or different grades of toxicity, and investigations become each and every day more important in this area (36). Furthermore, there have been reports showing the role of body composition, especially lean mass, on the pharmacokinetics of 5-FU (37).

On the other hand, low attenuation of muscles is a sign of triglyceride accumulation in muscle cells, and has also been shown to be associated with systematic inflammation (a hallmark of cancer cachexia) (5). The pathological accumulation of fat in muscles, also called myosteatosis, describes an abnormal retention of lipids within muscle tissue and has been associated with insulin resistance as well as decreased muscle activity (14). In our study, mean IMAT was 11.29 (± 12.86) cm^2 and total skeletal attenuation of muscle area was 29.02 (± 8.66) HU. According to our findings, myosteatosis was present in 89.89% of cancer patients.

However, obesity is a heterogeneous condition with individual differences in the pattern of adipose tissue deposition (6). Accumulation of abdominal fat, particularly in the visceral compartment, may confer the majority of obesity-associated health risks, being also associated with different types of cancers, such as colorectal or prostate malignancies (6,38,39). Because visceral adipose tissue (VAT), rather than subcutaneous adipose tissue (SAT), is recognized as the contributing factor in body insulin resistance, visceral abdominal obesity is viewed as the more clinically important type of abdominal obesity (6). Many studies have demonstrated a close relationship between body fat distribution and the occurrence of the metabolic syndrome or obesity-related complications, and the accumulation of heavy VAT can interrupt blood flow to abdominal organs and decrease organ function (40). In terms of fat composition the characteristics of the cancer patient presented in our study had an average of 131.92 (± 76.80) cm^2 of SAT, and 133.19 (± 85.28) cm^2 of VAT.

Nevertheless, low levels of muscle mass are not only seen in patients who appear cachectic, and it could also be present in individuals who are overweight or obese (7,9). This is due to cancer patients may develop simultaneous loss of skeletal muscle and gain of adipose tissue, culminating in the condition of "sarcopenic obesity" (8). The combination of sarcopenia and obesity has been associated with additive adverse effects related to physical disability in several epidemiologic studies (41). This dangerous term is strongly related to reduction in survival, worse prognosis, and increased adverse effects compared to sarcopenic or obese cancer patients (42). In our study, in total, there were 6 women (37.50%) and 11 men (33.33%) identified with a BMI ≥ 25 kg/m^2, being sarcopenic obese. Although this was noted in patients across the full range of body weight, sarcopenic obesity was particularly noted to have a strong association with poor survival when compared with non-sarcopenic obesity (9).

While other anthropometric quantification methods used to diagnose muscle depletion, such as bioelectrical impedance analysis (BIA), triceps or abdominal skinfolds, or waist circumference (WC), have a significant inter- and intra-observer variability, serum albumin or prealbumin are very expensive to quantify and depend on external factors such as body inflammation (2). Moreover, this has limited sensitivity for detecting VAT, SAT, IMAT or sarcopenic obesity (12,13). Because of that, CT scans are presently considered the most reliable methods for the analysis of body composition, because they can provide important quantitative information on muscle composition and distribution through their high pictorial quality, spatial accuracy, site specificity, and the ability to measure fat and muscle content from one abdominal cross-sectional slice (28,43).

The limitation of our study was that the delineation of muscles and adipose tissue was performed by a single researcher. On the other hand, different consensus groups who are working on sarcopenia as, for example, the European Working Group on Sarcopenia in Older People (EWGSOP), the Foundation for National Institutes of Health Sarcopenia Project, or the Society for Sarcopenia, Caquexia and Wasting Disorders, insist on the importance of evaluating muscle performance or muscle strength (2), which have not been collected in our patients. Likewise, the evaluation of body composition using CT scans may be a useful adjunct in managing patients with cancer, and may improve patient selection for therapies through the identification of high-risk individuals and appropriate initiation of early supportive care.

In conclusion, our study indicates that skeletal muscle and fat abnormalities are frequently present in cancer patients. On the other hand, sarcopenia may also exist even in the presence of overweight. To date, many studies have highlighted the importance of assessing malnutrition in cancer disease, and as CT planning scans are routinely used in the radiotherapy department, they can be used to assess skeletal muscle volume as well as adipose tissue in cancer patients undergoing radiotherapy.

REFERENCES

1. Kim JY, Wie GA, Cho YA, Kim SY, Kim SM, Son KH, et al. Development and validation of a nutrition screening tool for hospitalized cancer patients. Clinical Nutrition 2011;30:724-9. DOI: 10.1016/j.clnu.2011.06.001.
2. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis. Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39:412-23. DOI: 10.1093/ageing/afu115.
3. Fearon K, Strasser F, Anker S, Bosaeus I, Bruera E, Faisinger RL, et al. Definition and classification of cancer cachexia: an international consensus. Lan Oncology 2011;12:489-95. DOI: 10.1016/S1470-2045(10)70218-7.
4. Jung HW, Kim JW, Kim JY, Kim SW, Yang HK, Lee JW, et al. Effect of muscle mass toxicity and survival in patients with colon cancer undergoing adjuvant chemotherapy. Support Care Cancer 2015;23:687-94. DOI: 10.1007/s00520-014-2418-6.
5. Montano-Loza AJ, Angulo P, Meza-Junco J, Prado CMM, Sawyer MB, Beaumont C, et al. Sarcopenic obesity and myosteatosis are associated with higher mortality in patients with cirrhosis. Journal of Cachexia, Sarcopenia and Muscle 2016;7:126-35. DOI: 10.1002/jcsm.12039.
6. Kazemi-Bajestani SMR, Mazurak VC, Baracos V. Computed tomography-defined muscle and fat wasting are associated with cancer clinical outcomes. Seminars in Cell & Development Biology 2016;54:2-10. DOI: 10.1016/j.semcdb.2015.09.001.
7. Than BH, Birdsell LA, Marti L, Baracos VE, Fearon KC. Sarcopenia in an Overweight or Obese Patient Is an Adverse Prognostic Factor in Pancreatic Cancer. Clin Cancer Res 2009;15:6973-9. DOI: 10.1158/1078-0432.CCR-09-1525.
8. Carnicero IP, Mazurak VC, Prado CM. Clinical Implications of Sarcopenic Obesity in Cancer. Curr Oncol Rep 2016;18:62. DOI: 10.1007/s11912-016-0546-5.
9. González MC, Pastore CA, Orlandi SP, Heymsfield SB. Obesity paradox in cancer: new insights provided by body composition. Am J Clin Nutr 2014;99:999-1005. DOI: 10.3945/ajcn.113.071399.
10. Valente da Silva HG, Santos SO, Silva NO, Ribeiro FD, Josua LL, Moreira AS. Nutritional assessment associated with length of inpatients' hospital stay. Nutr Hosp 2012;27:542-7. DOI: 10.1590/S0212-16112012000200029.
11. Sergi G, Trevisan C, Veronese N, Lucato P, Manzato E. Imaging of sarcopenia, Eur. J. Radiol 2016; 85:1519-24. DOI: 10.1016/j.ejrad.2016.04.009.
12. Prado CM, Heymsfield SB. Lean Tissue Imaging: A New Era for Nutritional Assessment and Intervention. J Parenter Enteral Nutr 2014;38:940-53. DOI: 10.1177/0148607114550189.
13. Yip C, Dinkel C, Mahajan A, Siddique M, Cook J.R, Goh V. Imaging body composition in cancer patients: visceral obesity, sarcopenia and sarcopenic obesity may impact on clinical outcome. Insight Imaging 2015;6:489-97. DOI: 10.1007/s13244-015-0414-0.
14. Mourtzakis M, Prado MC, Lieffers RJ, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computered tomography images acquired during routine care. Physiol Nutr Metab 2008;33:997-1006. DOI: 10.1139/H08-075.
15. Peterson SJ, Braunschewing CA. Prevalence of sarcopenia and associated outcomes in clinical settings. Nutr Clin Pract 2016;31:40-8. DOI: 10.1177/0884533615622537.
16. Chu MP, Lieffers J, Ghosh S, Belch AR, Chua NS, Fontaine A, et al. Skeletal Muscle Radio-Density Is an Independent Predictor of Response and Outcomes in Follicular Lymphoma Treated with Chemoimmunotherapy. PLoS one 10 2015;10:0127589. DOI: 10.1371/journal.pone.0127589.
17. Aversa Z, Costelli P, Muscaritoli M. Cancer-induced muscle wasting: latest findings in prevention and treatment. Ther Adv Med Oncol 2017;9:369-82. DOI: 10.1177/1758834017698643.
18. Grossberg AJ, Chamchod S, Fuller DC, Mohamed ASR, Heukelom J, Eichelberger H, et al. Association of Body Composition with Survival and Locoregional Control of Radiotherapy-Treated Head and Neck Squamous Cell Carcinoma. JAMA Oncol 2016;2:782-9. DOI: 10.1001/jamaoncol.2015.6339.
19. Marín Caro MM, Gómez Candela C, Castillo Rabaneda R, Lourenço Nogueira T, García Huerta M, Loria Kohen V, et al. Nutritional risk evaluation and establishment of nutritional support in oncology patients according to the protocol of the Spanish Nutrition and Cancer Group. Nutr Hosp 2008;23:458.
20. Platek ME, Popp JV, Possinger CS, Denysschen CA, Horvarth P, Brown JK. Comparison of the prevalence of malnutrition diagnosis in head and neck, gastrointestinal and lung cancer patients by three classification methods. Cancer Nurs 2011;34:410-6. DOI: 10.1097/NCC.0b013e318206b013.
21. Porpurato PE. Understanding cachexia as a cancer metabolism syndrome. Oncogenesis 2016;5:1-10. DOI: 10.1038/oncsis.2016.3.
22. Wendrich AW, Swartz JE, Bril SI, Wegner I, De Graeffd A, Smid EJ, et al. Low skeletal muscle mass is a predictive factor for chemotherapy dose-limiting toxicity in patients with locally advanced head and neck cancer. Oral Oncol 2017; 71:26-33. DOI: 10.1016/j.oraloncology.2017.05.012.
23. Aversa Z, Costelli P, Muscaritoli M. Cancer-induced muscle wasting: latest findings in prevention and treatment. Ther Adv Med Oncol 2017;9:369-82. DOI:10.1177/1758834017698643.
24. Arends J, Baracos V, Bertz H, Bozzetti F, Calder PC, Deutz NEP, et al. Review ESPEN expert group recommendations for action against cancer related malnutrition. Clin Nutr 2017;36:1187-96. DOI: 10.1016/j.clnu.2017.06.017.
25. Talwar B, Donnelly R, Skelly R, Donaldson M. Nutritional management in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. J Laryngol Otol 2016;130:32-40. DOI: 10.1017/S0022215116000402.
26. Prado CM, Birdsell LA, Baracos VE. The emerging role of computerized tomography in assessing cancer cachexia. Curr Opin Support Palliat Care 2009;3:269-75. DOI: 10.1097/SPC.0b013e328331124a.
27. Andreoli A, Garaci F, Pio F, Guglielmi G. Body composition in clinical practice. Eur J Radiol 2016;85:1461-8. DOI: 10.1016/j.ejrad.2016.02.005.
28. Daly LE, Prado CM, Ryan AM. A window beneath the skin: how computed tomography assessment of body composition can assist in the identification of hidden wasting conditions in oncology that profoundly impact outcomes. Proceedings of the Nutrition Society 2018;77:135-51. DOI: 10.1017/S0029665118000046.
29. Paddon-Jones D, Sheffield-Moore M, Cree MG, Hewlings SJ, Aarsland A, Wolfe RR, et al. Atrophy and impaired muscle protein synthesis during prolonged inactivity and stress. J Clean Endocrinol Met 2006;91:4836-41. DOI: 10.1210/jc.2006-0651.
30. Peterson SJ, Braunschweig CA. Prevalence of Sarcopenia and Associated Outcomes in the Clinical Setting. Nutrition in Clinical Practice 2016;31:40-8. DOI: 10.1177/0884533615622537.
31. Vaughan VC, Martin P, Lewandowski PA. Cancer cachexia: impact, mechanisms and emerging treatments. J Cachexia Sarcopenia Muscle 2013;4:95-109. DOI: 10.1007/s13539-012-0087-1.
32. Nipp RD, Fuchs G, El-Jawahri A, Mario J, Troschel FM, Greer JA, et al. Sarcopenia Is Associated with Quality of Life and Depression in Patients with Advanced Cancer. Oncologist 2018;23:97-104. DOI: 10.1634/theoncologist.2017-0255.
33. Joglekar S, Nau PN, Mezhir JJ. The Impact of Sarcopenia on Survival and Complications in Surgical Oncology: A Review of the Current Literature. J Surg Oncol 2015;112:503-9. DOI: 10.1002/jso.24095.
34. Wendrich AW, Swartz JE, Bril SI, Wegner I, De Graeffd A, Smid EJ, et al. Low skeletal muscle mass is a predictive factor for chemotherapy dose-limiting toxicity in patients with locally advanced head and neck cancer. Oral Oncology 2017;71:26-33. DOI: 10.1016/j.oraloncology.2017.05.012.
35. Morgan DJ, Bray KM. Lean body mass as a predictor of drug dosage. Implications for drug therapy. Clinical pharmacokinetics 1994;26:292-307. DOI: 10.2165/00003088-199426040-00005.
36. Prado CM, Maia YLM, Ormesbee M, Sawyer M, Baracos VE. Assessment of nutritional status in cancer – The relationship between body composition and pharmacokinetics. Anti-cancer agents in medical chemistry 2013;13:000-000. DOI: 10.2174/18715206113139990322.
37. Prado CM, Baracos VE, McCargar LJ. Body composition as an independent determinant of 5-fluoracil – based chemotherapy toxicity. Clean Cancer Reas 2007;13:2634-8. DOI: 10.1158/1078-0432.CCR-06-3067.
38. Lee JY, Lee HS, Lee DC, Chu SH, Jeon JY, Kim NK, et al. Visceral Fat Accumulation Is Associated with Colorectal Cancer in Postmenopausal Women. PLoS One 2014;9:110587. DOI: 10.1371/journal.pone.0110587.
39. Von Hafe P, Pina F, Pérez A, Tavares M, Barros H. Visceral Fat Accumulation as a Risk Factor for Prostate Cancer. Obesity research 2004;12:1930-5. DOI: 10.1038/oby.2004.242.
40. Young JK, Ji WP, Jong WK, Chan-Soo P, John JPSG, Seung HL, et al. Computerized Automated Quantification of Subcutaneous and Visceral Adipose Tissue From Computed Tomography Scans: Development and Validation Study. JMIR Med Inform 2016;4:2. DOI: 10.2196/medinform.4923.
41. Bouchonville MF, Villareal DT. Sarcopenic Obesity – How Do We Treat It? Endocrinol Diabetes Obes 2013;20:412-9. DOI: 10.1097/01.med.0000433071.11466.7f.
42. Wannamethee SG, Atkins JL. Muscle loss and obesity: the health implications of sarcopenia and sarcopenic obesity. Proc Nutr Soc 2015;74:405-12. DOI: 10.1017/S002966511500169X.
43. Malietzis G, Aziz O, Bagnall NM, Johns N, Fearon KC, Jenkins JT. The role of body composition evaluation by computerizd outcomes: A systematic review. EJSO 2015;41:186-96. DOI: 10.1016/j.ejso.2014.10.056.

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Anthropometric cutoff points to identify lipodystrophy characteristics in people living with HIV/AIDS: an observational study

Puntos de corte antropométricos para identificar las características de la lipodistrofia en personas que viven con VIH/SIDA: un estudio observacional

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Abstract

Introduction: currently, there is no consensus regarding accurate and low-cost methods for diagnosing lipodystrophy in people living with HIV/AIDS (PLWHA). The aim of this study was to propose anthropometric cutoff points for the diagnosis of lipodystrophy among PLWHA.

Methods: we included 106 PLWHA (men = 65, women = 41) who are under antiretroviral therapy and have been clinically classified into either a "lipodystrophy" or "non-lipodystrophy" group. Anthropometric measurements included 19 regions of body perimeters and 6 skinfold thickness measures. The Youden index was used to establish anthropometric cutoff points for the diagnosis of lipodystrophy, using the mean values of the anthropometric data (referred to as "original") along with the "Z index" (ZI) values, which were adjusted by the "Phantom Strategy." The cutoff points were proposed when "original" anthropometric measurements and ZI values had a statistical significance of $p < 0.01$ and an area under the curve (AUC) higher than 70%. The size effect was assessed to verify the influence of lipodystrophy on each anthropometric measure.

Results: our data analysis proposes sex-specific cutoff points for the diagnosis of lipodystrophy in PLWHA – 17 points using the "original" anthropometric measurements, and 20 using the ZI values (average effect size between 1.0 and 1.1, and AUC = 76.7% and 78%).

Conclusions: our study proposes accurate cutoff points for the diagnosis of lipodystrophy using "original" anthropometric measurements and ZI values adjusted by the "Phantom Strategy." Our findings support the use of anthropometric measurements as a simplified method for diagnosing lipodystrophy and monitoring body composition alterations in people living with HIV/AIDS.

Key words:

HIV. Body composition. Anthropometry.

Resumen

Introducción: no existe consenso con respecto a métodos precisos y de bajo coste para diagnosticar la lipodistrofia en personas que viven con VIH/SIDA (PVVS). El objetivo de este estudio es proponer puntos de corte antropométricos para el diagnóstico de lipodistrofia entre las PVVS.

Métodos: se incluyeron 106 PVVS (hombres = 65, mujeres = 41) en tratamiento antirretroviral que se clasificaron clínicamente en dos grupos de "lipodistrofia" o "no lipodistrofia". Las mediciones antropométricas incluyeron 19 regiones de parámetros corporales y 6 medidas de pliegues cutáneos. El índice de Youden se utilizó para establecer puntos de corte antropométricos para el diagnóstico de lipodistrofia utilizando la media de los datos antropométricos (denominados "originales") junto con los valores del "índice Z" (IZ), que fueron ajustados por la "estrategia Phantom". Los puntos de corte se propusieron cuando las mediciones antropométricas "originales" y los valores de IZ fueron estadísticamente significativos con un valor $p < 0,01$ y un área bajo la curva (AUC) superior al 70%. Se evaluó el tamaño del efecto para verificar la influencia de la lipodistrofia en cada medida antropométrica.

Resultados: se propusieron puntos de corte específicos según el sexo para el diagnóstico de lipodistrofia en PVVS: 17 puntos usando las medidas antropométricas "originales" y 20 usando los valores de IZ (tamaño del efecto promedio entre 1.0 y 1.1, y AUC = 76.7% y 78%).

Conclusiones: se propusieron puntos de corte antropométricos para el diagnóstico de lipodistrofia. Las mediciones antropométricas son un método simplificado para diagnosticar y monitorear los cambios de composición corporal en las PVVS.

Palabras clave:

VIH. Composición corporal. Antropometría.

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INTRODUCTION

The human immunodeficiency virus (HIV) remains one of the most serious global health threats of our time. In the beginning of the 1980s, people living with HIV/AIDS (PLWHA) were given a short life expectancy. However, with the introduction of combined antiretroviral therapy (cART), mortality rates for PLWHA have dramatically decreased (1).

Without question, the introduction of the cART regimen is one of the greatest achievements in public health over the past few decades, and has caused HIV to shift from a death sentence to a chronic infection (2). However, an increase in morbidity and mortality as a result of HIV/AIDS, due to cardiovascular disease, kidney- and liver-related diseases, cognitive decline, and osteoporosis, has been reported (3-5). Additional adverse effects from exposure to cART and HIV infection include metabolic disorders (e.g., dyslipidemia and increases in blood glucose) and morphologic changes (central lipohypertrophy and/or peripheral lipoatrophy). These characteristics are known as the "lipodystrophy syndrome of HIV" (6,7). These changes represent serious problems because lipodystrophy increases the risk of developing cardiovascular diseases, may cause social and psychological distress, and may contribute to discontinuation of HIV treatment (8) among other problems. Thus, earlier identification and adequate treatment for lipodystrophy characteristics may improve the overall health and well-being of PLWHA.

To date there is no methodological consensus for identifying lipodystrophy characteristics. A clinical evaluation is the most widely used method for identifying and diagnosing lipodystrophy characteristics (9). However, this method is subjective and cannot identify body composition changes in the initial stages of lipodystrophy. Also, imaging methods (e.g., magnetic resonance imaging, computed tomography, and dual energy X-ray absorptiometry) have been used to identify and monitor lipodystrophy characteristics (10,11). Although some researchers agree that diagnosing lipodystrophy with imaging methods is accurate, the high operational cost of imaging technologies is an important factor that limits their utilization in clinical settings and in studies with large numbers of participants. This lack of consensus regarding accurate, low-cost methods for identifying lipodystrophy characteristics remains unresolved in the field.

Anthropometric methods such as skinfold thickness and body circumferences are typically used to measure body composition (12,13). These methods are easy to use, present a low operational cost, and have been validated in various populations. However, there is no current literature on the utilization of these methods to identify lipodystrophy characteristics in PLWHA. Thus, our study proposes to fill this gap in the literature by developing a simplified method to identify lipodystrophy characteristics in Brazilians living with HIV/AIDS. In what follows, we propose anthropometric cutoff points for the identification of lipodystrophy characteristics in this population. We believe this information may assist health professionals in accurately identifying lipodystrophy characteristics at a low cost, and thus works towards decreasing the adverse health effects on body composition associated with cART.

MATERIAL AND METHODS

STUDY POPULATION

In this study we adopted a cross-sectional design and evaluated 106 individuals (mean age = 46.2 years). All of them were diagnosed with HIV/AIDS and were on treatment at the University Hospital of Ribeirao Preto School of Medicine, University of Sao Paulo, Brazil (HC-FMRP-USP/UETDI). The study was conducted from November 2013 to November 2014. During the period of the study, 1,298 people living with HIV/AIDS were receiving treatment at the HC-FMRP-USP/UETDI. To achieve a power range of 0.75 to 0.80 with a significance level of $p < 0.05$ for detecting differences between people living with HIV/AIDS, with and without lipodystrophy, a sample size of 100 to 112 patients was recommended. Accordingly, we reached out to 125 people living with HIV/AIDS at the HC-FMRP-USP/UETDI, and after their meeting inclusion and exclusion criteria we were able to collect complete data from 106 individuals. The inclusion criteria adopted for this study were: participants diagnosed with HIV/AIDS as adults, aged between 18 and 69 years, under cART treatment, with or without physical characteristics of lipodystrophy. Exclusion criteria included: being treated for opportunistic diseases or cancer, immune inflammatory diseases, wasting syndrome, rare metabolic disorders, use of ergogenic products that could cause body composition alterations, being pregnant or breast feeding, using prostheses, amputated, and engaged in an exercise program during the past 6 months or experiencing rapid weight loss over the past 6 months.

Our study was in agreement with the Helsinki declaration. All participants volunteered for the study, were informed about the scope of the study, and provided their written consent. The study was approved by the Ethics Review Board at University Hospital of Ribeirao Preto School of Medicine, University of Sao Paulo, Brazil, process number: 7082/2011.

PROCEDURES

We collected from medical records the following information; age (years), time from HIV diagnosis (years since the diagnosis), and time on cART (years since the beginning of treatment). The self-reported race/ethnicity of the participants in our sample was broadly consistent with those reported nationally by the Brazilian Institute of Geography and Statistics (14).

DIAGNOSIS OF LIPODYSTROPHY

People living with HIV/AIDS were classified as with or without lipodystrophy based on a clinical evaluation of lipodystrophy. In this method of diagnosis, the presence or absence of visceral fat accumulation in the trunk is not considered (9). Rather, the clinical evaluation is made by achieving a consensus about the loss of subcutaneous fat between the evaluator and the participant. A trained evaluator asked the participant whether she/he had experienced

a reduction in peripheral subcutaneous fat in areas of the face, buttocks, arms, and legs after receiving a diagnosis of HIV infection and after beginning cART. A lipodystrophy diagnosis was made if the participant stated that she/he had lost fat in at least one of these areas, and if the evaluator, after a visual assessment of the participant, also perceived a reduction of fat in the same areas. However, if the visual assessment of the evaluator did not agree with the report made by the participant, lipodystrophy was not diagnosed (9). This clinical evaluation process is a commonly adopted method in Brazil both in research and clinical practice (10,15-18).

STUDY GROUPS

In order to propose cutoff points for identifying lipodystrophy characteristics, we studied people living with HIV/AIDS, with and without lipodystrophy. After a clinical evaluation considering only alterations in areas of the face, buttocks, arms, and legs, participants were assigned to either a lipodystrophy (LD) or a non-lipodystrophy (NLD) group. In this study we included 41 women (LD = 12 and NLD = 29) and 65 men (LD = 29 and NLD = 36).

MEASUREMENTS

"Original" measurements

In order to establish anthropometric cutoff points for identifying lipodystrophy characteristics we used anthropometric measurements, referred to in this manuscript as "original." Skinfold thickness was measured in six regions: triceps, subscapular, suprailiac, abdomen (horizontal), thigh, and medial calf. The Prime® caliper (Harpenden Scientific model) was used to measure each participant's skinfolds. During the assessment of skinfold thickness, the fold is raised perpendicular to the surface of the body at the measurement site. The long axis of the fold is aligned in agreement with the instructions for each skinfold. The basic principle is that the long axis be parallel to the natural cleavage lines of the skin in the region of the measurement. The fold is kept elevated until the measurement has been completed. More details can be found in Harrison et al. (1988) (19), who present guidelines for carrying out these measures.

Body circumferences were measured at nineteen regions: shoulder (largest diameter), breast (fourth sternocostal joint), waist (smallest diameter), abdomen (umbilical scar), hip (largest diameter), right arm extended, right arm contracted, right forearm, right wrist, left arm extended, left arm contracted, left forearm, left wrist, right thigh (proximal), right medial calf (largest diameter), right ankle (smallest circumference from the ankle, nearest to the malleoli), left thigh (proximal), left medial calf (largest diameter), and left ankle (lower circumference from the ankle, nearest to the malleoli). A 2 m Sanny® brand metal band with a latex device at the end was used, which was replaced every 20 participants evaluated. The guidelines for carrying out the measurements are those described by Callaway et al. (1988) (20).

Skinfold thickness and body circumference measurements were performed in triplicate, and the median value was recorded. If there was a variation greater than 5% between measures, a new series of measures was carried out.

"Phantom Z-score" values adjusted by the Phantom Strategy

In addition to using the "original" anthropometric measurements to establish anthropometric cutoff points for identifying lipodystrophy characteristics, we assessed body composition differences between the groups through body proportionality. The most commonly used method is the "Phantom Strategy," an asexual and arbitrary human reference model for body proportionality with specific anthropometric characteristics for both men and women (21). The main application of the Phantom Strategy is quantifying possible differences expressed in body proportionality indicators between anthropometric measurements as assessed in the participant and in a human reference model for body proportionality.

The first step in application of the Phantom strategy is the adjustment of each anthropometric measurement to the corresponding "Phantom size," and expressing the difference from the Phantom reference value in Z-scores. The adjusted anthropometric measurement, referred to in this manuscript as "Phantom Z-score," indicates a score value of the difference between an anthropometric measurement and its reference model (21).

DATA QUALITY CONTROL

Data quality control was carried out in three steps. First, all the anthropometric measures listed above were collected by the same evaluator at three sequential measurements, and the median values were used. In addition, the measures were conducted in 6 patients at a time, and were then re-tested an hour later to confirm accuracy. Finally, the technical error of measurement (TEM) was calculated (22). TEM values were assessed for body circumferences (TEM $\leq$ 0.71 cm) and skinfold thickness (TEM $\leq$ 0.60 mm), ensuring the reliability of the measurements within established limits (22).

STATISTICS

Prior to conducting a data analysis, we checked the database and cleaned for errors of data entry and impossible/inconsistent values. The Shapiro Wilks test was used to examine the normality of the distribution among continuous variables. Data with normally distributed parameters are presented as mean and standard deviation by sex for all variables, with a 95% confidence interval. Data that displayed a skewed distribution are presented as median and interquartile range ($p25^{th}$ to $p75^{th}$). For comparison of differences in data between the LD and NLD groups we adopted Student's t-test, and the Mann-Whitney U-test for normal and skewed distributions, respectively. The Cohen's effect size was assessed to compare the lipodystrophy magnitude

for age, time from HIV diagnosis, and time under cART, and for the anthropometric measurements between both groups. The effect size, known as "d," was used to determine the significance level comparing the groups, ranging from small ($0.20 \leq d < 0.50$), to moderate ($0.50 \leq d < 0.80$), to large ($d \geq 0.80$) (23).

After comparing age, time from HIV diagnosis, time under cART, and the anthropometric measurements between the LD and NLD groups, we selected only anthropometric measurements for calculating the cutoff points due to the purpose of our study. We elected for this study only anthropometric measurements for proposing cutoff points, which were considered statistically significant with p-values of < 0.01 and when the area under the curve (AUC) was greater than 70% following the Receiver Operator Characteristic (ROC) curve analysis. The accuracy requirement adopted in this study is due to the large number of anthropometric measurements assessed, and our goal of identifying any differences between the LD and NLD groups with a high level of accuracy. In addition, cutoff points were established for these anthropometric measurements by using the Youden index (24). The Youden index is a function that includes the sum of the highest values for sensitivity and specificity minus one. The Youden index ranges from 0 (zero) to 1 (one). Values close to 1 indicate a relatively large efficacy, and values close to 0 limited efficacy (24). The software used for data analysis was the SPSS 23.0 package.

RESULTS

Our sample was composed of white Brazilians (n = 67, 63.2%), *pardo* (brown) Brazilians (n = 20, 18.9%), black Brazilians (n = 10, 9.4%), and Asian Brazilians (n = 9, 8.5%). Table I lists a descriptive analysis by sex, age, time from diagnosis with HIV, and time of exposure to cART. These are important variables to consider because of the accelerated aging process associated with cART and its effects on body composition in people living with HIV/AIDS.

Table I shows a comparison between people clinically diagnosed with and without lipodystrophy (LD *vs.* NLD groups, respectively). The results show that age was not significantly different between LD and NLD for both men and women, with the majority of participants being in their 40s. Among men, the results showed a significant association of lipodystrophy with time from HIV diagnosis and use of cART. In comparison to those without lipodystrophy, men with lipodystrophy showed ($p < 0.001$) an average of six more years for their time from diagnosis with HIV (LD = 12.5 *vs.* NLD = 6.6 years) and use of cART (LD = 11 *vs.* NLD = 5 years). Even though there was no significant statistical difference between the LD and NLD groups among women, a similar trend between time from HIV diagnosis (LD = 11.3 *vs.* NLD = 7.6 years) and use of cART (LD = 9.2 *vs.* NLD = 5.5 years) was observed ($p = 0.223$ and $p = 0.115$, respectively).

Tables II and III show anthropometric differences by sex for those with and without lipodystrophy, with results reported only for variables with $p < 0.01$ and AUC higher than 70%. Between-group analyses indicate that our proposed cutoff points tend to have greater sensitivity than specificity. This reflects a higher probability of identifying lipodystrophy characteristics using the proposed cutoff points when PLWHA have these anthropometric characteristics. In addition, the effect size for all anthropometric variables was either moderate or large ($d \geq 0.7$). This leads us to believe that PLWHA will be accurately identified for lipodystrophy charac-

Table I. Descriptive analysis and differences test for the variables age, time of exposure to HIV and cART, by sex, and lipodystrophy diagnosis in 106 people living with HIV/AIDS

Variables	Men LD (n = 29)	NLD (n = 36)	Differences test (t or U)	p-value	d[a]
Age (years)[b]	47.6 ± 7.2 (45.1 to 50.1)	45.2 ± 9.9 (41.8 to 48.4)	-1.1	0.274	0.3
Diagnosis of HIV (months)[c]	151.3 (131.6 to 183.2)	79.5 (67.7 to 107.2)	-3.5	< 0.001*	1.0
Exposure to cART (months)[c]	132.6 (110.0 to 153.3)	60.2 (46.2 to 77.8)	-4.3	< 0.001*	1.4
Variables	**Women LD (n = 12)**	**NLD (n = 29)**	**Differences test**	**p-value**	**d[a]**
Age (years)[b]	49.5 ± 7.4 (44.9 to 54.1)	45.0 ± 12.1 (40.4 to 49.5)	-1.2	0.233	0.5
Diagnosis of HIV (months)[c]	135.9 (92.0 to 184.0)	90.9 (62.7 to 125.4)	-1.2	0.223	0.5
Exposure to cART (months)[c]	110.1 (74.5 to 153.5)	65.7 (45.8 to 88.1)	-1.6	0.115	0.7

*[a]Results of Cohen effect size test; [b]Values expressed as mean ± standard deviation, confidence interval of 95%, and results of differences test by using Student's t-test; [c]Values expressed as median and interquartile range ($p25^{th}$ to $p75^{th}$), and results of differences test by using Mann Whitney U-test. *p < 0.01 considered significant based on Mann Whitney U-test.*

HIV: Human Immunodeficiency Virus; cART: Combined AntiRetroviral Therapy; AIDS: Acquired ImmunoDeficiency Syndrome; LD: LipoDystrophy group; NLD: Non-LipoDystrophy group.

teristics when their anthropometric measurements are lower than the cutoff points proposed. The further down the anthropometric values go in comparison to the cutoff points, the greater the probability of lipodystrophy. Table II shows a data analysis based on the "original" anthropometric measurements, which includes our proposed cutoff points for identifying lipodystrophy characteristics. Out of the 6 skinfold thickness regions and 19 body circumferences measured, we found significant accuracy (AUC $> 70\%$; $p < 0.01$) in 3 skinfold thickness measurements for both sexes, and in 7 body circumferences for men and 4 for women.

In men, the optimum (high sensitivity and high specificity) cutoff points for identifying lipodystrophy characteristics were found when skinfold thickness measurements were ≤ 16.3 mm in the suprailiac, ≤ 21.4 mm in horizontal abdomen, and ≤ 9.2 mm in the thigh; and when body circumferences were ≤ 94.7 cm in the hip, ≤ 29.4 cm in the right arm extended, ≤ 16.6 cm in the right wrist, ≤ 29.2 cm in the left arm extended, ≤ 30.4 cm in the left arm contracted, ≤ 16.1 cm in left wrist, and ≤ 50.2 cm in the left thigh. In women, the optimum cutoff points for identifying lipodystrophy characteristics were reached when skinfold thickness measurements were ≤ 17.5 mm in the triceps, ≤ 22.5 mm in the thigh, and ≤ 8.6 mm in the medial calf; and when body circumferences were ≤ 53.6 cm in the right thigh, ≤ 34.1 cm in the right medial calf, ≤ 56.4 cm in the left thigh, and ≤ 32.4 cm in the left medial calf.

Table III shows the data analysis and cutoff points based on anthropometric measurements adjusted by Phantom Z-score values. We found significant accuracy (AUC $> 70\%$; $p < 0.01$) in 4 skinfold thickness measurements for men and 3 for women, and in 8 body circumferences for men and 5 for women. Table III lists these cutoff point values. In comparison to our proposed cutoff points for lipodystrophy characteristics based on the "original" anthropometric measurements, the adjusted model has an additional body circumference item (Phantom Z-score for the right arm contracted for men, and Phantom Z-score for the right ankle for women), and an additional skinfold thickness score for men (Phantom Z-score for the triceps).

Our analysis found a similar effect size ($d = 1.0$ and $d = 1.1$) and accuracy (AUC% = 76.7% and AUC% = 78%) when using the "original" anthropometric measurements and the Phantom Z-score measurements, respectively. These results indicate that both methods have accurate cutoff points to identify lipodystrophy characteristics in people living with HIV/AIDS.

DISCUSSION

Simplified methods for identifying lipodystrophy characteristics in people living with HIV/AIDS will positively impact public health. With an accessible method, the adverse health effects of infection with HIV and its treatment (cART) can be monitored and treated outside the hospital setting. It will expand the care of people living with HIV/AIDS by multidisciplinary health professionals who work to decrease the comorbidities associated with lipodystrophy. In this manuscript we propose anthropometric cutoff points for identifying lipodystrophy characteristics. So far, to the best of our knowledge, the present study is the first to propose anthropometric cutoff points for identifying and monitoring lipodystrophy characteristics in people living with HIV/AIDS. Our study advances the field by proposing a simplified method that uses anthropometric measurements and that is enhanced by the "Phantom Strategy" of body proportionality.

The length of exposure to cART is an important variable to consider when studying the body composition of people living with HIV/AIDS. Some researchers have published on accelerated lipodystrophy when patients are exposed longer to cART (25,26). Tetteh et al. (2016) (25) followed people living with HIV/AIDS for one year and reported significant changes in metabolic and nutrition disorders, as well as in body composition, due to cART. In our study we confirmed a positive association of exposure to cART and a diagnosis of HIV with the development of lipodystrophy. When compared to men without lipodystrophy, men with lipodystrophy showed an average of six more years since the time of diagnosis of their HIV and their use of cART. Chitu-tisu et al. (2017) (26) compared people living with HIV/AIDS with those without HIV, and concluded that after an average of 5 years since diagnosis and using cART, people living with HIV/AIDS started showing significantly accelerated lipodystrophy. Alves et al. (2016) (27) documented the influence of time of exposure to cART on the diagnosis of HIV in women (27). However, our study could not confirm this association among women. Further research is needed to clarify this association in women. It seems that lipodystrophy affects women more than men based on the higher overall effect size observed in our study.

Our findings indicate that our proposed anthropometric cutoff points are accurate for the identification of lipodystrophy characteristics in people living with HIV/AIDS. Our findings support the use of cutoff points that include 17 and 20 anthropometric measurements for "original anthropometric measurements" and "Phantom Z-score" values, respectively. The cutoff points proposed are especially important during the clinical evaluation of lipodystrophy when the patient and the evaluator are not in agreement, and when the evaluator has doubts about lipodystrophy severity. In the early stages of lipodystrophy cutoff points can serve as valuable tools to help health professionals confirm lipodystrophy characteristics among people living with HIV/AIDS. In addition, cutoff points can also be used to monitor body composition changes by comparing results in subsequent evaluations. Thus, an earlier identification and adequate treatment for lipodystrophy characteristics can prevent or delay the development of cardiovascular diseases, thereby leading to better overall health and well-being for people living with HIV/AIDS (28,29).

Whether to use cutoff points from the "original" measurements or from the Phantom Z-score values remains an open question. However, in practical terms, using the cutoff points based on the "original" measurements is the most simplified way and would require the least amount of time and effort.

Our study had some limitations worth noting. We acknowledge that there are other factors that may influence body composition that were not addressed in this study, including nutritional patterns, socio-economic status, heredity, and previous opportunistic diseases.

Table II. Cutoff points[a] using original measurements to identify lipodystrophy characteristics for 106 people living with HIV/AIDS, by sex

Men									
Measurements	**LD (n = 29)**	**NLD (n = 36)**	**Differences test (t or U)**	**p-value**	**d[b]**	**AUC%[c]**	**95% CI[d]**	**Cutoff point**	**Sensibility / Specificity %**
Body circumferences (cm)									
Hip[e]	88.5 ± 6.4 (86.4 to 91.1)	93.9 ± 7.7 (91.9 to 96.9)	3.1	0.003*	0.8	71.4	58.1 to 83.3	94.7	86.2 / 52.8
Right arm extended[e]	27.8 ± 2.8 (26.8 to 28.9)	29.9 ± 2.9 (29.2 to 31.0)	2.9	0.006*	0.7	72.5	59.7 to 85.2	29.4	79.3 / 66.7
Right wrist[e]	16.2 ± 0.9 (15.8 to 16.5)	16.9 ± 0.9 (16.7 to 17.3)	2.9	0.005*	0.7	71.8	58.6 to 84.2	16.6	75.9 / 69.4
Left arm extended[e]	27.3 ± 2.7 (25.6 to 28.1)	29.8 ± 2.9 (28.9 to 30.8)	3.6	0.001*	0.9	75.6	63.2 to 88.5	29.2	82.8 / 66.7
Left arm contracted[e]	28.2 ± 2.5 (27.2 to 29.1)	30.7 ± 2.8 (29.7 to 31.6)	3.7	< 0.001*	0.9	74.4	62.2 to 86.7	30.4	82.8 / 61.4
Left wrist[e]	15.9 ± 1.0 (15.6 to 16.3)	16.8 ± 0.9 (16.6 to 18.1)	3.4	0.001*	0.8	72.1	60.3 to 85.7	16.1	65.5 / 75.2
Left thigh[e]	48.9 ± 5.4 (46.0 to 50.1)	52.8 ± 5.4 (47.0 to 53.8)	3.4	0.001*	0.9	72.9	60.1 to 84.5	50.2	65.5 / 66.7
Skinfold thickness (mm)									
Suprailiac[e]	11.5 ± 5.9 (9.8 to 13.9)	18.5 ± 9.2 (15.9 to 22.0)	3.5	0.001*	0.9	72.6	60.2 to 84.5	16.3	79.3 / 52.8
Abdomen horizontal[e]	15.4 ± 8.2 (12.7 to 18.6)	21.8 ± 8.0 (19.2 to 24.5)	3.2	0.002*	0.8	71.7	58.3 to 83.8	21.4	75.9 / 55.6
Thigh[f]	8.3 (6.5 to 10.4)	14.5 (11.8 to 17.7)	-3.0	0.003†	0.8	72.9	59.6 to 84.4	9.2	69.0 / 63.9
Women									
Measurements	**LD (n = 12)**	**NLD (n = 29)**	**Differences test (t)**	**p-value**	**d[b]**	**AUC%[c]**	**95% CI[d]**	**Cutoff point**	**Sensibility / Specificity %**
Body circumferences (cm)									
Right thigh[e]	49.5 ± 6.1 (45.8 to 52.9)	58.1 ± 7.1 (55.5 to 60.8)	3.7	0.001*	1.3	84.6	71.2 to 96.7	53.6	83.3 / 78.6
Right medial calf[e]	31.5 ± 3.4 (29.4 to 33.4)	35.6 ± 3.6 (34.2 to 36.8)	3.4	0.002*	1.2	80.0	66.6 to 95.2	34.1	83.3 / 72.4
Left thigh[e]	49.3 ± 6.5 (38.8 to 52.5)	57.5 ± 6.9 (55.1 to 60.1)	3.5	0.001*	1.2	82.5	69.9 to 96.3	56.4	91.7 / 51.7
Left medial calf[e]	31.7 ± 3.4 (29.7 to 33.5)	35.4 ± 3.6 (34.0 to 36.7)	3.1	0.004*	1.1	77.3	61.8 to 93.6	32.4	66.7 / 86.2
Skinfold thickness (mm)									
Triceps[e]	12.4 ± 5.6 (9.3 to 15.7)	19.9 ± 7.9 (16.6 to 22.6)	2.9	0.005*	1.1	79.1	65.0 to 93.4	17.5	91.7 / 58.6
Thigh[e]	15.9 ± 9.9 (10.7 to 21.7)	28.1 ± 9.3 (24.5 to 31.4)	3.7	0.001*	1.3	83.3	69.4 to 96.1	22.5	75.0 / 78.6
Medial calf[e]	6.7 ± 5.6 (3.9 to 9.9)	16.8 ± 6.3 (14.4 to 19.0)	4.8	< 0.001*	1.7	88.8	76.2 to 100.0	8.6	75.0 / 89.7

*[a]Results only for variables with p < 0.01 and area under the curve (AUC) higher than 70%; [b]Results of Cohen effect size test; [c]Area under the curve in percentage value; [d]Confidence interval of 95% from the area under the curve; [e]Values expressed as mean ± standard deviation, 95% confidence interval, and results of differences test by using Student's t-test; [f]Values expressed as median and interquartile range ($p25^{th}$ to $p75^{th}$), and results of differences test by using Mann Whitney U-test; *p < 0.01 considered significant based on Student's t-test; †p < 0.01 considered significant based on Mann Whitney U-test.*

Abbreviations: HIV: Human Immunodeficiency Virus; AIDS: Acquired ImmunoDeficiency Syndrome; LD: LipoDystrophy group; NLD: Non LipoDystrophy group; cm: centimeters; mm: millimeters.

Table III. Cutoff points[a] using Phantom Z-score measurements to identify lipodystrophy characteristics for 106 people living with HIV/AIDS, by sex

Men								
Measurements	**NLD (n = 36)**	**t-test**	**p-value**	**d[b]**	**AUC%[c]**	**95% CI[d]**	**Cutoff point**	**Sensitivity / Specificity %**
Body circumferences (cm)								
Phantom Z-score, hip[e]	-0.1 ± 1.2 (-0.5 to 0.3)	3.9	< 0.001*	1.0	76.3	65.1 to 88.6	-0.4	86.2 / 66.7
Phantom Z-score, right arm extended[e]	1.3 ± 1.2 (0.9 to 1.7)	3.2	0.002*	0.8	73.4	61.9 to 86.2	1.2	86.2 / 61.1
Phantom Z-score, right arm contracted[e]	0.7 ± 1.2 (0.2 to 1.1)	2.9	0.006*	0.7	72.4	60.6 to 85.7	0.4	82.8 / 69.4
Phantom Z-score, right wrist[e]	0.9 ± 1.5 (0.4 to 1.3)	3.1	0.003*	0.8	70.9	58.5 to 83.4	0.9	79.3 / 52.9
Phantom Z-score, left arm extended[e]	1.3 ± 1.2 (0.9 to 1.7)	4.1	< 0.001*	1.0	78.7	67.5 to 89.3	0.9	82.8 / 66.7
Phantom Z-score, left arm contracted[e]	0.6 ± 1.2 (0.2 to 0.9)	4.1	< 0.001*	1.1	77.1	66.5 to 89.3	0.2	79.3 / 69.4
Phantom Z-score, left wrist[e]	0.6 ± 1.4 (0.3 to 2.3)	3.7	< 0.001*	0.9	74.5	62.8 to 86.3	0.2	79.3 / 63.9
Phantom Z-score, right thigh[e]	-0.6 ± 1.1 (-0.9 to -0.2)	3.8	< 0.001*	1.0	75.2	63.4 to 87.8	-1.1	69.0 / 75.0
Skinfold thickness (mm)								
Phantom Z-score, triceps[e]	-1.3 ± 1.0 (-1.6 to -1.0)	2.9	0.006*	0.7	71.7	58.6 to 84.5	-1.6	86.2 / 55.6
Phantom Z-score, suprailiac[e]	0.7 ± 2.0 (0.1 to 1.4)	3.7	0.001*	0.9	73.4	60.1 to 85.7	0.2	79.3 / 55.7
Phantom Z-score, abdomen horizontal[e]	-0.5 ± 1.0 (-0.8 to -0.2)	3.3	0.002*	0.8	72.5	60.7 to 84.6	-0.4	79.3 / 52.8
Phantom Z-score, thigh[e]	-1.5 ± 1.1 (-1.9 to -1.1)	3.2	0.002*	0.8	72.0	60.1 to 84.3	-1.9	72.4 / 55.6
Women								
Measurements	**NLD (n = 29)**	**t-test**	**p-value**	**d[b]**	**AUC%[c]**	**95% CI[d]**	**Cutoff point**	**Sensibility / Specificity %**
Body circumferences (cm)								
Phantom Z-score, right thigh[e]	1.8 ± 1.8 (1.1 to 2.5)	3.8	0.001*	1.4	87.3	76.5 to 98.9	0.7	91.7 / 82.1
Phantom Z-score, right medial calf[e]	1.5 ± 1.8 (0.8 to 2.1)	3.3	0.002*	1.2	81.5	67.6 to 95.9	0.6	91.7 / 71.4
Phantom Z-score, right ankle[e]	1.0 ± 1.1 (0.5 to 1.4)	2.8	0.008*	1.0	74.8	57.5 to 91.6	0.8	83.3 / 51.7
Phantom Z-score, left thigh[e]	1.6 ± 1.8 (0.9 to 2.3)	3.7	0.001*	1.3	85.1	72.3 to 98.7	0.7	91.7 / 85.7
Phantom Z-score, left medial calf[e]	1.4 ± 1.8 (0.8 to 2.1)	3.1	0.004*	1.2	77.7	61.0 to 93.5	0.7	91.7 / 67.9
Skinfold thickness (mm)								
Phantom Z-score, triceps[e]	1.4 ± 2.0 (0.6 to 2.1)	2.9	0.005*	1.1	79.6	65.4 to 93.2	1.0	91.7 / 62.1
Phantom Z-score, thigh[e]	0.4 ± 1.2 (-0.1 to 0.9)	3.8	0.001*	1.2	82.0	69.3 to 96.5	-0.1	75.0 / 78.6
Phantom Z-score, medial calf[e]	0.5 ± 1.5 (-0.1 to 1.1)	4.7	< 0.001*	1.7	87.2	75.4 to 99.2	1.4	75.1 / 89.7

*[a]Results only for variables with p < 0.01 and area under the curve (AUC) higher than 70%; [b]Results of Cohen effect size test; [c] Area under the curve in percentage value; [d]Confidence interval of 95% from the area under the curve; [e]Values expressed as mean ± standard deviation, 95% confidence interval, and results of differences test by using Student's t-test. *p < 0.01 considered significant based on Student's t-test.*

HIV: Human Immunodeficiency Virus; AIDS: Acquired ImmunoDeficiency Syndrome; LD: LipoDystrophy group; NLD: Non LipoDystrophy group; cm: centimeters; mm: millimeters.

Also, it is important to note that we did not include in this study HIV/AIDS patients that were in treatment for opportunistic diseases. So, caution is warranted when generalizing our proposed cutoff points for lipodystrophy characteristics to all HIV/AIDS patients. In addition, accelerated aging is commonly experienced by people living with HIV/AIDS. Both aging and HIV status have been shown to influence body composition; however, to date, there are no studies in the literature that explore the nature of the interaction between these two variables.

We did not use body mass index or waist circumference as inclusion criteria in our study. Instead, we chose to utilize clinical evaluation procedures to identify the presence or absence of lipodystrophy. In this approach the presence or absence of visceral fat accumulation in the trunk is not considered. However, when we analyzed the differences in body mass index and waist circumference between lipodystrophy and non-lipodystrophy groups, we found statistical differences at $p < 0.01$ only for body mass index. We found lower values for body mass index in the lipodystrophy group and no statistical significant difference in value for waist circumference among groups (data not shown). All cutoff points proposed for body circumferences are from upper and lower body segments, and not from the trunk. Thus, our cutoff points may fit better for identifying lipoatrophy characteristics in lipodystrophy.

We did not perform an external sample validation for our anthropometric cutoff points to confirm the accuracy of the cutoff points used to identify lipodystrophy characteristics in people living with HIV/AIDS. However, we decided to select and propose in this manuscript only anthropometric measurements, which after difference tests and ROC curve analyses better distinguish the lipodystrophy and non-lipodystrophy groups at $p < 0.01$ and AUC $> 70\%$, respectively. The accuracy requirement adopted for selecting the anthropometric variables for proposing cutoff points may minimize the absence of an external sample validation. Our sample has a similar proportion of white, *pardo*, black, and Asian Brazilians as the national population (14). While there are demographic differences across Brazil's regions, our study did not address the impact of these differences on the identified cutoff points. To the best of our knowledge there are no anthropometric cutoff points to identify lipodystrophy characteristics in people living with HIV/AIDS from other countries. Accordingly, our study may also have clinical value elsewhere, particularly for individuals from low- and middle-income countries. Future studies should continue investigating body composition alterations in people living with HIV/AIDS and confirm the broad use of our findings.

In summary, the findings presented here support the use of cutoff points that include 17 and 20 anthropometric measurements, namely "original anthropometric measurements" and "Phantom Z-score" values, respectively, as a simplified method for identifying lipodystrophy characteristics in people living with HIV/AIDS in Brazil, with similar race/ethnicity characteristics as in the national population. This information provides an important clinical tool for monitoring adverse health effects among people living with HIV/AIDS, and for the development of future care strategies for implementation by multidisciplinary teams working in this area.

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REFERENCES

1. FDA UFDA. Antiretroviral drugs used in the treatment of HIV infection. 2016. https://www.fda.gov/forpatients/illness/hivaids/treatment/ucm118915.htm. Acessed in 05/05/2017.
2. Eyawo O, Franco-Villalobos C, Hull MW, Nohpal A, Samji H, Sereda P, et al. Changes in mortality rates and causes of death in a population-based cohort of persons living with and without HIV from 1996 to 2012. BMC infectious diseases 2017;17(1):174. DOI: 10.1186/s12879-017-2254-7.
3. Strijdom H, De Boever P, Walzl G, Essop MF, Nawrot TS, Webster I, et al. Cardiovascular risk and endothelial function in people living with HIV/AIDS: design of the multi-site, longitudinal EndoAfrica study in the Western Cape Province of South Africa. BMC Infectious Diseases 2017;17(1):41. DOI: 10.1186/s12879-016-2158-y.
4. Perazzo H, Luz PM. Liver disease and healthy life-expectancy with HIV. The Lancet HIV 2017;4(6):e236-e7. DOI: 10.1016/S2352-3018(17)30030-9.
5. Gonciulea A, Wang R, Althoff KN, Palella FJ, Lake J, Kingsley LA, et al. An increased rate of fracture occurs a decade earlier in HIV+ compared with HIV– men. Aids 2017;31(10):1435-43. DOI: 10.1097/QAD.0000000000001493.
6. Carr A, Samaras K, Burton S, Law M, Freund J, Chisholm DJ, et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. Aids 1998;12(7):F51-8. DOI: 10.1097/00002030-199807000-00003.
7. Hengel R, Watts N, Lennox J. Benign symmetric lipomatosis associated with protease inhibitors. The Lancet 1997;350(9091):1596. DOI: 10.1016/S0140-6736(05)64011-1.
8. Gagnon M. Understanding the experience of reconstructive treatments from the perspective of people who suffer from facial lipoatrophy: a qualitative study. International journal of nursing studies 2012;49(5):539-48. DOI: 10.1016/j.ijnurstu.2011.11.001.
9. Sutinen J, Yki-Järvinen H. Increased resting energy expenditure, fat oxidation, and food intake in patients with highly active antiretroviral therapy-associated lipodystrophy. American Journal of Physiology-Endocrinology and Metabolism 2007;292(3):E687-92. DOI: 10.1152/ajpendo.00219.2006.
10. Beraldo R, Vassimon H, Aragon D, Navarro A, de Paula FA, Foss-Freitas M. Proposed ratios and cutoffs for the assessment of lipodystrophy in HIV-seropositive individuals. European journal of clinical nutrition 2015;69(2):274-8. DOI: 10.1038/ejcn.2014.149.
11. Mialich MS, dos Santos AP, da Silva BR, de Paula FJA, Jordão AA, Navarro AM. Relationship between adiposity indices, lipodystrophy, and sarcopenia in HIV-positive individuals with and without lipodystrophy. Journal of Clinical Densitometry 2017;20(1):73-81. DOI: 10.1016/j.jocd.2016.06.007.
12. Florindo AA, Latorre Mdo R, Santos EC, Borelli A, Rocha Mde S, Segurado AA. Validation of methods for estimating HIV/AIDS patients' body fat. Revista de saude publica 2004;38(5):643-9. DOI: 10.1590/S0034-89102004000500005.
13. Segatto AFM, Junior IFF, Santos VRD, Alves KC, Barbosa DA, P Filho AM, et al. Indices of body fat distribution for assessment of lipodysthrophy in people living with HIV/AIDS. BMC research notes 2012;5(1):543. DOI: 10.1186/1756-0500-5-543.
14. Instituto Brasileiro de Geografia e Estatística (IBGE). Características Étnico-Raciais da População. Um estudo das categorias de classificação de cor ou raça. Instituto Brasileiro de Geografia e Estatística Brasília; 2013. https://biblioteca.ibge.gov.br/index.php/biblioteca-catalogo?id=249891&view=detalhes. Acessed in 02/15/2018.
15. Vassimon H, Deminice R, A Machado A, P Monteiro J, A Jordao A. The association of lipodystrophy and oxidative stress biomarkers in HIV-infected men. Current HIV research 2010;8(5):364-9. DOI: 10.2174/157016210791330347.
16. Vassimon HS, de Paula FJA, Machado AA, Monteiro JP, Jordão Jr AA. Hypermetabolism and altered substrate oxidation in HIV-infected patients with lipodystrophy. Nutrition 2012;28(9):912-6. DOI: 10.1016/j.nut.2011.12.010.
17. dos Santos W, Paes P, dos Santos A, Machado D, Navarro A, Frenandes A. Impact of progressive resistance training in Brazilian HIV patients with lipodystrophy. J Aids Clin Res 2013;4(204):2. DOI: 10.4172/2155-6113.1000204.
18. Dos Santos AP, Navarro AM, Schwingel A, Alves TC, Abdalla PP, Venturini ACR, et al. Lipodystrophy diagnosis in people living with HIV/AIDS: prediction

and validation of sex-specific anthropometric models. BMC public health 2018;18(1):806. DOI: 10.1186/s12889-018-5707-z.
19. Harrison GG, Buskirk E, Carter JL, Johnston F, Lohman T, Pollock M, et al. Skinfold thicknesses and measurement technique. Anthropometric standardization reference manual 1988;1988:55-80.
20. Callaway CW, Chumlea W, Bouchard C, Himes J, Lohman T, Martin A, et al. Circumferences. Anthropometric standardization reference manual 1988;1988:39-54.
21. Ross W, Wilson N. A strategem for proportional growth assessment. Acta Paediatrica Belgica 1974;28:169.
22. Norton K, Olds T, Albernaz NMFd. Antropométrica: um livro sobre medidas corporais para o esporte e cursos da área de saúde. Antropométrica: um livro sobre medidas corporais para o esporte e cursos da área de saúde: Artmed; 2005.
23. Cohen J. Statistical power analysis. Current directions in psychological science. 1992;1(3):98-101. DOI: 10.1111/1467-8721.ep10768783.
24. Schisterman EF, Perkins NJ, Liu A, Bondell H. Optimal cut-point and its corresponding Youden Index to discriminate individuals using pooled blood samples. Epidemiology 2005:73-81. DOI: 10.1097/01.ede.0000147512.81966.ba.
25. Tetteh RA, Nartey ET, Lartey M, Mantel-Teeuwisse AK, Leufkens HG, Yankey BA, et al. Association Between the Occurrence of Adverse Drug Events and Modification of First-Line Highly Active Antiretroviral Therapy in Ghanaian HIV Patients. Drug Safety 2016;39(11):1139-49. DOI: 10.1007/s40264-016-0460-7.
26. Chitu-Tisu CE, Barbu EC, Lazar M, Bojinca M, Tudor AM, Hristea A, et al. Body composition in HIV-infected patients receiving highly active antiretroviral therapy. Acta clinica Belgica 2017;72(1):55-62. DOI: 10.1080/17843286.2016.1240426.
27. Alves TC, de Moraes C, dos Santos AP, Venturini ACR, de Carvalho Santana R, Navarro AM, et al. Chance aumentada de síndrome metabólica em mulhe-res vivendo com HIV/AIDS e Síndrome da Lipodistrofia. Medicina (Ribeirão Preto Online) 2016;49(5):421-8. DOI: 10.11606/issn.2176-7262.v49i5p421-428.
28. Non LR, Escota GV, Powderly WG. HIV and its relationship to insulin resistance and lipid abnormalities. Translational Research 2017;183:41-56. DOI: 10.1016/j.trsl.2016.12.007.
29. Guaraldi G, Stentarelli C, Zona S, Santoro A, Beghetto B, Carli F, et al. The natural history of HIV-associated lipodystrophy in the changing scenario of HIV infection. HIV Med 2014;15(10):587-94. DOI: 10.1111/hiv.12159.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Efecto de factores contextuales en la composición corporal de jugadores profesionales de fútbol. Un estudio retrospectivo

Effect of contextual factors on body composition in professional soccer players. A retrospective study

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Resumen

La exigencia de las demandas físicas en el fútbol ha evolucionado en los últimos años, poniendo de manifiesto la necesidad de investigar sobre aquellos aspectos que condicionan el rendimiento deportivo. Es por esto que el objetivo de este estudio fue describir la incidencia del entrenamiento individualizado, la compañía en las comidas, la raza y la demarcación sobre las variables antropométricas en jugadores de fútbol profesional. Para ello se desarrolló un estudio retrospectivo sobre 51 jugadores profesionales de la Segunda División B española durante las temporadas de 2015/2016, 2016/2017 y 2017/2018. La valoración antropométrica se realizó bajo las normas técnicas de medición recomendadas por el International Working Group of Kinanthropometry, adoptadas por la International Society for the Advancement of Kinanthropometry (ISAK). Los resultados revelaron que el entrenamiento individualizado y la compañía en las comidas fueron los factores que más influyeron sobre las variables antropométricas. Los valores de masa grasa y de masa muscular, y el sumatorio de pliegues son sensibles al efecto de la intervención sobre dichos factores. Los mayores niveles de interacción se producen entre la compañía en las comidas y el entrenamiento individualizado, y entre la demarcación y la compañía en las comidas. Considerando la composición corporal como un aspecto a tener en cuenta en el desarrollo del rendimiento, se concluye que la aplicación de ciertos contenidos del entrenamiento según las características individuales y el estilo de vida de los jugadores es un factor que posee una influencia significativa sobre los futbolistas profesionales.

Palabras clave:

Nutrición.
Grasa corporal.
Antropometría.
Entrenamiento.
Fútbol.

Abstract

The requirements of physical demands in soccer have evolved in recent years, determining the need to investigate those aspects that condition athletic performance. The objective of this study was to describe the incidence of individualized training, company at meals, race, and demarcation on the anthropometric variables of professional soccer players since these four factors affect body composition, which is considered a predictor of performance and an indicator of lifestyle in these individuals. For this purpose, a retrospective study was developed in 51 professional players of the Spanish Football League Second Division B during the 2015/2016, 2016/2017, and 2017/2018 seasons. The anthropometric assessment was carried out under the technical standards of measurement recommended by the International Working Group of Kinanthropometry, adopted by the International Society for the Advancement of Kinanthropometry (ISAK). The results revealed that individualized training and company during meals were the factors that most influence exerted on the anthropometric variables that were collected. The values of fat mass and muscle mass, and the sum of fold measurements are sensitive to the effect of the intervention with these factors. The highest levels of interaction occurred between company during the meals and individualized training, and between demarcation and company during the meals. Considering body composition as an aspect to be taken into account in the development of performance, it should be considered that the application of certain training contents according to the individual characteristics and lifestyle of players are factors that may have a significant influence on professional soccer players.

Key words:

Nutrition. Body fat.
Anthropometry.
Training. Soccer.

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INTRODUCCIÓN

La naturaleza evolutiva del fútbol ha puesto de manifiesto la necesidad de investigar sobre aquellos aspectos que condicionan el rendimiento de los deportistas (1). Sin embargo, el fútbol es un deporte complejo de alta competitividad donde existen interacciones entre los diferentes factores que afectan al éxito deportivo (2,3). El diseño de estrategias para identificar con eficacia los factores relacionados con el rendimiento individual y colectivo debe tener un carácter multifactorial de acuerdo con las características fisiológicas y anatómicas de los deportistas y el contexto en el que se encuentran (3-5).

La composición corporal es uno de los factores que se integran en esa concepción holística de la detección de talentos en el fútbol (3,5-7). Más concretamente, el perfil antropométrico se ha usado repetidamente como método eficaz de evaluación de la composición corporal, considerándose un predictor relevante en la identificación del talento entre los futbolistas jóvenes (4,8). La valoración de la composición corporal y la antropometría facilita el estudio entre variables morfológicas y rendimiento (9), existiendo líneas de investigación donde se han podido identificar dichas variables como factores de riesgo con repercusión sobre la salud de los deportistas (10).

La literatura nos muestra que no existe un único perfil antropométrico que garantice el éxito deportivo, pues el somatotipo de los futbolistas es diferente atendiendo a las características individuales. Sin embargo, los resultados determinan en el futbolista un somatotipo mesomorfo-equilibrado de acuerdo con los diferentes niveles de rendimiento y las ligas profesionales, existiendo una excepción con respecto a los porteros, quienes muestran un aspecto endomórfico (11,12).

Las exigencias competitivas en el fútbol (13-15) y los esfuerzos realizados por los jugadores profesionales de acuerdo con el rol que desempeñan sobre el terreno de juego se han documentado ampliamente en la literatura científica (16-18), observándose diferencias significativas entre las diferentes demarcaciones (19). Este hallazgo podría dar respuesta a los diferentes planes de entrenamiento específicos desarrollados en función del perfil de rendimiento competitivo y, como consecuencia, podría ser una de las razones por las que se ha hipotetizado acerca de la posibilidad de que la demarcación sobre el terreno de juego o las características del rol del jugador se asocien a un determinado perfil antropométrico y/o fisiológico (20).

Mantener una composición corporal óptima se relaciona positivamente con el desarrollo deportivo (5,21). Los niveles altos en el porcentaje de grasa, los niveles insuficientes de masa libre de grasa y los índices de masa corporal (IMC) elevados pueden afectar al rendimiento y la salud de los deportistas (21,22). Sin embargo, se considera que existen factores externos que pueden condicionar el éxito deportivo y, posiblemente, la composición corporal de los deportistas (2,3). Considerando la importancia de la interacción entre los diferentes factores y su relación con el rendimiento, el objetivo de este estudio fue analizar el efecto que tienen factores contextuales tales como la demarcación en el terreno de juego, la etnia del deportista, la compañía durante las comidas y el entrenamiento individualizado sobre los parámetros antropométricos del jugador de fútbol profesional, así como la interacción entre ellos.

MATERIAL Y MÉTODOS

DISEÑO

Estudio de tipo retrospectivo donde se registraron los datos obtenidos durante tres temporadas completas (2015/2016, 2016/2017 y 2017/2018).

POBLACIÓN DEL ESTUDIO

Un total de 51 futbolistas profesionales de la Segunda División B española formaron parte de este estudio. Los valores promedio de la edad, la altura, el peso y el $VO_{2máx}$ (Yo-Yo Intermittent Recovery Test, level 2) fueron de 25,36 ± 3,1 años, 177 ± 4.2 cm, 73.76 ± 8.0 kg y 54.3 ± 5.1 mL·kg^{-1}, respectivamente. Todos los participantes tenían como mínimo 8 años de experiencia en el entrenamiento del fútbol, de manera estructurada y organizada por una entidad deportiva, y 3 años de experiencia en un club profesional. Los jugadores entrenaron un mínimo de 4 sesiones semanales durante las temporadas del estudio, con al menos 85 minutos de duración por sesión, realizando un partido de competición el fin de semana.

Todos los participantes se clasificaron según su demarcación sobre el terreno de juego (porteros, n = 4; defensas, n = 16; centrocampistas, n = 19; delanteros, n = 12), según la raza (negra, n = 8; mestiza, n = 11; blanca, n = 32) y según la compañía que tuvieron durante las comidas (padres, n = 15; pareja, n = 19; ninguna, n = 17); además, dado que todos los jugadores habían tenido un entrenamiento individualizado, ajustado a sus necesidades iniciales como complemento condicional al entrenamiento con el equipo, los jugadores también se clasificaron según dichos entrenamientos individualizados (coordinación/agilidad, n = 5; velocidad de reacción, n = 6; fuerza-potencia, n = 7; capacidad aeróbica, n = 4; velocidad, n = 7; potencia aeróbica, n = 8; habilidad para resistir sprints (RSA), n = 9, y fuerza-resistencia, n = 5). Este entrenamiento individual se había realizado un promedio de 5 veces al mes con el preparador físico, repartido entre una o dos sesiones de 20-25 minutos a la semana, antes o después de la sesión de entrenamiento del equipo, durante toda la temporada. Cada jugador se incluyó dentro de este contenido de entrenamiento complementario de acuerdo con los criterios establecidos por el preparador físico, entre los que se tuvieron en cuenta las características individuales de los jugadores (edad, datos antropométricos y resultados de los tests de valoración) y las exigencias físicas de la demarcación de acuerdo con los últimos estudios publicados sobre el análisis del tiempo de movimiento *(time motion analysis)* (16-19).

Todos los jugadores recibieron y firmaron el consentimiento informado después de una explicación detallada del estudio de investigación. El club involucrado aprobó la investigación antes de comenzar con ella. El estudio cumplió con los criterios éticos de la Universidad de Córdoba, estando en consonancia con la última versión de la Declaración de Helsinki.

INSTRUMENTOS

La masa corporal se midió con una báscula digital TANITA© BC-601 y la altura con un estadiómetro SECA© 213. Los pliegues cutáneos se documentaron en milímetros con un plicómetro Harpenden, los perímetros se midieron con una cinta métrica Lufkin Executive Thinline W606PM y los diámetros se determinaron con un antropómetro pequeño RealMet BCN. El registro de los datos se llevó a cabo a través de una hoja de cálculo Excel, formulada para evitar cualquier tipo de error matemático o en la introducción de datos, que no obstante se comprobaron posteriormente de manera visual.

PROCEDIMIENTO

La composición corporal se evaluó una vez al mes durante cada temporada, registrándose un total de 8 mediciones por cada jugador. Los jugadores fueron citados bajo las mismas condiciones para evitar variabilidad entre los sujetos y entre las mediciones, siendo evaluados por el mismo profesional y con los mismos instrumentos. En la valoración antropométrica se siguieron las normas técnicas de medición recomendadas por el International Working Group of Kinanthropometry, adoptadas por la International Society for the Advancement of Kinanthropometry (ISAK) (23). Todos los jugadores hubieron de someterse a varias mediciones de la composición corporal: masa corporal, talla, pliegues cutáneos, perímetros y diámetros.

La recogida de los datos personales necesarios para la valoración antropométrica fue realizada por el dietista-nutricionista del club, acreditado por la ISAK con un nivel II, teniendo en cuenta que no debía superarse el error técnico de medición (ETM) intraobservador indicado por la ISAK (2011), del 5% para los pliegues y del 1% para los perímetros y diámetros (23). Se registraron los pliegues cutáneos (subescapular, tríceps braquial, bíceps braquial, cresta ilíaca, supraespinal, abdominal, muslo anterior y pierna medial), los perímetros (brazo relajado, brazo contraído, mínimo de la cintura, máximo de la cadera, parte anterior del muslo y máximo de la pierna) y los diámetros óseos pequeños (biepicondíleo del húmero, biestiloideo y bicondíleo del fémur). También se calcularon los sumatorios de 6 y 8 pliegues cutáneos. Mediante las fórmulas descritas en el consenso de cineantropometría del GREC (24) se calculó la composición corporal mediante modelos de los siguientes componentes: la masa grasa mediante las ecuaciones Faulkner (25), la masa muscular mediante la propuesta de Lee (26) y la masa ósea mediante la técnica de Rocha (27).

ANÁLISIS ESTADÍSTICO

Se utilizó el programa estadístico SPSS (v.22.0, SPSS, Inc., Chicago, IL, EE. UU.) para el análisis de los datos. El análisis estadístico se basó en un análisis de la varianza mediante un Modelo Lineal General (MLG) multivariante y multifactorial (Hotelling's Trace, Roy's Largest Root, Pillai's Trace y Wilks' Lambda). Se realizó el test de homogeneidad de las medias a posteriori, a través de la prueba de Tukey ($p < 0,05$), para crear agrupaciones, además de observar las interacciones entre dos o más factores para todas las variables del estudio con más de dos factores de clasificación. La precisión de la estimación se indicó con un intervalo de confianza del 95% y con un nivel de significación de $p \leq 0,05$.

RESULTADOS

Los resultados se determinaron a partir del análisis de la varianza mediante un Modelo Lineal General (MLG) multivariante y multifactorial. Los resultados de los tests multivariantes (Hotelling's Trace, Roy's Largest Root, Pillai's Trace y Wilks' Lambda) determinaron que todos los factores estudiados producen diferencias estadísticamente significativas para el conjunto de las variables del estudio, así como para la mayoría de las interacciones entre ellas.

En la tabla I se resumen los efectos de los factores, de forma individualizada, sobre los diferentes parámetros antropométricos recogidos. El entrenamiento es el factor más determinante sobre las variables de la composición corporal, seguido de la compañía en las comidas, la etnia y la demarcación sobre el terreno de juego. El pliegue abdominal, el porcentaje de masa grasa (Yuhasz) y la suma de 6 y 8 pliegues se vieron significativamente afectados ($p < 0,001$) por todos los factores contextuales estudiados.

La demarcación sobre el terreno de juego tuvo influencia sobre las variables antropométricas de los jugadores. Se obtuvieron resultados estadísticamente significativos con todos los parámetros antropométricos excepto con los perímetros (el perímetro de la cadera fue el único que mostró diferencias significativas) y el diámetro del húmero.

La etnia condicionó significativamente las variables antropométricas. Sin embargo, no se observaron resultados significativos ni en el peso, ni en el perímetro de la cintura y de la pierna, ni en el peso residual. Los jugadores de etnia blanca tenían estaturas superiores a las de los jugadores de etnia negra y mestiza. El IMC fue mayor en los jugadores de etnia negra.

La compañía durante las comidas es uno de los factores que más influencia tienen sobre las variables antropométricas de los jugadores de fútbol. El diámetro del húmero, el peso graso y el porcentaje de masa muscular no mostraron resultados significativos, a diferencia del resto de las variables. Los valores más elevados en los pliegues se observaron cuando los futbolistas comían en compañía de los padres. Los futbolistas que comían con la pareja mostraron resultados en los pliegues inferiores a los obtenidos cuando comían sin ninguna compañía. Los futbolistas

Tabla I. Nivel de significación del efecto de los factores estudiados sobre las variables antropométricas

Parámetro	Demarcación	Etnia	Compañía	Entrenamiento
Peso	0,019*	0,137	0,000‡	0,000‡
Altura	0,001†	0,000‡	0,010*	0,000‡
PL Tríceps	0,000‡	0,009†	0,000‡	0,000‡
PL Subescapular	0,000‡	0,041*	0,000‡	0,000‡
PL Bíceps	0,000‡	0,012*	0,000‡	0,000‡
PL Cresta iliaca	0,000‡	0,000‡	0,000‡	0,000‡
PL Supraespinal	0,000‡	0,001†	0,002†	0,005†
PL Abdominal	0,000‡	0,000‡	0,000‡	0,000‡
PL Muslo	0,000‡	0,000‡	0,000‡	0,000‡
PL Medial pierna	0,003†	0,003†	0,000‡	0,000‡
PR Brazo relajado	0,430	0,002†	0,004†	0,429
PR Brazo contraído	0,453	0,009†	0,000‡	0,384
PR Cintura (mínimo)	0,450	0,743	0,017*	0,013
PR Cadera (máximo)	0,029*	0,046*	0,000‡	0,000‡
PR Pierna (máximo)	0,397	0,194	0,000‡	0,000‡
D Húmero (biepicondíleo)	0,371	0,017*	0,051	0,000‡
D Biestiloideo	0,000‡	0,000‡	0,000‡	0,000‡
D Fémur (biepicondíleo)	0,010*	0,000‡	0,002†	0,000‡
Suma de 6 pliegues	0,000‡	0,000‡	0,000‡	0,000‡
Suma de 8 pliegues	0,000‡	0,000‡	0,000‡	0,000‡
IMC	0,007†	0,000‡	0,000‡	0,000‡
% Masa grasa (Yuhasz, 1974)	0,000‡	0,000‡	0,000‡	0,000‡
% Masa grasa (Faulkner)	0,000‡	0,004†	0,000‡	0,000‡
% Masa muscular	0,000‡	0,000‡	0,171	0,000‡
% Masa ósea	0,001†	0,000‡	0,001†	0,000‡
Peso graso	0,000‡	0,010*	0,602	0,000‡
Peso muscular (Matiegka, 1921)	0,044*	0,026*	0,000‡	0,000‡
Peso óseo (Rocha, 1974)	0,000‡	0,000‡	0,000‡	0,000‡
Peso residual (Würch, 1974)	0,020*	0,126	0,000‡	0,000‡

*PL: pliegue; PR: perímetro; D: diámetro. *Valor de p < 0,05; †Valor de p < 0,01; ‡Valor de p < 0,001.*

que comían con los padres presentaban un mayor porcentaje de masa grasa y un menor porcentaje de masa muscular.

El entrenamiento fue el factor que más influencia tuvo sobre los parámetros antropométricos registrados, existiendo diferencias significativas en todas las variables excepto en el perímetro del brazo relajado y del brazo contraído. Los jugadores que habían realizado a nivel individual un entrenamiento de coordinación/agilidad presentaron pliegues y perímetros más elevados, y un porcentaje de masa grasa mayor que los de aquellos que habían realizado un trabajo de potencia aeróbica, RSA y fuerza-resistencia.

En la tabla II se muestran los niveles de significación del análisis de las interacciones entre los factores para todas las variables estudiadas. La etnia fue un factor que presentó excesivas interacciones vacías (por el bajo número de individuos), por lo que no se tuvo en cuenta en el análisis estadístico. Como se puede observar en la tabla II, muchas de las interacciones dobles no resultaron significativas, mostrándose que no existe interferencia de un factor sobre otro y que sus influencias se comportan como efectos independientes. Los mayores niveles de interacción se producen entre los factores de compañía en la comida y entrenamiento (CxE) y entre la demarcación sobre el terreno de juego y la compañía durante la comida (DxC).

En la figura 1 se presenta la interacción entre el contenido del entrenamiento individualizado y la compañía durante las comidas sobre el sumatorio de 8 pliegues. Los jugadores que se habían

Tabla II. Interacción de variables en la composición corporal

Parámetro	DxC	DxE	RxE	CxE
Peso	0,799	0,992	0,006†	0,126
Altura	0,001†	0,998	0,003†	0,021*
PL Tríceps	0,002†	0,518	0,199	0,000‡
PL Subescapular	0,000‡	0,481	0,334	0,146
PL Bíceps	0,008†	0,058	0,300	0,234
PL Cresta iliaca	0,553	0,281	0,240	0,701
PL Supraespinal	0,012*	0,589	0,535	0,034*
PL Abdominal	0,248	0,597	0,801	0,009†
PL Muslo	0,010*	0,441	0,843	0,001†
PL Medial pierna	0,000‡	0,008†	0,229	0,013*
PR Brazo relajado	0,909	0,648	0,909	0,353
PR Brazo contraído	0,630	0,659	0,601	0,828
PR Cintura (mínimo)	0,921	0,115	0,838	0,989
PR Cadera (máximo)	0,031*	0,801	0,004†	0,019*
PR Pierna (máximo)	0,119	0,634	0,065	0,001
D Húmero (biepicondíleo)	0,048*	0,299	0,000‡	0,000‡
D Biestiloideo	0,000‡	0,039	0,206	0,008†
D Fémur (biepicondíleo)	0,080	0,884	0,000‡	0,000‡
Suma de 6 pliegues	0,003†	0,699	0,816	0,001†
Suma de 8 pliegues	0,004†	0,483	0,698	0,012*
IMC	0,000‡	0,887	0,019*	0,000‡
% Masa grasa[1]	0,002†	0,739	0,762	0,002†
% Masa grasa[2]	0,006†	0,857	0,712	0,001†
% Masa muscular	0,000‡	0,565	0,762	0,000‡
% Masa ósea	0,000‡	0,210	0,522	0,000‡
Peso graso	0,367	0,934	0,216	0,081
Peso muscular[3]	0,188	0,968	0,011*	0,064
Peso óseo[4]	0,004†	0,453	0,000‡	0,004†
Peso residual[5]	0,773	0,977	0,006†	0,110

*PL: pliegue; PR: perímetro; D: diámetro; DxC: demarcación y compañía; DxE: demarcación y entrenamiento; RxE: etnia y entrenamiento; CxE: compañía y entrenamiento. [1]Yuhasz, 1974; [2]Faulkner; [3]Matiegka, 1921; [4]Rocha, 1974; [5]Würch, 1974. *Valor de p < 0,05; †Valor de p < 0,01; ‡Valor de p < 0,001.*

sometido a entrenamiento de la velocidad de reacción mostraban un sumatorio de pliegues mayor cuando comían solos o en compañía de los padres. Sin embargo, aquellos que comían con su pareja y realizaban entrenamientos de fuerza-potencia presentaban valores más bajos en la suma de pliegues. La interacción DxC mostró diferencias significativas para los pliegues del tríceps, subescapular, del bíceps y medial de la pierna, así como en el sumatorio de 6 y 8 pliegues, en el IMC, en el porcentaje de masa grasa, en el porcentaje de masa muscular y en el porcentaje de masa ósea. Los delanteros que comían en compañía de la pareja o sin compañía mostraron resultados más elevados de masa muscular. El porcentaje de masa muscular tuvo una distribución creciente entre los porteros, los defensas, los centrocampistas y los delanteros que comían solos, tal y como se muestra en la figura 2.

DISCUSIÓN

Considerando la importancia que tienen los estudios descriptivos sobre la composición corporal de los deportistas a lo largo del periodo competitivo (4,5), en el presente estudio se decidió analizar, sin intervención, la variabilidad de los parámetros antropométricos de una serie de jugadores profesionales de fútbol en relación con ciertos factores que, de acuerdo con la literatura, podrían tener influencia sobre dichas variables (5,20,28). Además,

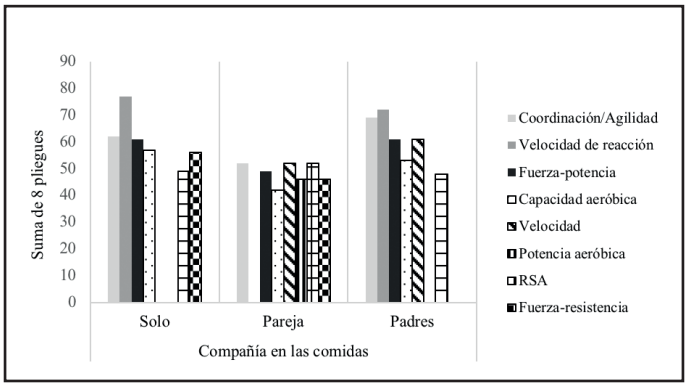

Figura 1.
Interacción entre los factores de compañía en las comidas y el entrenamiento individualizado sobre la variable antropométrica "suma de 8 pliegues".

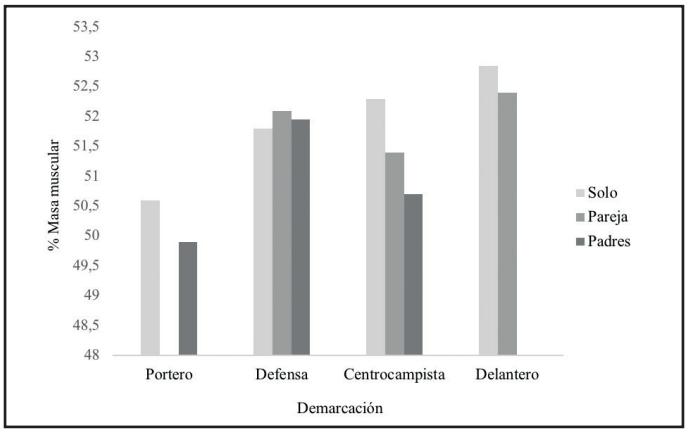

Figura 2.
Interacción entre los factores de demarcación y compañía en las comidas sobre el porcentaje de masa muscular.

respetando la concepción holística del deportista en los procesos de rendimiento (3,7), en dicho estudio se han pretendido buscar interacciones entre los factores externos y averiguar cómo influyen estas sobre las características antropométricas de los futbolistas.

La composición corporal y la cantidad y calidad del entrenamiento son algunos de los aspectos que se integran en el puzzle del rendimiento en los futbolistas (16). El rendimiento físico se correlaciona negativamente con el grosor de los pliegues cutáneos en aquellos deportes donde el deportista debe desplazar su cuerpo repetidas veces ante dificultades interpuestas por el adversario, siendo la masa libre de grasa un factor influyente sobre la capacidad de producir fuerza en actividades de alta intensidad (29). La composición corporal tiene influencia sobre la eficiencia biomecánica, la capacidad fisiológica y la salud de los deportistas (6,10,21,30-32), considerándose relevantes dichos aspectos para la práctica del fútbol ya que los equipos que ocuparon los mejores puestos en la clasificación mostraron valores inferiores de componente graso (33). Recientemente se ha realizado un análisis crítico de los estudios de aquellos factores que influyen en el rendimiento de los futbolistas, entre los que se encuentran los factores antropométricos (34), si bien dicha investigación se centra demasiado en las metodologías de análisis y menos en los resultados, como argumentan Carling y cols. en 2013 (35).

De acuerdo con lo que asegura la literatura mencionada, la metodología utilizada en este estudio para el registro de las variables antropométricas resulta potencialmente favorable para conocer la composición corporal con fiabilidad y validez. Se consideró que el tipo y el número de las variables registradas eran suficientes para proporcionar información relevante con respecto a la composición corporal de los futbolistas profesionales, sabiendo que las modificaciones del peso en los deportistas tienen que aportar conocimiento sobre el peso graso y muscular (22,28).

De acuerdo con el conocimiento científico, los futbolistas poseen un porcentaje de grasa corporal del 10-11% (± ≈2 DE), tal y como ocurrió en este estudio. Sin embargo, existen diferencias antropométricas entre los futbolistas de acuerdo con la etnia (5),

la madurez (3,6), el estilo de vida, la demarcación sobre el terreno de juego (3,6,28) o el tipo de entrenamiento complementario que se realice (16,20).

Los futbolistas estudiados mostraron diferencias significativas en la composición corporal de acuerdo con la demarcación sobre el terreno de juego, aspecto que ya había sido estudiado con anterioridad en otras investigaciones (3,6,28,36-37). Sutton y cols. (2009) (6) no encontraron diferencias significativas entre los jugadores según su demarcación, a excepción de los porteros. Sin embargo, Rodríguez Rodríguez (2019) (37) encontró diferencias en cuanto al peso entre todas las demarcaciones a excepción de entre los defensas y los delanteros, mientras que en el sumatorio de 6 pliegues solo hubo diferencias significativas entre los porteros con respecto al resto. Las diferencias antropométricas de los porteros con respecto a los jugadores de campo se han puesto de manifiesto con frecuencia en la literatura (3,28), pudiéndose justificar dicho hallazgo con el tipo de esfuerzos que demanda la competición para las diferentes demarcaciones. Rodríguez Rodriguez (2019) (37) indica que los porteros presentan valores superiores de peso, masa magra y masa muscular (sobre todo en los brazos), siendo sus resultados estadísticos, en aquellos parámetros antropométricos coincidentes, muy similares a los que presentamos en nuestro estudio.

La especialización desde edades tempranas ha propiciado la necesidad de categorizar el perfil antropométrico en función de la demarcación y de las exigencias específicas de esta con el objetivo de desarrollar programas de entrenamiento efectivos que fomenten el completo desarrollo de los deportistas profesionales (4,8). Sin embargo, existe controversia entre los estudios al determinar que existe un morfotipo ideal que asegure el rendimiento deportivo (20,28), no encontrando diferencias significativas en dicho morfotipo entre varios estudios (36,37).

Los resultados de esta investigación demostraron que el entrenamiento es el factor que más influye sobre las variables antropométricas. La modificación de los porcentajes de masa grasa y masa muscular a través de la actividad física está bien documentado en la literatura científica. Al ejercicio regular de los deportistas se le añadió un entrenamiento individualizado de acuerdo con los criterios profesionales del preparador físico y con el único objetivo de mejorar el perfil de rendimiento específico. Sin embargo, los hallazgos de este estudio demostraron que ciertos contenidos tuvieron mayor repercusión que otros sobre el sumatorio de pliegues, el porcentaje de masa grasa y el porcentaje de masa muscular. Los jugadores que desarrollaron un entrenamiento de potencia aeróbica, RSA y fuerza-resistencia obtuvieron mejores efectos sobre los valores antropométricos. De acuerdo con la literatura (38,39), el gasto calórico se ve aumentado por los estímulos de alta intensidad, el entrenamiento intermitente y el entrenamiento de fuerza combinado con el trabajo de resistencia, lo cual podría explicar los hallazgos encontrados en este estudio.

La compañía durante las comidas es un factor que hace referencia a si el jugador come habitualmente solo, en pareja o con sus padres. Los resultados del estudio mostraron el efecto de dicho factor sobre la composición corporal de los jugadores. Las normas dominantes en muchas sociedades prescriben que las comidas deben compartirse, que se debe comer simultánea e idealmente cara a cara con los miembros de la familia u otras personas cercanas. Las personas que hacen la mayoría de sus comidas sin compañía tienen una tendencia a comer con menos calidad (40). Esto se podría explicar cómo una falta de motivación para elegir o preparar los alimentos en comparación con lo que sucede cuando se cohabita con alguien más y cuando se consumen los alimentos en pareja.

CONCLUSIÓN

A través de esta investigación se describen las variables antropométricas de unos jugadores profesionales de fútbol a lo largo de una temporada completa, respetando los métodos utilizados en otras investigaciones. Además se establecieron, de forma estadística, las posibles interacciones entre las variables registradas con el fin de aproximarnos a la concepción holística del rendimiento.

De acuerdo con los hallazgos de este estudio, se observa que el entrenamiento es el factor más influyente en las variables antropométricas de los deportistas, existiendo aspectos característicos en el día a día de los futbolistas que podrían tener repercusión sobre las variables registradas (compañía durante las comidas, edad o niveles de motivación).

Por último, considerando la necesidad de exigir rendimiento a los deportistas profesionales para aumentar las probabilidades de éxito individual y colectivo, se considera que este estudio puede servir de referencia para los cuerpos técnicos dentro del marco del concepto de trabajo multidisciplinar, para que estos puedan intervenir en la gestión de los factores que afectan a la composición corporal de los jugadores de fútbol.

BIBLIOGRAFÍA

1. Barnes C, Archer D, Hogg B, Bush M, Bradley P. The Evolution of Physical and Technical Performance Parameters in the English Premier League. Int J Sports Med 2014;35(13):1095-100. DOI: 10.1055/s-0034-1375695
2. Chena M, Pérez-López A, Bores-Cerezal A, Ramos-Campo D. Associations between body composition and neuromuscular performance in young soccer players. IV NSCA International Conference, Murcia, Spain. Oral Abstract Presentations 2014;11:128.
3. Chena Sinovas M, Pérez-López A, Álvarez Valverde I, Bores Cerezal A, Ramos-Campo DJ, Rubio-Arias JA, et al. Influencia de la composición corporal sobre el rendimiento en salto vertical dependiendo de la categoría de la formación y la demarcación en futbolistas. Nutr Hosp 2015;32(1):299-307.
4. Reilly T, Bangsbo J, Franks A. Anthropometric and physiological predispositions for elite soccer. J Sports Sci 2000;18(9):669-83. DOI: 10.1080/02640410050120050
5. Sutton L, Scott M, Wallace J, Reilly T. Body composition of English Premier League soccer players: Influence of playing position, international status, and ethnicity. J Sports Sci 2009;27(10):1019-26. DOI: 10.1080/02640410903030305
6. Pérez-López A, Pérez-López A, Sinovas MC, Álvarez-Valverde I, Valades D. Relationship between body composition and vertical jump performance in young spanish soccer players. J Sport Hum Perform 2015;3(3).
7. Unnithan V, White J, Georgiou A, Iga J, Drust B. Talent identification in youth soccer. J Sports Sci 2012;30(15):1719-26. DOI: 10.1080/02640414.2012.731515
8. Gil S, Ruiz F, Irazusta A, Gil J, Irazusta J. Selection of young soccer players in terms of anthropometric and physiological factors. J Sports Med Phys Fitness 2007;47(1):25-32.

9. Brocherie F, Girard O, Forchino F, Al Haddad H, Dos Santos GA, Millet GP. Relationships between anthropometric measures and athletic performance, with special reference to repeated-sprint ability, in the Qatar national soccer team. J Sports Sci 2014;32(13):1243-54. DOI: 10.1080/02640414.2013.862840
10. Ehrmann FE, Duncan CS, Sindhusake D, Franzsen WN, Greene DA. GPS and Injury Prevention in Professional Soccer. J Strength Cond Res 2016;30(2):360-7. DOI: 10.1519/JSC.0000000000001093
11. Asín-Izquierdo I. Las Necesidades Condicionales en el Fútbol. Metodología Integrada en la Planificación de la Preparación Física - Revista de Entrenamiento Deportivo. Rev Entren Deport 2016;30(3).
12. Zuñiga Galavíz U, de León Fierro LG. Somatotipo en futbolistas semiprofesionales clasificados por su posición de juego. Int J Sport Sci 2007;3:29-36.
13. Stølen T, Chamari K, Castagna C, Wisløff U. Physiology of Soccer. Sport Med 2005;35(6):501-36. DOI: 10.2165/00007256-200535060-00004
14. Bangsbo J, Nørregaard L, Thorsø F. Activity profile of competition soccer. Can J Sport Sci 1991;16(2):110-6.
15. Bangsbo J, Iaia FM, Krustrup P. Metabolic response and fatigue in soccer. Int J Sports Physiol Perform 2007;2(2):111-27. DOI: 10.1123/ijspp.2.2.111
16. Bradley PS, Di Mascio M, Peart D, Olsen P, Sheldon B. High-Intensity Activity Profiles of Elite Soccer Players at Different Performance Levels. J Strength Cond Res 2010;24(9):2343-51. DOI: 10.1519/JSC.0b013e3181aeb1b3
17. DellaL A, Wong DP, Moalla W, Chamari K. Physical and technical activity of soccer players in the French First League - with special reference to their playing position. Int Sport J FIMS ISMJ 2010;11(2):278-90.
18. Di Salvo V, Baron R, Tschan H, Calderon Montero F, Bachl N, Pigozzi F. Performance Characteristics According to Playing Position in Elite Soccer. Int J Sports Med 2007;28(3):222-7. DOI: 10.1055/s-2006-924294
19. Bradley PS, Ade JD. Are Current Physical Match Performance Metrics in Elite Soccer Fit for Purpose or Is the Adoption of an Integrated Approach Needed? Int J Sports Physiol Perform 2018;13(5):656-64. DOI: 10.1123/ijspp.2017-0433
20. Lago-Peñas C, Casais L, Dellal A, Rey E, Domínguez E. Anthropometric and Physiological Characteristics of Young Soccer Players According to Their Playing Positions: Relevance for Competition Success. J Strength Cond Res 2011;25(12):3358-67. DOI: 10.1519/JSC.0b013e318216305d
21. Bunc V, Hráský P, Skalská M. Changes in Body Composition, During the Season, in Highly Trained Soccer Players. Open Sports Sci J 2015;8(1):18-24. DOI: 10.2174/1875399X01508010018
22. Perroni F, Vetrano M, Camolese G, Guidetti L, Baldari C. Anthropometric and Somatotype Characteristics of Young Soccer Players. J Strength Cond Res 2015;29(8):2097-104. DOI: 10.1519/JSC.0000000000000881
23. Stewart A, Marfell-Jones M. International Society for Advancement of Kinanthropometry. International standards for anthropometric assessment. International Society for the Advancement of Kinanthropometry; 2011.
24. Esparza Ros F. Manual de cineantropometria. Madrid: Grupo Español de Cineantropometria; 1993.
25. Faulkner JA. Physiology of Swimming. Res Quarterly Am Assoc Heal Phys Educ Recreat 1966;37(1):41-54. DOI: 10.1080/10671188.1966.10614734
26. Lee RC, Wang Z, Heo M, Ross R, Janssen I, Heymsfield SB. Total-body skeletal muscle mass: development and cross-validation of anthropometric prediction models. Am J Clin Nutr 2000;72(3):796-803. DOI: 10.1093/ajcn/72.3.796
27. Rocha MSL. Peso ósseo do brasileiro de ambos os sexos de 17 a 25 años. Arq Anat Antropol 1975;1:445-51.
28. Slimani M, Nikolaidis PT. Anthropometric and physiological characteristics of male soccer players according to their competitive level, playing position and age group: a systematic review. J Sports Med Phys Fitness 2018;59(1):141-63. DOI: 10.23736/S0022-4707.17.07950-6
29. Mala L, Maly T, Zahalka F, Bunc V, Kaplan A, Jebavy R, et al. Body composition of elite female players in five different sports games. J Hum Kinet 2015;45:207-15. DOI: 10.1515/hukin-2015-0021
30. Bosco C. La fuerza muscular : aspectos metodológicos. INDE; 2000.
31. Sporis G, Jukic I, Ostojic SM, Milanovic D. Fitness Profiling in Soccer: Physical and Physiologic Characteristics of Elite Players. J Strength Cond Res 2009;23(7):1947-53. DOI: 10.1519/JSC.0b013e3181b3e141
32. Wong DP, Wong SH. Physiological Profile of Asian Elite Youth Soccer Players. J Strength Cond Res 2009;23(5):1383-90. DOI: 10.1519/JSC.0b013e3181a4f074
33. Kalapotharakos VI, Strimpakos N, Vithoulka I, Karvounidis C, Diamantopoulos K, Kapreli E. Physiological characteristics of elite professional soccer teams of different ranking. J Sports Med Phys Fitness 2006;46(4):515-9.
34. Mackenzie R, Cushion C. Performance analysis in football: A critical review and implications for future research. J Sports Sci 2013;31(6):639-76. DOI: 10.1080/02640414.2012.746720
35. Carling C, Wright C, Nelson LJ, Bradley PS. Comment on 'Performance analysis in football: A critical review and implications for future research.' J Sports Sci 2014;32(1):2-7. DOI: 10.1080/02640414.2013.807352
36. Jorquera Aguilera C, Rodríguez Rodríguez F, Torrealba Vieira MI, Campos Serrano J, Gracia Leiva N, Holway F. Características Antropométricas de Futbolistas Profesionales Chilenos. Int J Morphol 2013;31(2):609-14. DOI: 10.4067/S0717-95022013000200042
37. Rodríguez Rodríguez F, López-Fuenzalida A, Holway F, Jorquera-Aguilera C. Diferencias antropométricas por posición de juego en futbolistas profesionales chilenos. Nutr Hosp 2019;36(4). DOI: 10.20960/nh.02474
38. Andreato LV, Esteves JV, Coimbra DR, Moraes AJP, Carvalho T. The influence of high-intensity interval training on anthropometric variables of adults with overweight or obesity: a systematic review and network meta-analysis. Obes Rev 2019;20(1):142-55. DOI: 10.1111/obr.12766
39. Badawy HM, Muaidi QI. Perfil aeróbico durante el rendimiento de alta intensidad en atletas sauditas profesionales. Pak J Biol Sci 2018;21:24-8.
40. Yates L, Warde A. Eating together and eating alone: meal arrangements in British households. Br J Sociol 2017;68(1):97-118. DOI: 10.1111/1468-4446.12231

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Nutritional assessment of female patients newly diagnosed with breast cancer in a northern region of Spain

Evaluación nutricional de mujeres recién diagnosticadas de cáncer de mama en una cohorte del norte de España

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Abstract

Background: evidence from research suggests that the development of cancer disease is associated with environmental factors. There are few studies evaluating nutritional status in women suffering from cancer in Spain.

Objectives: this study aimed to assess the nutritional status in breast cancer female patients at diagnosis in a northern region of Spain (Asturias), where breast cancer rates are particularly high when compared to the rest of Spain.

Material and methods: a cross-sectional study was conducted in a sample of 76 newly diagnosed female cancer patients. Lifestyle factors, anthropometry, biochemical, and dietary intake data were collected immediately after diagnosis and prior to the initiation of the prescribed treatment.

Results: a high percentage of these women diagnosed with cancer were sedentary (59.2%). Their average body mass index (BMI) was 27.3 ± 5.5 kg/m^2. They also showed a high percentage of body fat, 38.3%, as well as a large waist circumference of 92.2 cm. Patients reported a low intake of fruits, vegetables, legumes, and nuts, and a high intake of red meat, meat products, and sweet foodstuffs as compared to the Spanish dietary guidelines ($p < 0.01$).

Conclusion: the results showed a low intake of folate, calcium, and vitamin D, which is particularly relevant in women. In conclusion, these breast cancer patients showed overweight and high sedentarism levels, and reported unbalanced dietary patterns at the time of diagnosis.

Key words:

Breast cancer.
Nutritional status.
Dietary intake.
Women.

Resumen

Introducción: la evidencia actual indica que el desarrollo de algunos tipos de cáncer está asociado a factores ambientales. Pocos estudios realizados en España han evaluado el estado nutricional de las mujeres con cáncer.

Objetivos: el objetivo de este estudio ha sido evaluar el estado nutricional de las mujeres en el momento de ser diagnosticadas de cáncer de mama (CM) en una región del norte de España (Asturias), donde las cifras de cáncer de mama son particularmente elevadas en comparación con el resto de España.

Material y métodos: se realizó un estudio transversal con una muestra de 76 mujeres recién diagnosticadas de cáncer de mama. Se recopilaron datos sobre su estilo de vida, antropometría, ingesta, bioquímica y dieta de forma inmediata tras el diagnóstico y antes del inicio del tratamiento.

Resultados: un alto porcentaje de estas mujeres diagnosticadas de cáncer eran sedentarias (59,2%). El valor medio de su índice de masa corporal (IMC) era de 27,3 ± 5,5 kg/m^2. Asimismo, estas pacientes mostraron un alto porcentaje de grasa corporal, del 38,3%, y un elevado perímetro de la cintura, de 92,2 cm. La dieta de todas las pacientes incluía una escasa ingesta de frutas, verduras, legumbres y frutos secos, y en cambio una ingesta elevada de carnes rojas y procesadas y alimentos dulces, en comparación con las recomendaciones dietéticas españolas ($p < 0,01$).

Conclusión: los resultados también mostraron unas escasas ingestas de folato, calcio y vitamina D, particularmente preocupantes en las mujeres. En conclusión, la mayoría de las voluntarias con CM presentaban sobrepeso, altos niveles de sedentarismo y un patrón de dieta no equilibrada en el momento del diagnóstico.

Palabras clave:

Cáncer de mama.
Estado nutricional.
Dieta. Mujeres.

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INTRODUCTION

According to the World Health Organization, 40 million people die from noncommunicable diseases (NCDs) each year, which is equivalent to 70% of all deaths globally (1). Cancer is the second leading cause of death after cardiovascular disease. In 2018, the International Agency for Research on Cancer (IARC) estimated 18.1 million new cancer cases and 9.6 million deaths (2). Cancer incidence varies according to gender and different geographic locations, among other factors. In women, the most commonly diagnosed type worldwide is breast cancer (BC), both in developed and developing countries. In 2018, approximately 2.0 million new cases were diagnosed (24.2% of all cancer cases were diagnosed in women). The same year in Spain, the incidence of female BC was 24.7% (2).

The World Cancer Research Fund (WCRF) has concluded that healthy lifestyles may help to prevent up to 70% of cancer cases. These include healthy diet eating, regular physical activity, a healthy weight, and avoiding smoking and alcohol drinking (3). There is growing and consistent epidemiological evidence, with robust confirmation for mechanisms operating in humans, that greater body fatness is a cause of postmenopausal breast cancer (3).

At the same time, malnutrition is very common in these cancer patients after the disease has been diagnosed. The prevalence of disease-related malnutrition ranges from 20% to 80% in patients with cancer, and increases the risk of adverse outcomes, including poor prognosis, treatment response, and quality of life (4,5).

Early identification of malnutrition and an appropriate nutritional intervention are essential in this population to avoid the potential pathological effects of deficient nutrition, and to reduce the cytotoxic effects and other associated complications (6).

In Spain, although a preliminary assessment of the nutritional status is recommended at the time of diagnosis with any cancer (6), the clinical care of cancer patients focuses mainly on the medical treatment. A dietitian assesses only patients with severe malnutrition, but not those who are newly diagnosed, thus limiting the benefits of an earlier nutritional intervention. To date, few Spanish studies have addressed this assessment of nutritional status in newly diagnosed cancer patients, before a therapy is established (7,8). There is some information during periods of treatment such as chemotherapy, or concerning malnutrition in terminal stages. But current studies deal only with diet, or physical activity, or lifestyle, and not enough studies are performed to provide an integral evaluation of all these environmental factors (7,8). Furthermore, there are no previous nutritional assessment studies in women with breast cancer in the northern Spanish region of Asturias, which exhibits the highest cancer-related mortality rate among all Spanish regions (9).

Therefore, the aim of the present study was to assess the nutritional status of newly diagnosed female patients with breast cancer in the north-western coast of Spain (Asturias), as well as specific information on their physical activity and body composition.

METHODS

STUDY DESIGN AND PARTICIPANTS

A cross sectional study was conducted in newly diagnosed female patients with breast cancer attending the Oncology Unit at Centro Médico de Asturias and the Surgery Unit at Hospital Universitario Central de Asturias. The Spanish region of Asturias has the highest obesity rates for adults in the country (25.7%, aged between 24-65 years) (10). The population sample of female cancer patients was recruited on their first hospital visit after cancer diagnosis, between February 2016 and July 2017. Therefore, the recruitment took place prior to any type of therapeutic intervention. The inclusion criteria considered women aged 18 years or older with an initial diagnosis and a confirmed result of breast cancer. Patients with nutritional support, supplementation, or psychiatric illness were excluded. The Ethics Committee of Universidad CEU San Pablo approved the study. Informed consent was obtained from all participants before enrolment. A single dietitian performed all measurements and administered all questionnaires, thus variability between observers was avoided.

PHYSICAL ACTIVITY AND ANTHROPOMETRIC DATA

The validated International Physical Activity Questionnaire (IPAQ, short version) was used to obtain information about each patient's physical activity before their diagnosis during a face-to-face interview (11).

Anthropometric measures such as height, weight, waist, hip and arm circumferences, and triceps skin fold thickness were obtained according to the methodology described by the International Society for the Advancement of Kinanthropometry (ISAK) (12). A trained dietitian performed these measurements. Patients were weighed in light clothing without shoes on an In Body 230 (Microcaya) weighing scale with a graduation of 0.1 kg. Patient height was determined with a mechanical height rod stadiometer (Wunder HRi) using a graduation of 1.0 mm. All measurements were obtained in duplicate. The measurements of waist, hip, and arm circumferences were made in triplicate by using a Cescorf flexible steel tape measure with a graduation of 1.0 mm. The triceps skinfold thickness was measured by using a Holtain skinfold caliper (0.2 mm). Arm strength was determined with the Takei 5401 Hand Grip Dynamometer (graduation of 0.1 kg). The mean arm circumference and triceps skinfold thickness were used to calculate the mid-arm muscle circumference and the corrected arm muscle area using standard equations. The corrected arm muscle area $\leq$ 21.6 cm^2 for females was used to determine the risk of malnutrition (13). Fat and lean mass were determined using an InBody 230 multi-frequency (20 kHz, 100 kHz, Microcaya) measurement, according to the recommendations issued by the European Society for Parenteral and Enteral Nutrition (ESPEN) for the assessment of patients conforming to the bioelectrical impedance test (14). The participants were classified according to their BMI and waist/hip index as described in the Spanish Society for the Study of Obesity (SEEDO) classification (15).

NUTRIENT INTAKE ASSESSMENT AND CLINICAL DATA

A trained dietitian collected and processed the dietary data using standardized questionnaires of 24-hour recall for three different days – two week days and one weekend day (16). The 24-hour dietary recall was carried out prior to the initiation of the prescribed treatment. Participants were asked for detailed descriptions of the foods and beverages they had consumed, as well as their portions, cooking methods, and recipes. The 24-hour recall interviewer used visual aids, food models, food portions and probing questions to overcome the memory lapses of the respondents (17). The food weights obtained were converted to nutrient intake estimates per day by using the DIAL programme, based on the Spanish food composition database (version 3.0.0.5) (18).

Diet quality and intake adequacy were assessed according to the recommended food portions and the nutritional targets authorized by the Spanish Society for Community Nutrition (19). Dietary energy and nutrients were compared to the recommended intakes for the Spanish population (20). Patients were also administered the Patient Generated Subjective Global Assessment (PG-SGA), a validated tool for nutritional diagnosis, simple and effective, that is currently considered the standard reference for the assessment of nutritional status in cancer patients (21). In addition, medical records were collected in the PG-SGA too (e.g., type of tumor and stage data) in order to complete their clinical status assessment.

STATISTICAL ANALYSIS

The size of the sample was determined according to the incidence of BC amongst women in Asturias (9). A sample of 72 subjects was calculated, with a 95% confidence interval, α error of 5%, β error of 20%, and a power of 80%, by using the McNemar test. With a prediction of percentage loss of 20%, an initial sample consisting of 76 subjects was proposed. All statistical tests were performed using the IBM SPSS Statistics for Windows, Version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics (mean, standard deviation, proportions, and absolute number and percentage) were computed for each investigated variable.

RESULTS

GENERAL CHARACTERISTICS

A total of 76 female participants finally joined the study. All participants completed the study (100% response rate) and none of them suffered from pre-existing comorbidities. All had a diagnosis of breast cancer. Their baseline characteristics (Table I) showed that most patients were > 50 years old (average age: 56.9 years). The patients were diagnosed with stage I (n = 57; 75%), stage II (n = 18; 24%) or stage III (n = 1; 3%) malignancies. Most of the cancers had hormone receptors and were of the luminal A/B type (n = 60, 79%). Twenty-four percent of these BC patients were smokers (n = 18) or ex-smokers (n = 26; 34%), and more than half of the sample (n = 49) drank alcohol regularly. The physical activity level was low, and the patients were currently sedentary (59%, n = 45). According to the PG-SGA criteria, 98% of patients were well-nourished at the time of diagnosis.

Table I. Selected baseline characteristics of newly diagnosed breast cancer female patients in Asturias

Baseline characteristics		(n = 76)
Age (yrs): mean (standard deviation, SD)		56.9 (9.3)
		n (%)
Menopausal status	Pre-menopausal	26 (34)
	Post-menopausal	50 (66)
Cancer stage	I	57 (75)
	IIA-IIB	18 (24)
	IIIA-IIIB-IIIC	1 (3)
Tumor grade*	I	30 (40)
	II	30 (40)
	III	16 (20)
	IV	0 (0)
Hormone receptor status	Luminal A/B	60 (79)
	HER2†	11 (14)
	Basal	5 (7)
Current alcohol use	None	27 (35)
	Some	21 (28)
	Moderate	28 (37)
Smoking status	Never	32 (42)
	Current	18 (24)
	Past	26 (34)
Physical activity level‡	High	9 (12)
	Moderate	22 (29)
	Low	45 (59)

*Number of patients (percentage), n (%). *Tumor grade: I = well differentiated, II = moderately differentiated, III = poorly differentiated, IV = undifferentiated. †HER2: human epidermal growth factor receptor 2. ‡Physical activity levels (11).*

ANTHROPOMETRIC MEASURES

According to their body mass index, nearly one-third (31.6%) of the participants were considered obese at diagnosis. Anthropometric measures are summarized in table II. The body fat percentage was higher than recommended (38.3%). Waist circumference and waist/hip ratio data were also higher than the reference values in all participants (17). The average mid-arm muscle circumference was 29.4 cm. Our BC patients aged 60-69 years showed greater strength in their right arm (p = 0.02) when compared to references (22).

Table II. Anthropometric measures of newly diagnosed breast cancer female patients in Asturias

	n = 76	Reference value†	
BMI: mean (SD)*	27.3 (5.6)		
BMI: n (%)†	Underweight	1 (1.3)	< 18.5 kg/m^2
	Normal weight	29 (38.2)	18.5-24.9 kg/m^2
	Overweight	22 (28.9)	24.9-29.9 kg/m^2
	Obese	24 (31.6)	> 29.9 kg/m^2
Hand grip strength (kg) according to age (yrs) and right (R) or left (L) arm; mean (SD)	18-39 yrs	R 28.9 (0.0) L 25.5 (0.0)	P50 (27.4-27.6)
	40-49 yrs	R 25.7 (5.1) L 25.4 (5.2)	P50 (26.9)
	50-59 yrs	R 23.6 (3.6) L 22.1 (4.9)	P50 (24.3)
	60-69 yrs	R 24.2 (4.4) L 22.7 (4.8)	P50 (21.7)
	≥ 70 yrs	R 17.8 (3.7) L 16.8 (2.1)	P50 (16.8)
Mid-arm muscle circumference (cm): mean (SD)	29.4 (3.5)	> 21.6	
% Body fat: mean (SD)	38.3 (8.1)	< 30%	
Waist circumference (cm): mean (SD)	92.2 (13.3)	< 88	
Waist/Hip ratio: mean (SD)	0.86 (0.06)	< 0.85	

*Number of patients; mean values (standard deviation). *BMI (body mass index): weight (kg)/height^2 (m^2). †Consensus SEEDO 2007 (15).*

Table III. Biochemical markers of newly diagnosed breast cancer female patients in Asturias

	Mean SD		Reference values*
Hemoglobin (g/dL)	13.7	1.1	12.0-16.0
Hematocrit (%)	40.8	3.2	36.0-48.0
Glucose (mg/dL)	95.9	12.1	70.0-110.0
Total cholesterol (mg/dL)	212.6	40.9	< 200.0
HDL cholesterol (mg/dL)	68.4	20.1	> 46.0
LDL cholesterol (mg/dL)	125.9	34.2	< 160.0
Triglycerides (mg/dL)	104.1	55.9	< 150.0
Albumin (g/L)	39.9	6.2	35.0-52.0
Iron (µg/dL)	87.1	28.9	37.0-45.0
C-reactive protein (mg/dL)	1.7	3.2	0.0-0.5

*Mean values (standard deviation). *Reference values (23).*

Table IV. Daily frequency of food groups consumption in newly diagnosed breast cancer female patients in Asturias

Food group	Recommended intake, portions/day*	Intake, portions/day n = 76	
		Mean	SD
Fruits	3	1.21	0.9
Vegetables	2	0.75	0.5
Cereals, grains, potatoes	≥ 6	3.85	1.4
Legumes	0.5	0.21	0.2
Nuts	0.4	0.15	0.2
Oils	3-4	3.64	0.7
Beverages (water)	≥ 8	5.62	2.3
Dairy products	≥ 2	1.72	0.9
Lean meats	0.4	0.41	0.3
Fish and seafood	0.5	0.39	0.3
Eggs	0.4	0.35	0.3
Fat meats and meat products	0.07	0.39	0.4
Sweets and candies	0.07	0.75	0.6

*Mean values (standard deviation). *Daily consumption recommended by Spanish nutritionists (19).*

BIOCHEMICAL PARAMETERS

At diagnosis, the values of the measured biochemical parameters (Table III) were considered clinically normal for hemoglobin, hematocrit, glucose, triglycerides, albumin, and iron in all participants (23). Total cholesterol levels (212.6 mg/dL) were higher than the reference values (200.0 mg/dL).

NUTRIENT INTAKE ASSESSMENT AND ADEQUACY OF THE REPORTED INTAKE

The results obtained for the intake frequency of food groups among these newly diagnosed BC female patients in Asturias are presented in table IV. All participants had an insufficient intake

of plant-based foods (fruits, vegetables, cereals and potatoes, legumes, and nuts). In contrast, they had adequate intakes for lean meats, and for olive and sunflower oils.

The intakes of macronutrients and selected micronutrients are summarized in table V. The dietary assessment showed an unbalanced energy and macronutrient distribution in the patients. Energy and carbohydrate intakes were lower than recommended ($p < 0.05$) (20). The average carbohydrate intake was particularly low (39.6%).

Table V. Total energy intake and the contributions of macronutrients and lipids (%) in newly diagnosed breast cancer female patients in Asturias

	n = 76		
	Mean	**SD**	**Nutritional objectives***
Energy (kcal/day)	1,785.9	336.2	2,075
% Proteins	16.5	3.0	15
% Carbohydrates	39.6	7.0	50
% Sugars	19.3	5.6	
% Lipids	39.7	6.2	35
% SFA	12.1	2.8	8
% MUFA	18.7	4.2	20
% PUFA	5.2	1.6	5
% n-6	4.3	1.4	3%
% n-3	0.8	0.4	1-2%
% Alcohol	2.1	2.4	< 10%
% Fiber	2.0	0.7	

*SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids. Mean values (standard deviation). *Nutritional objetives for the Spanish population (19).*

The reported intakes of minerals and vitamins (Table VI) were compared to Spanish recommendations (20). The daily intake of vitamins and minerals did not meet the recommendations for folate (62.3% of recommended intake), vitamin D (13.1%), vitamin E (36.6%), calcium (66.6%), and zinc (54.8%).

DISCUSSION

The present study provides the first data available on the baseline characteristics and lifestyle factors (physical activity, tobacco use, and alcohol intake), anthropometry, biochemical parameters, and nutrient intake of women newly diagnosed with breast cancer (BC) in Asturias, northern Spain, prior to any therapeutic intervention. Actually, very few studies in Spain have evaluated the nutritional status of oncologic female patients at diagnosis (7,8). Some studies have analyzed the nutritional status of cancer patients in a terminal stage, or during chemotherapy and radiotherapy interventions. Other studies have considered only some parameters separately, like quality of life, or diet, or physical activity (7,8).

In the present study, sedentarism rates were high among our patients. The evidence suggests an inverse relationship between physical exercise, aerobic and strength, and the risk for relapse in cancer survivors (24). Travier et al., in 2015, studied the effect of an 18-week exercise programme during BC treatment. They reported positive effects on physical fatigue, submaximal cardiorespiratory fitness, and muscle strength (24).

A high percentage of newly diagnosed female patients with cancer were smokers and regular alcohol drinkers. The World Cancer Research Fund (WCRF)/American Institute of Cancer Research (AICR) report from 2018 showed that alcohol intake is strongly linked to the risk of developing BC in postmenopausal women (25). Furthermore, high alcohol intakes reduce folate absorption (26). This could explain why BC risk is higher in women

Table VI. Reported intake of vitamins and minerals in newly diagnosed breast cancer female patients in Asturias, and its adequacy with regards to the daily intakes recommended for the Spanish population

	n = 76		% Adequacy to recommended daily intake*	
	Intake (daily)			
	Mean	**SD**	**Mean**	**SD**
Vitamin B_1 (mg)	1.2	0.4	151.6	51.1
Vitamin B_2 (mg)	1.6	0.5	130.7	38.2
Niacin (mg)	29.7	7.7	212.6	55.6
Vitamin B_5 (mg)	4.6	1.0	92.8	19.8
Vitamin B_6 (mg)	1.6	0.5	103.3	30.4
Folate (µg)	250.0	80.0	62.3	19.9
Vitamin B_{12} (µg)	25.3	7.8	273.2	183.9
Vitamin C (mg)	115.4	61.5	191.9	102.9
Vitamin A (µg)	636.1	271.6	79.3	34.0
Vitamin D (µg)	1.9	1.5	13.1	10.5
Vitamin E (mg)	7.3	2.8	36.6	14.4
Vitamin K (µg)	132.7	92.2	147.5	102.4
Calcium (mg)	800.3	240.9	66.6	20.0
Phosphorus (mg)	1,233.8	304.5	175.9	42.9
Potassium (mg)	2,594.2	581.2	74.1	16.6
Magnesium (mg)	262.2	65.2	87.2	21.6
Iron (mg)	11.7	3.2	117.3	32.2
Zinc (mg)	8.0	2.3	54.8	15.0
Iodine (µg)	97.5	37.8	88.6	34.4

**Spanish reference intake (20).*

with a regular alcohol intake and a folate-deficient dietary intake (26). Interestingly, the present study showed deficient folate intakes at diagnosis (Table VI). This result follows the same trend than that found by the ANIBES study for the general female population in Spain (27).

According to the PG-SGA method used to assess the nutritional status of participants in this study, 97.8% of participants were well-nourished at diagnosis. The prevalence of malnutrition in the current study was lower than that reported in other studies. Bering T et al. found that 80.8% of BC female patients were well nourished before starting chemotherapy or radiotherapy (28).

Despite this result, in the present study it is important to note that there is a high prevalence of overweight and obesity, with high body fat percentages and high waist circumference values in the study patients. This result follows the same pattern shown by the ENPE study for the Spanish population, which recently reported a prevalence of overweight and obesity of 25.7% among healthy adults aged 24-65 years living in Asturias (10). Also, our results are similar to those obtained for the general population of Spain according to the ANIBES study, which revealed a high prevalence of overweight and obesity in women (31.5% and 17.2%, respectively) (29).

Overweight and obesity could increase the risk of several types of cancers, such as BC. Ewertz M et al. have established that the higher the BMI value ($\geq$ 30 kg/m^2) of BC patients at diagnosis, the higher the cancer risk (30). In addition, a study on obesity and BC risk indicated that general and central obesity were positively associated with BC risk in pre- and post-menopausal BC women (31). Along the same lines of our BMI results, 61.8% of the patients had abdominal obesity as based on waist circumference. A high percentage of overweight and obesity (66.5%) was also reported in a study among Malaysian BC patients after 1 year post-diagnosis (32). Excessive abdominal fat and large waist circumference values are associated with an increased risk of postmenopausal BC (33).

The assessment of muscle strength using the handgrip strength test has been widely utilized in BC survivors. In the present study, BC patients (60-69 years) showed greater strength in their right arm when compared to references (22). A good status for this indicator could be considered particularly interesting, primarily considering that previous studies have showed a markedly impaired muscle strength after treatment in BC patients (34). To our knowledge, no studies have thus far reported handgrip strength in cancer patients at diagnosis.

Regarding biochemical markers, BC patients showed increased total cholesterol (TC) levels when compared to references values. Several studies have investigated the relationship between TC and HDL-C and the risk for BC. A meta-analysis (35) confirmed the evidence of a modest but statistically significant inverse association between HDL-C and BC. Ni et al. (35) suggested that serum HDL-C protects against breast carcinogenesis only among postmenopausal women.

Recent research has reported a protective role against cancer of some dietary patterns, specifically those including a high intake of vegetables, fruits, whole grains, fish, olive oil, and nuts (36). The Mediterranean diet is an example of this. However, in the current study, we found that BC female patients evaluated in the northwestern region of Spain did not follow the classical, recommended Mediterranean dietary pattern. The patients' dietary intake was poor in plant-based foods such as fruits, vegetables, cereals, grains, legumes, and nuts, and was instead rich in red meats and meat derivatives, as well as sweet foodstuffs. These findings are consistent with those of other studies in cancer female patients on treatment, which reported a low consumption of fruits, vegetables, and wholegrain cereals (36). Consistently with this pattern, the energy and macronutrient distribution of these patients was unbalanced when compared to the Spanish Nutritional Objectives (19), with an excessive intake of lipids and a low proportion of energy provided by carbohydrates. The contribution of lipids to total energy intake was higher than the values stated in the Spanish Nutritional Objectives because of a higher intake of MUFAs. Our data follow the current typical western dietary patterns, actually quite similar to those reported by the ANIBES study for the general Spanish population (37).

Regarding micronutrients, as a consequence of the low intake of fruits and vegetables, folate dietary intake was markedly lower when compared to the Spanish reference intakes (20). Other authors (38) have also reported similar results in BC patients undergoing treatment. Vitamin E and vitamin D intakes were also definitely low in these patients' diets. Several studies in cancer patients also reported an inadequate intake of these vitamins (13). Vitamin D dietary intake results were dramatically low, indeed. As a matter of fact, reported calcium intakes were low, underscoring another weakness in their diet. These results are of particular concern and could lead to many potential implications, since folate, calcium, and vitamin D are critical nutrients specifically involved in the nutritional status and health of women. Zinc and potassium dietary intakes were also suboptimal. A diet poor in vegetables also led these patients to have a reduced intake of fiber. Several studies have demonstrated the protective effect of fiber against BC, among other types of cancer (39). A strong evidence suggests that dietary intervention could reduce nutritional status failure during intensive treatment (5,40).

CONCLUSIONS

In summary, this study provides for the first time specific knowledge on the nutritional status at diagnosis of breast cancer (BC) female patients in a northern region of Spain (Asturias), a region where breast cancer rates are particularly high when compared to the rest of Spain. Most of these participants showed overweight and high sedentarism levels, and reported unbalanced dietary patterns, quite far from the Mediterranean model. All of them reported a low intake of vegetables and a high intake of red meat. Patients also showed an alarming low intake of folate, vitamin D, and calcium. These results are particularly concerning, since folate, calcium, and vitamin D are critical nutrients involved in the nutritional status and health of women.

An early identification of malnutrition risk, and a timely nutritional intervention, are critical for cancer patients at diagnosis. Such

an intervention – before, during, and after cancer therapy – might well be critical not only to cover the nutritional requirements of cancer patients, but also to reduce the cytotoxic effects and complications associated with cancer treatment, whose effects have an impact on nutritional status. Longitudinal studies evaluating the evolution of the nutritional status of patients are also needed.

REFERENCES

1. World Health Organization. Noncommunicable diseases 2017. http://www.who.int/mediacentre/factsheets/fs355/en/ (accessed on 30 October 2018).
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: a Cancer Journal for Clinicians 2018;49:509-31. DOI: 10.3322/caac.21492
3. World Cancer Research Fund American Institute for Cancer Research. Diet, Nutrition, Physical Activity and Cancer: a Global Perspective. Continuous Update Project Expert Report 2018. 2018.
4. Gupta D, Lis CG, Granick J, Grutsch JF, Vashi PG, Lammersfeld CA. Malnutrition was associated with poor quality of life in colorectal cancer: a retrospective analysis. Journal of Clinical Epidemiology 2006;59:704-9. DOI: 10.1016/j.jclinepi.2005.08.020
5. Ravasco P, Monteiro Grillo I, Camilo M. Cancer wasting and quality of life react to early individualized nutritional counselling! Clinical Nutrition 2007;26:7-15. DOI: 10.1016/j.clnu.2006.10.005
6. Gómez Candela C, Pérez LML, Aunon PZ, Suarez LR, Perez SC, Monzon AZ, et al. Algoritmos de evaluación y tratamiento nutricional en el paciente adulto con cáncer. Soporte Nutricional en El Paciente Oncologico 2004:1-20.
7. López MTF, Fernández CAS, de Sas Prada MT, Urrutia SA, Alonso mLB, Pérez MTA, et al. Desnutrición en pacientes con cáncer; una experiencia de cuatro años. Nutr Hosp 2013:1-10.
8. Suárez-Varela M, Simón AR, López-Antón AB, Tormo SB, Climente IP, Redondo Bautista M, et al. Protein intake in women with breast cancer before, during, and after treatment. Annals of Clinical Nutrition 2018:1-7.
9. Galcerán J, Ameijide A, Carulla M, Mateos A, Quirós JR, Rojas D, et al. Cancer incidence in Spain, 2015. Clinical and Translational Oncology 2017:1-27. DOI: 10.1007/s12094-016-1607-9
10. Aranceta-Bartrina J, Pérez-Rodrigo C, Alberdi-Aresti G, Ramos-Carrera N, Lázaro-Masedo S. Prevalencia de obesidad general y obesidad abdominal en la población adulta española (25-64 años) 2014-2015: estudio ENPE. Revista Española de Cardiología 2016;69:579-87. DOI: 10.1016/j.recesp.2016.02.010
11. Gómez-Conesa A, Mantilla Toloza SC. El Cuestionario Internacional de Actividad Física. Un instrumento adecuado en el seguimiento de la actividad física poblacional International Physical Activity Questionnaire. An adequate instrument in population physical activity monitoring. Rev Iberoam Fisioter Kinesol 2015:1-5.
12. Stewart A, Marfell-Jones M, Olds T, De Ridder H. International Standards for Anthropometric Assessment. 3rd ed. 2001.
13. Menon K, Razak S, Ismail KA, Krishna BV. Nutrient intake and nutritional status of newly diagnosed patients with cancer from the East Coast of Peninsular Malaysia. BMC Research Notes 2014;7:680-9. DOI: 10.1186/1756-0500-7-680
14. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Manuel Gómez J, et al. Bioelectrical impedance analysis—part II: utilization in clinical practice. Clinical Nutrition 2004;23:1430-53. DOI: 10.1016/j.clnu.2004.09.012
15. Rubio MA, Salas-Salvado J, Barbany M, Moreno B, Aranceta J, Bellido D, et al. Consenso SEEDO 2007 para la evaluación del sobrepeso y la obesidad y el establecimiento de intervención terapéutica. Revista Española De Obesidad 2007:1-52. DOI: 10.1016/S0025-7753(07)72531-9
16. Gómez Candela C, Roldán JO, García M, Marín M, Madero R, Pérez-Portabella C, et al. Utilidad de un método de cribado de malnutrición en pacientes con cáncer. Nutr Hosp 2010:1-6.
17. Russolillo G MI. Álbum Fotográfico de Porciones de Alimentos. Madrid: 2008.
18. Ortega RM, López-Sobaler AM, Andrés P, Requejo A, Aparicio AA, Molinero LM. DIAL software for assessing diets and food calculations. Department of Nutrition (UCM) & Alce Ingeniería, S.L. Madrid, Spain. Available on line: http://www.alceingenieria.net/nutricion/descarga.htm 2008:1-111.
19. Aranceta J, Serra-Majem L. Objetivos nutricionales para la población española. Consenso de la Sociedad Española de Nutrición Comunitaria. Rev Esp Nutr Com 2012:1-24.
20. Moreiras O, Carbajal A, Cabrera L, Cuadrado C. Ingestas recomendadas de energía y nutrientes para la población española. In: Ediciones Pirámide Grupo Anaya SE, editor. 17 ed., Madrid, Spain: Tablas de composición de alimentos; 2017, pp. 258-9.
21. Barbosa-Silva M, Barros AJ. Indications and limitations of the use of subjective global assessment in clinical practice: an update. Curr Opin Clin Nutr Metab Care 2006:1-7.
22. Schlüssel MM, Anjos dos LA, de Vasconcellos MTL, Kac G. Reference values of handgrip dynamometry of healthy adults: A population-based study. Clinical Nutrition 2008;27:601-7. DOI: 10.1016/j.clnu.2008.04.004
23. Francisco AV. Biblioteca de pruebas Hospital Universitario Central de Asturias. 2016.
24. Travier N, Fonseca-Nunes A, Javierre C, Guillamo E, Arribas L, Peiró I, et al. Effect of a diet and physical activity intervention on body weight and nutritional patterns in overweight and obese breast cancer survivors. Med Oncol 2013;31:931-41.
25. World Cancer Research Fund American Institute for Cancer Research. Continuous Update Project Expert Report. Alcoholic drinks and the risk of cancer 2018:1-85.
26. Islam T, Ito H, Sueta A, Hosono S, Hirose K, Watanabe M, et al. Alcohol and dietary folate intake and the risk of breast cancer. European Journal of Cancer Prevention 2013;22:358-66. DOI: 10.1097/CEJ.0b013e32835b6a60
27. Partearroyo T, Samaniego-Vaesken mL, Ruiz E, Olza J, Aranceta-Bartrina J, Gil A, et al. Dietary sources and intakes of folates and vitamin B12 in the Spanish population: Findings from the ANIBES study. PLoS ONE 2017;12:e0189230-19. DOI: 10.1371/journal.pone.0189230
28. Bering T, Mauricio SF, da Silva JB, Davisson MIT. Nutritional and metabolic status of breast cancer women. Nutr Hosp 2015:1-8.
29. López-Sobaler AM, Aparicio A, Aranceta-Bartrina J, Gil A, González-Gross M, Serra-Majem L, et al. Overweight and General and Abdominal Obesity in a Representative Sample of Spanish Adults: Findings from the ANIBES Study. BioMed Research International 2016;2016:1-11. DOI: 10.1155/2016/8341487
30. Ewertz M, Jensen M-B, Gunnarsdóttir KÁ, Højris I, Jakobsen EH, Nielsen D, et al. Effect of Obesity on Prognosis After Early-Stage Breast Cancer. Journal of Clinical Oncology 2011;29:25-31. DOI: 10.1200/JCO.2010.29.7614
31. Chen GC, Chen SJ, Zhang R, Hidayat K, Qin JB, Zhang YS, et al. Central obesity and risks of pre- and postmenopausal breast cancer: a dose-response meta-analysis of prospective studies. Obes Rev 2016;17(11):1167-77. DOI: 10.1111/obr.12443
32. Yaw YH, Shariff ZM, Kandiah M, Mun CY, Yusof RM, Othman Z, et al. Weight changes and lifestyle behaviors in women after breast cancer diagnosis: a cross-sectional study. BMC Public Health 2011;11:309. DOI: 10.1186/1471-2458-11-309
33. Gaudet MM, Carter BD, Patel AV, Teras LR, Jacobs EJ, Gapstur SM. Waist circumference, body mass index, and postmenopausal breast cancer incidence in the Cancer Prevention Study-II Nutrition Cohort. Cancer Causes & Control 2014;25:737-45. DOI: 10.1007/s10552-014-0376-4
34. Klassen O, Schmidt ME, Ulrich CM, Schneeweiss A, Potthoff K, Steindorf K, et al. Muscle strength in breast cancer patients receiving different treatment regimes. J Cachexia Sarcopenia Muscle 2016;8:305-16. DOI: 10.1002/jcsm.12165
35. Ni H, Liu H, Gao R. Serum Lipids and Breast Cancer Risk: A Meta-Analysis of Prospective Cohort Studies. PLoS ONE 2015;10:e0142669-15. DOI: 10.1371/journal.pone.0142669
36. He J, Gu Y, Zhang S. Consumption of vegetables and fruits and breast cancer survival: a systematic review and meta- analysis. Sci Rep 2017;7:1-10. DOI: 10.1038/s41598-017-00635-5
37. Ruiz E, Ávila J, Valero T, del Pozo S, Rodríguez P, Aranceta-Bartrina J, et al. Energy Intake, Profile, and Dietary Sources in the Spanish Population: Findings of the ANIBES Study. Nutrients 2015;7:4739-62. DOI: 10.3390/nu7064739
38. Jung S, Spiegelman D, Baglietto L, et al. Fruit and Vegetable Intake and Risk of Breast Cancer by Hormone Receptor Status. JNCI Journal of the National Cancer Institute 2013;105(3):219-236. DOI: 10.1093/jnci/djs635
39. Aune D, Chan DSM, Greenwood DC, et al. Dietary fiber and breast cancer risk: a systematic review and meta-analysis of prospective studies. Annals of Oncology 2012;23(6):1394-1402. DOI: 10.1093/annonc/mdr589
40. Isenring EA, Capra S, Bauer JD. Nutrition intervention is beneficial in oncology outpatients receiving radiotherapy to the gastrointestinal or head and neck area. British Journal of Cancer 2004;91:447-52. DOI: 10.1038/sj.bjc.6601962

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Epidemiología y dietética

Conducta alimentaria y su relación con el estrés, la ansiedad, la depresión y el insomnio en estudiantes universitarios

Eating behavior and its relationship with stress, anxiety, depression, and insomnia in university students

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Resumen

Introducción: existe evidencia creciente que relaciona la alimentación con la salud psicológica de la población adulta. Esta asociación no se ha explorado suficientemente entre los estudiantes universitarios.

Objetivos: los objetivos de este estudio fueron analizar la calidad de la dieta en una población universitaria y cuantificar su asociación con la prevalencia de ansiedad, depresión, estrés e insomnio.

Métodos: estudio descriptivo transversal sobre una muestra de 1055 estudiantes universitarios. Se utilizaron tres cuestionarios validados: el Índice de Alimentación Saludable (IAS), la escala breve de Depresión, Ansiedad y Estrés (DASS-21) y el Índice de Severidad del Insomnio.

Resultados: la puntuación media del IAS fue de 68,57 ± 12,17. La prevalencia de la alimentación no saludable fue del 82,3%, mayor en las mujeres (84,8% *vs.* 76,4%). La alimentación no saludable se relacionó de forma significativa con la prevalencia de ansiedad, depresión y estrés. El consumo excesivo de dulces y el bajo de lácteos se asociaron a una mayor prevalencia de alteraciones psicológicas y del sueño.

Conclusiones: los patrones alimentarios no saludables son comunes en la población universitaria y se relacionan con la presencia de ansiedad, estrés y depresión. Las intervenciones educativas dirigidas a disminuir el consumo de alimentos no saludables en estudiantes universitarios pueden conllevar una mejora de la salud psicológica y/o viceversa.

Palabras clave:

Nutrición, alimentación y dieta. Estudiantes. Depresión. Estrés psicológico. Ansiedad. Trastornos del inicio y del mantenimiento del sueño.

Abstract

Introduction: there is growing evidence linking food consumption with psychological health in adult people. This association has not been well explored among university students.

Objectives: the aims of this study were to analyze diet quality in a university population, and to assess its association with the prevalence of anxiety, stress, depression, and insomnia.

Methods: a cross-sectional study of a sample of 1,055 university students. Three validated questionnaires were used: the Healthy Eating Index (HEI), the Depression Anxiety Stress Scale (DASS 21), and the Insomnia Severity Index.

Results: the average HEI score was 68.57 ± 12.17. The prevalence of unhealthy eating was 82.3%, higher in women (84.8% *vs.* 76.4%). Unhealthy eating was significantly associated with prevalence of anxiety, depression, and stress. Excessive intake of sweets and low of dairy products were associated with a higher prevalence of psychological and sleep disturbances.

Conclusions: unhealthy eating patterns are common among the university population, and related to anxiety, stress, and depression. Educational interventions to reduce unhealthy food consumption in university students may also result in psychological health improvements and/or vice versa.

Key words:

Diet, food and nutrition. Students. Depression. Stress, psychological. Anxiety. Sleep initiation and maintenance disorders.

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INTRODUCCIÓN

Para muchos estudiantes, el paso de la educación secundaria a la universidad supone una transición cargada de exigencia. La competencia y la presión por los resultados académicos (1), los cambios en las cargas de trabajo y en las redes de apoyo, y en ocasiones estar lejos de la familia durante un periodo en el que pueden desencadenarse conductas de riesgo (2) pueden derivar en estados de estrés, ansiedad, depresión o insomnio (3,4).

En estudios anteriores sobre la población general, parece haberse detectado una asociación entre la forma de alimentarse y el estado del ánimo (5). De esta forma, y con independencia de la razón subyacente del trastorno del ánimo, la forma de alimentarse puede afectar a la forma en que se sienten las personas (6) y, probablemente, viceversa (7). La evidencia acerca de la relación entre la salud psicológica y la ingesta de ciertos nutrientes y grupos de alimentos es abundante. Así, se han detectado asociaciones inversas entre la ingesta de ácidos grasos polinsaturados (8), proteínas (9) y ciertos micronutrientes (10-12) con la sintomatología depresiva. Por el contrario, la ingesta de alimentos procesados y carbohidratos simples se ha asociado de forma directa (9-13). La ingesta baja en ácidos grasos ω-3 (14) y minerales como el manganeso, el cobre o el zinc (15) se ha relacionado con mayores niveles de ansiedad. La calidad del sueño se ha asociado de forma directa con la ingesta de algunos nutrientes como el selenio, la vitamina C o el calcio (16). Sin embargo, la investigación es escasa acerca de la relación existente entre la calidad de la dieta en general y la salud psicológica, especialmente en poblaciones específicas como la adolescente o la adulta joven.

En España, los problemas derivados de una mala alimentación están creciendo en la población infantil, adolescente y adulta joven. Se ha estimado en un 38,6% la prevalencia del sobrepeso/obesidad en la población menor de 17 años (17), y en un 26,8% entre la población universitaria (18). Del mismo modo, los problemas de salud mental son muy prevalentes en la población adolescente y adulta joven española. Dos estudios recientes (19,20) sitúan la prevalencia de los trastornos de tipo ansioso y depresivo en la adolescencia precoz por encima del 11%. En la época universitaria, Balanza y cols. (21) han reportado hasta un 55,6% y un 47,1% de casos probables de depresión y ansiedad, respectivamente. Por todo ello, resulta de interés la investigación acerca de la relación entre la alimentación y el estado de ánimo en diversas poblaciones de estudiantes. La mayoría de los estudiantes universitarios se encuentran al inicio de la edad adulta. En esta época es cuando se forman los estilos de vida y los comportamientos relacionados con la salud, que pueden tener un impacto mantenido a lo largo de sus vidas (9). Bajo este prisma, el objetivo de esta investigación fue evaluar la asociación entre la calidad de la dieta y varios indicadores relativos a la salud psicológica y el sueño de los universitarios de nuestro medio.

METODOLOGÍA

DISEÑO Y POBLACIÓN DE ESTUDIO

Se llevó a cabo un estudio descriptivo transversal. La población de referencia fue la de estudiantes de diferentes titulaciones del campus de la Universidad San Jorge en Zaragoza, España. La captación de los participantes se realizó en el aula durante el periodo lectivo del primer cuatrimestre del curso 2018-19. Todos los estudiantes fueron informados de los objetivos de la investigación al inicio de una de sus clases, y al finalizar la misma se les hizo entrega de los cuestionarios. Durante el periodo de recogida de datos, que se prolongó por 6 semanas, se invitó a participar en el estudio a un total de 1311 estudiantes. De estos, 1055 (744 mujeres y 311 varones) dieron su consentimiento para entrar en esta investigación y cumplimentaron con arreglo a lo solicitado el cuestionario propuesto.

COLECCIÓN DE DATOS

El cuestionario de recogida de datos se compuso de 4 secciones: datos sociodemográficos (incluyendo antropometría y hábitos), alimentación, salud psicológica y sueño.

Se recopiló información sobre la edad, sexo, área de estudio, residencia habitual, situación de pareja, altura, peso, situación económica percibida, tabaquismo, consumo de alcohol, práctica de actividad física y sedentarismo de los participantes. La actividad física desarrollada y el tiempo dedicado a estar sentado o tumbado (no se incluye el sueño) se evaluaron mediante la versión breve del *International Physical Activity Questionnaire* (IPAQ breve) en su versión en español. Este instrumento se ha validado en la población española (22) y se ha utilizado en repetidas ocasiones en una población joven y universitaria (23,24). El IPAQ breve permite registrar la intensidad, frecuencia y duración de la actividad física desarrollada en los últimos 7 días. A partir de esta información se calcularon los equivalentes metabólicos de tarea (MET) por semana multiplicando el gasto energético medio por minuto y semana por la intensidad de cada actividad física realizada (3,3 MET para caminar, 4,0 MET para las actividades de intensidad moderada y 8,0 MET para las vigorosas). Los resultados de cada categoría de actividad física (caminar + moderada + vigorosa) se sumaron para obtener la actividad física total en MET/semana (25).

La valoración de la alimentación de los participantes se realizó mediante el Índice de Alimentación Saludable (IAS) a partir de la metodología descrita por Norte y cols. (26), que incluyeron ligeras modificaciones en el cuestionario original de Kennedy y cols. (27) con el fin de adaptarlo a los alimentos más habitualmente ingeridos por la población española. El IAS consta de 10 variables puntuables de 0 a 10 puntos cada una. De este modo, la puntuación final del cuestionario oscila entre 0 y 100 puntos. La clasificación por categorías se realiza en base a los siguientes criterios: puntuación > 80, alimentación saludable; entre 50 y 80 puntos, necesita cambios; menor de 50 puntos, poco saludable.

Además, se comparó la frecuencia de la ingesta de cada grupo de alimentos de los participantes con las recomendaciones recogidas en la Guía de la Alimentación Saludable de la Sociedad Española de Nutrición Comunitaria (SENC) (28).

La sintomatología relativa a la ansiedad, el estrés y la depresión de los participantes se evaluó mediante el cuestionario DASS-21,

versión corta del DASS-42. El DASS-21 está conformado por las subescalas DASS-A (ansiedad), DASS-E (estrés) y DASS-D (depresión). El DASS-21 es un instrumento compuesto de 21 ítems, 7 para cada subescala, con evaluación de tipo Likert de 0 a 3 puntos (0 significa "no me es aplicable en absoluto" y 3 "me es aplicable mucho o la mayoría del tiempo"). La suma de las puntuaciones obtenidas en cada subescala se multiplica por 2 al objeto de hacer comparables los resultados del DASS-21 y el DASS-42. A partir de las puntuaciones obtenidas se clasifica a los participantes en cada una de las 3 subescalas de la siguiente manera:

- Ansiedad: normal (0-7 puntos), leve (8-9), moderada (10-14), severa (15-19) y extremadamente severa (> 19)
- Depresión: normal (0-9 puntos), leve (10-13), moderada (14-20), severa (21-27) y extremadamente severa (> 27).
- Estrés: normal (0-14 puntos), leve (15-18), moderado (19-25), severo (26-33) y extremadamente severo (> 33).

El cuestionario DASS-21 fue validado con anterioridad en la población universitaria española con unos valores de consistencia interna para las tres subescalas que oscilaron entre $\alpha = 0,73$ y $\alpha = 0,81$ (29).

La calidad del sueño y el insomnio de los participantes se evaluaron mediante el Índice de Severidad del Insomnio (ISI). Este cuestionario consta de 7 ítems que estudian la naturaleza, severidad e impacto del insomnio. Cada ítem se puntúa mediante una escala de tipo Likert de 0 a 4 puntos. La puntuación total se obtiene sumando las respuestas de los 7 ítems, pudiendo obtenerse un mínimo de 0 y un máximo de 28 puntos. A partir de esta puntuación puede establecerse la siguiente clasificación:

- De 0 a 7 puntos: ausencia de insomnio clínico
- De 8 a 14 puntos: insomnio subclínico
- De 15 a 21 puntos: insomnio clínico (moderado)
- De 22 a 28 puntos: insomnio clínico (grave).

La validación del ISI en la población española obtuvo un valor de consistencia interna de $\alpha = 0,91$ (30). Además, este cuestionario se ha utilizado en repetidas ocasiones en muestras de estudiantes universitarios (31-33).

ANÁLISIS DE LOS DATOS

Las características de la muestra se resumieron usando la media y la desviación estándar para las variables continuas, y el número y el porcentaje para las cualitativas.

El test de Kolmogorov-Smirnov se usó para comprobar la normalidad de las distribuciones de cada variable. El análisis bivariante se ejecutó mediante las pruebas Chi-cuadrado, t de Student y ANOVA, según correspondiera. El análisis de la correlación bivariada entre variables cuantitativas se efectuó mediante el test de Pearson. Además se realizó un análisis multivariante con objeto de determinar el impacto de la calidad de la alimentación y la adherencia a las recomendaciones de ingesta semanal de diferentes grupos de alimentos sobre el sueño y la salud psicológica de los participantes (presencia de ansiedad, estrés, depresión o insomnio). Para ello se construyeron diferentes modelos de regresión logística binaria (método *Intro*) ajustados por posibles factores de confusión como el género, la edad, el peso (IMC), la titulación, la actividad física desarrollada, la situación económica percibida, el tiempo dedicado a patrones sedentarios, el tabaquismo o la situación de pareja.

El análisis estadístico de los datos se realizó con el paquete estadístico SPSS para Windows (versión 21, Chicago, IL, EE.UU.), aceptando un nivel de significación de $p < 0,05$.

RESULTADOS

CARACTERÍSTICAS DE LA MUESTRA

En total, 1055 estudiantes (70,5% mujeres y 29,5% varones) participaron en el estudio. El rango de edad osciló entre los 18 y los 42 años, con una media de 21,74 ± 5,15 años. La mayoría de ellos cursaba una titulación sanitaria (58,3%), no fumaba (75,3%), refería un consumo ocasional de alcohol (67,7%), no mantenía una relación estable (53,2%) y vivía con su familia (66,4%) (Tabla I).

Tabla I. Características de los participantes (n = 1055)

		n (%)
Edad, media ± DE		21,74 ± 5,15
Género	Mujer	744 (70,5%)
	Varón	311 (29,5%)
Titulación	Sanitaria	615 (58,3%)
	No sanitaria	440 (41,7%)
Residencia	Vive solo/a	64 (6,1%)
	Vive con compañeros	291 (27,6%)
	Vive con padres/familiares	700 (66,4%)
Pareja estable	Sí	494 (46,8%)
	No	561 (53,2%)
Nivel económico percibido	Muy bajo	28 (2,7%)
	Bajo	94 (8,9%)
	Medio	789 (74,8%)
	Alto	144 (13,6%)
IMC, media ± DE		22,15 ± 3,48
Categorías IMC	Bajo peso	160 (15,1%)
	Normopeso	732 (69,4%)
	Sobrepeso/Obesidad	163 (15,4%)
Tabaquismo	Sí	261 (24,7%)
	No	794 (75,3%)
Cigarrillos/día en fumadores; media ± DE		8,42 ± 6,31
Consumo de alcohol	Nunca	27 (2,6%)
	Ocasionalmente	714 (67,7%)
	1 vez/semana	263 (24,9%)
	2 veces/semana	22 (2,1%)
	≥ 3 veces/semana	29 (2,7%)
Actividad física (MET/sem), media ± DE		2377,03 ± 2466,54
Sedentarismo (horas/día), media ± DE		6,76 ± 2,45

CALIDAD DE LA DIETA

La puntuación media en el IAS fue de 68,57 ± 12,17. El 82,3% de los participantes presentaron una alimentación poco saludable o necesitada de cambios. En el análisis por géneros, las mujeres mostraron una alimentación significativamente menos saludable que los varones (Tabla II).

Los criterios del cuestionario en los que se evidenció un menor nivel de adherencia fueron los relativos al consumo de carnes magras, pescados y huevos, y al de embutidos y fiambres. En sentido opuesto, la mayor adherencia se observó en el consumo de legumbres y lácteos (Tabla III).

La puntuación del cuestionario IAS fue significativamente superior en los no fumadores, en los alumnos sin pareja estable y en las personas que vivían acompañadas ya sea por compañeros o por familiares. Por categorías de IMC, los participantes con bajo peso y con exceso de peso mostraron puntuaciones medias más elevadas que las de aquellos con normopeso. La titulación cursada y el nivel económico percibido no se asociaron significativamente a la puntuación del IAS (Tabla IV).

SALUD PSICOLÓGICA Y SUEÑO

El 23,5%, 18,6% y 33,9% de los participantes mostraron, en mayor o menor medida, niveles de ansiedad, depresión y estrés, respectivamente. Además, hasta un 43,1% presentaban insomnio en alguna de sus categorías. Por géneros, las mujeres obtuvieron peores puntuaciones en las escalas de estrés, ansiedad e insomnio ($p < 0,05$) (Tabla II).

Tabla II. Resultados por géneros de los cuestionarios IAS, DASS-21 e ISI

Cuestionario		Total (n = 1055)	Varones (n = 311)	Mujeres (n = 744)	p
IAS	Alimentación saludable	186 (17,6%)	73 (23,4%)	113 (15,1%)	0,002
	Necesita cambios	794 (75,2%)	213 (68,4%)	581 (78,1%)	
	Poco saludable	75 (7,1%)	25 (8,0%)	50 (6,7%)	
	Media ± DE	68,57 ± 12,17	69,96 ± 12,02	67,98 ± 12,19	0,016
DASS-E	Sin estrés	697 (66,1%)	253 (81,3%)	444 (59,7%)	0,000
	Leve	121 (11,5%)	28 (9,0%)	93 (12,5%)	
	Moderado	174 (16,5%)	30 (9,6%)	144 (19,4%)	
	Severo	46 (4,4%)	0 (0%)	46 (6,2%)	
	Extremadamente severo	17 (1,6%)	0 (0%)	17 (2,3%)	
	Media ± DE	12,39 ± 8,08	9,80 ± 6,13	13,48 ± 8,54	0,000
DASS-A	Sin ansiedad	807 (76,5%)	266 (85,5%)	541 (72,7%)	0,000
	Leve	83 (7,9%)	16 (5,1%)	67 (9,0%)	
	Moderada	95 (9,0%)	29 (9,3%)	66 (8,9%)	
	Severa	9 (0,9%)	0 (0%)	9 (1,2%)	
	Extremadamente severa	61 (5,8%)	0 (0%)	61 (8,2%)	
	Media ± DE	4,84 ± 5,75	3,35 ± 3,33	5,46 ± 6,41	0,000
DASS-D	Sin depresión	859 (81,4%)	251 (80,7%)	608 (81,7%)	0,000
	Leve	80 (7,6%)	31 (10,0%)	49 (6,6%)	
	Moderada	48 (4,5%)	0 (0%)	48 (6,5%)	
	Severa	38 (3,6%)	14 (4,5%)	24 (3,2%)	
	Extremadamente severa	30 (2,8%)	15 (4,8%)	15 (2,0%)	
	Media ± DE	5,45 ± 7,12	5,44 ± 8,28	5,46 ± 6,58	NS*
ISI	Sin insomnio	600 (56,9%)	220 (70,7%)	380 (51,1%)	0,000
	Insomnio leve	333 (31,6%)	58 (18,6%)	275 (37,0%)	
	Insomnio moderado	114 (10,8%)	33 (10,6%)	81 (10,9%)	
	Insomnio grave	8 (0,8%)	0 (0%)	8 (1,1%)	
	Media ± DE	7,91 ± 4,88	6,22 ± 4,70	8,62 ± 4,78	0,000

**NS: no significativo.*

Tabla III. Grado de incumplimiento de las recomendaciones de la SENC (28)

Grupo de alimentos	Recomendación	Grado de incumplimiento
Cereales y derivados	Consumo diario	64,8%*
Verduras y hortalizas	Diario	67,5%*
Frutas	Diario	55,7%*
Leche y derivados	Diario	31,3%*
Carnes (incluye magras, pescados y huevos)	2-3 veces/semana	80,9%*
Legumbres	2-3 veces/semana	38,7%*
Embutidos y fiambres	Ocasional	77,7%†
Dulces	Ocasional	75,5%†
Refrescos con azúcar	Ocasional	48,6%†

**Por defecto. †Por exceso.*

ASOCIACIÓN ENTRE CALIDAD DE LA DIETA, SALUD PSICOLÓGICA E INSOMNIO

El análisis de la correlación bivariada mostró una asociación significativa e inversa entre las puntuaciones del IAS y las del DASS-A, DASS-E e ISI (Tabla V).

En el análisis de regresión logística binaria, ajustado por posibles factores de confusión, la alimentación no saludable se relacionó de forma significativa con la presencia de depresión, ansiedad y estrés. Por grupos alimentarios, la falta de adherencia a las recomendaciones de ingesta de verduras y hortalizas se asoció a la presencia de ansiedad, depresión e insomnio. Además, el consumo deficitario de productos lácteos y el excesivo de dulces se asociaron a un mayor riesgo de sufrir ansiedad, estrés, depresión e insomnio (Tabla VI).

DISCUSIÓN

Según nuestro conocimiento, el presente estudio es el primero que evalúa la relación entre calidad general de la dieta y múltiples

Tabla IV. Relación entre tipo de alimentación según el IAS y características de los participantes. Análisis bivariante

Puntuación IAS				Tipo de alimentación según el IAS			
		Media ± DE	p	Alimentación poco saludable	Necesita cambios	Alimentación saludable	p
Género	Varones (n = 311)	69,96 ± 12,02	0,016	25 (8,0%)	213 (68,4%)	73 (23,4%)	0,002
	Mujeres (n = 744)	67,98 ± 12,19		50 (6,7%)	581 (78,1%)	113 (15,1%)	
Categorías IMC	Bajo peso (n = 160)	69,41 ± 12,23	0,000	11 (6,9%)	133 (83,1%)	16 (10,0%)	0,000
	Normopeso (n = 732)	67,48 ± 11,55		49 (6,7%)	569 (77,7%)	114 (15,5%)	
	Sobrepeso/Obesidad (n = 163)	72,75 ± 13,91		15 (9,2%)	94 (57,6%)	54 (33,1%)	
Titulación	Sanitaria (n = 615)	68,38 ± 12,28	NS*	42 (6,8%)	469 (76,2%)	104 (16,9%)	NS
	No sanitaria (n = 440)	68,82 ± 12,02		32 (7,2%)	326 (74,1%)	82 (18,6%)	
Residencia	Vive solo/a (n = 64)	59,36 ± 11,11	0,000	14 (21,9%)	50 (78,1%)	0 (0%)	0,000
	Con compañeros (n = 291)	69,95 ± 12,54		23 (7,9%)	219 (75,3%)	49 (16,8%)	
	Con padres/familiares (n = 700)	68,83 ± 11,76		36 (5,2%)	523 (75,4%)	135 (19,5%)	
Situación de pareja	Pareja estable (n = 494)	67,28 ± 12,84	0,001	40 (8,1%)	356 (72,1%)	98 (19,8%)	NS
	Sin pareja (n = 561)	69,69 ± 11,44		34 (6,0%)	439 (78,2%)	88 (15,7%)	
Nivel económico percibido	Muy bajo (n = 28)	72,50 ± 2,54	NS	0 (0%)	28 (100%)	0 (0%)	0,000
	Bajo (n = 94)	68,96 ± 14,40		7 (7,4%)	58 (61,7%)	29 (30,9%)	
	Medio (n = 789)	68,09 ± 12,54		66 (8,4%)	577 (73,1%)	146 (18,5%)	
	Alto (n = 144)	70,13 ± 9,07		1 (0,7%)	131 (90,9%)	12 (8,33%)	
Tabaquismo	Fumadores (n = 261)	66,82 ± 12,20	0,008	7 (2,7%)	216 (82,7%)	38 (14,6%)	0,001
	No fumadores (n = 794)	69,14 ± 12,11		67 (8,4%)	579 (72,9%)	148 (18,6%)	
Consumo de alcohol	Nunca (n = 27)	66,83 ± 7,86	0,000	0 (0%)	27 (100%)	0 (0%)	0,000
	Ocasionalmente (n = 714)	68,84 ± 12,57		59 (8,2%)	530 (74,2%)	125 (17,5%)	
	1 vez/semana (n = 263)	67,21 ± 10,27		8 (3,0%)	217 (82,5%)	38 (14,4%)	
	2 veces/semana (n = 22)	80,36 ± 2,21		0 (0%)	8 (36,4%)	14 (63,6%)	
	≥3 veces/semana (n = 29)	66,65 ± 19,23		7 (24,1%)	14 (48,2%)	8 (27,6%)	

**NS: no significativo.*

Tabla V. Correlaciones bivariadas entre las puntuaciones de los cuestionarios IAS, DASS-21, Rosenberg e ISI

		IAS	DASS-E	DASS-A	DASS-D	ISI
IAS	Coeficiente de correlación	1,00	-0,07*	-0,10†	-0,03	-0,23†
DASS-E	Coeficiente de correlación	-0,07*	1,00	0,50†	0,50†	0,51†
DASS-A	Coeficiente de correlación	-0,10†	0,50†	1,00	0,57†	0,33†
DASS-D	Coeficiente de correlación	-0,03	0,50†	0,57†	1,00	0,39†
ISI	Coeficiente de correlación	-0,23†	0,51†	0,33†	0,39†	1,00

**p < 0,05 bilateral. †p < 0,01 bilateral.*

Tabla VI. OR (IC 95%) ajustadas* de la asociación entre conducta alimentaria y salud psicológica de los participantes

	Presencia de estrés (DASS-E > 14)	Presencia de depresión (DASS-D > 9)	Presencia de ansiedad (DASS-A > 7)	Presencia de insomnio (ISI > 7)
Alimentación saludable (IAS > 80)	Referencia	Referencia	Referencia	Referencia
Necesita cambios alimenticios (IAS 50-80)	1,35 (0,74-2,43)	*2,95 (1,28-6,77)*	*2,42 (1,14-5,10)*	1,69 (0,95-2,99)
Alimentación poco saludable (IAS < 50)	*1,87 (1,22-2,84)*	*3,73 (1,53-9,06)*	*3,51 (1,19-10,44)*	1,97 (0,80-4,86)
Componentes IAS (falta de adherencia a las recomendaciones)				
Cereales y derivados	1,05 (0,69-1,59)	1,67 (0,96-2,91)	0,96 (0,56-1,64)	1,03 (0,71-1,49)
Verduras y hortalizas	1,16 (0,73-1,82)	*2,01 (1,08-3,71)*	*3,09 (1,83-5,19)*	*1,78 (1,22-2,62)*
Frutas	1,31 (0,88-1,95)	1,68 (0,92-3,07)	1,39 (0,86-1,62)	1,10 (0,76-1,59)
Leche y derivados	*1,56 (1,03-2,35)*	*2,01 (1,19-3,42)*	*1,59 (1,00-2,52)*	*2,13 (1,49-3,04)*
Carnes (incluye magras, pescados y huevos)	0,94 (0,59-1,49)	1,06 (0,56-2,01)	1,40 (0,87-2,27)	0,92 (0,61-1,39)
Legumbres	0,90 (0,59-1,36)	1,10 (0,65-1,87)	*2,40 (1,54-3,74)*	1,14 (0,79-1,63)
Embutidos y fiambres	*1,84 (1,19-2,85)*	1,64 (0,77-3,47)	1,01 (0,58-1,76)	1,12 (0,72-1,74)
Dulces	*2,27 (1,50-3,44)*	*2,73 (1,62-4,59)*	*3,33 (2,07-5,35)*	*1,60 (1,09-2,36)*
Refrescos con azúcar	1,26 (0,86-1,83)	0,97 (0,58-1,62)	1,21 (0,78-1,87)	1,16 (0,84-1,60)

**Ajustado por género, edad, IMC, titulación, actividad física, situación económica percibida, sedentarismo, tabaquismo y situación de pareja. Las celdas en cursiva indican significación estadística, p < 0,05.*

dimensiones de la salud psicológica y el sueño en una población universitaria. Nuestros hallazgos evidencian una elevada prevalencia de estrés (33,9%), ansiedad (23,5%), depresión (18,6%) e insomnio (43,1%) entre los universitarios de nuestro medio, mayor en las mujeres que en los varones (a excepción de la sintomatología depresiva). Aizpurua y cols. (34), utilizando también el cuestionario DASS-21, hallaron en universitarios españoles prevalencias aún mayores de depresión, ansiedad y estrés, con valores del 38,2%, 45,4% y 42,5%, respectivamente. A nivel mundial, una revisión sistemática de 24 estudios estimó una prevalencia media de depresión entre los universitarios del 30,5%, con un rango que oscilaba entre el 10,4% y el 80,5% (35).

Estudios previos sobre universitarios españoles, empleando el IAS como instrumento de medida de la calidad de la dieta, evidenciaron un elevado número de universitarios con patrones alimentarios no saludables (18,36,37). En este estudio, hasta el 82,3% de los participantes presentaban una alimentación no saludable o necesitada de cambios. Por grupos de alimentos, el consumo más alejado de las recomendaciones fue el de carnes magras, pescados y huevos (por defecto), y el de embutidos y fiambres (por exceso). La calidad general de la dieta se asoció de forma significativa e inversa a la presencia de algún nivel de ansiedad, estrés o depresión, no así con el insomnio. Por grupos de alimentos, encontramos que la prevalencia de las alteraciones del bienestar psicológico y el sueño se asocia esencialmente con la falta de adherencia a las recomendaciones de ingesta de verduras y hortalizas, lácteos y dulces.

La discusión de los resultados relativos a la calidad general de la dieta es compleja ya que únicamente un estudio previo ha analizado la relación entre esta dimensión y la prevalencia de síntomas depresivos en una población universitaria, concretamente femenina. En ese estudio, Quehl y cols. (38) detectaron una relación lineal inversa y significativa entre la puntuación del IAS (versión canadiense) y la puntuación de la *Center for Epidemiologic Studies Depression Scale*. Existe mayor evidencia en relación al consumo de diferentes grupos de alimentos y su relación con la salud psicológica. Mikolajczyk y cols. (9) observaron, solo en universitarias, una relación significativa entre el estrés percibido, por un lado, y el consumo

elevado de dulces y comida rápida, y bajo de frutas y verduras, por el otro. Otros estudios (7,40) hacen extensiva la asociación a los estudiantes varones. Lazarevich y cols. (13) y Liu y cols. (39) detectaron mayores niveles de depresión en los universitarios con consumo más elevado de comida rápida y dulces. A diferencia de los resultados obtenidos en nuestro estudio, ninguno de estos estudios reporta relaciones significativas entre el estrés, la ansiedad o la depresión y el consumo de lácteos.

Este estudio presenta varias limitaciones. No analiza el tamaño de las raciones ni cuantifica la ingesta total de calorías, proteínas, grasas y carbohidratos. Además, su naturaleza transversal permite establecer asociaciones pero no relaciones de causalidad. En este sentido, futuras investigaciones deberán aclarar la relación temporal entre la alimentación y las alteraciones de la salud mental. Pese a estas limitaciones, nuestros hallazgos sugieren una alta prevalencia de universitarios con alimentación inadecuada, que además se relaciona con la salud psicológica. Estos datos manifiestan la necesidad de aplicar estrategias de prevención y promoción de la salud en el ámbito universitario. En este sentido, cualquier intervención dirigida a minimizar los niveles de ansiedad, depresión o estrés en esta población debe incluir contenidos dirigidos a mantener una alimentación saludable.

BIBLIOGRAFÍA

1. El Ansari W, Stock C. Is the health and wellbeing of university students associated with their academic performance? Cross sectional findings from the United Kingdom. Int J Environ Res Public Health 2010;7(2):509-27.
2. Piko B. Perceived social support from parents and peers: which is the stronger predictor of adolescent substance use? Subst Use Misuse 2000;35(4):617-30.
3. Schlarb AA, Claßen M, Grünwald J, Vögele C. Sleep disturbances and mental strain in university students: results from an online survey in Luxembourg and Germany. Int J Ment Health Syst 2017;11:24.
4. Shamsuddin K, Fadzil F, Ismail WS, Shah SA, Omar K, Muhammad NA, et al. Correlates of depression, anxiety and stress among Malaysian university students. Asian J Psychiatr 2013;6(4):318-23.
5. Meyer BJ, Kolanu N, Griffiths DA, Grounds B, Howe PR, Kreis IA. Food groups and fatty acids associated with self-reported depression: an analysis from the Australian National Nutrition and Health Surveys. Nutrition 2013;29(7-8):1042-7.
6. Low Dog T. The role of nutrition in mental health. Altern Ther Health Med 2010;16(2):42-6.
7. El Ansari W, Adetunji H, Oskrochi R. Food and mental health: relationship between food and perceived stress and depressive symptoms among university students in the United Kingdom. Cent Eur J Public Health 2014;22(2):90-7.
8. Akbaraly TN, Sabia S, Shipley MJ, Batty GD, Kivimaki M. Adherence to healthy dietary guidelines and future depressive symptoms: evidence for sex differentials in the Whitehall II study. Am J Clin Nutr 2013;97(2):419-27.
9. Mikolajczyk RT, El Ansari W, Maxwell AE. Food consumption frequency and perceived stress and depressive symptoms among students in three European countries. Nutr J 2009;8:31.
10. Murakami K, Miyake Y, Sasaki S, Tanaka K, Arakawa M. Dietary folate, riboflavin, vitamin B-6, and vitamin B-12 and depressive symptoms in early adolescence: the Ryukyus Child Health Study. Psychosom Med 2010;72(8):763-8.
11. Park JY, You JS, Chang KJ. Dietary taurine intake, nutrients intake, dietary habits and life stress by depression in Korean female college students: a case-control study. J Biomed Sci 2010;17(Suppl 1):S40.
12. Yary T, Aazami S. Dietary intake of zinc was inversely associated with depression. Biol Trace Elem Res 2012;145(3):286-90.
13. Lazarevich I, Irigoyen Camacho ME, Velázquez-Alva MC, Flores NL, Nájera Medina O, Zepeda Zepeda MA. Depression and food consumption in Mexican college students. Nutr Hosp 2018;35(3):620-6.
14. Larrieu T, Layé S. Food for mood: Relevance of nutritional Omega-3 fatty acids for depression and anxiety. Front Physiol 2018;9:1047.
15. Nakamura M, Miura A, Nagahata T, Shibita Y, Okada E, Ojima T. Low zinc, copper and manganese intake is associates with depression and anxiety symptoms in the Japanese working population: Findings from the Eating Habit and Well-Being Study. Nutrients 2019;11(4):E847.
16. Grandner MA, Jackson N, Gerstner JR, Knutson KL. Sleep symptoms associated with intake of specificdietary nutrients. J Sleep Res 2014;23(1):22-34.
17. Sánchez-Cruz JJ, Jiménez-Moleón JJ, Fernández-Quesada F, Sánchez MJ. Prevalencia de obesidad infantil y juvenil en España en 2012. Rev Esp Cardiol 2013;66(5):371-6.
18. Navarro-Prado S, González-Jiménez E, Perona JS, Montero-Alonso MA, López-Bueno M, Schmidt-RioValle J. Need of improvement of diet and life habits among university student regardless of religion professed. Appetite 2017;114:6-14.
19. Canals J, Voltas N, Hernández-Martínez C, Cosi S, Arija V. Prevalence of DSM-5 anxiety disorders, comorbidity, and persistence of symptoms in Spanish early adolescents. Eur Child Adolesc Psychiatry 2019;28(1):131-43.
20. Canals-Sans J, Hernández-Martínez C, Sáez-Carles M, Arija-Val V. Prevalence of DSM-5 depressive disorders and comorbidity in Spanish early adolescents: Has there been an increase in the last 20 years? Psychiatry Res 2018;268:328-34.
21. Balanza Galindo S, Morales Moreno I, Guerrero Muñoz J, Conesa Conesa A. Fiabilidad y validez de un cuestionario para medir en estudiantes universitarios la asociación de la ansiedad y depresión con factores académicos y psicosociofamiliares durante el curso 2004-2005. Rev Esp Salud Publica 2008;82(2):189-200.
22. Román Viñas B, Ribas Barba L, Ngo J, Serra Majem L. Validación en población catalana del cuestionario internacional de actividad física. Gac Sanit 2013;27(3):254-7.
23. Varela-Mato V, Cancela JM, Ayan C, Martín V, Molina A. Lifestyle and health among Spanish university students: differences by gender and academic discipline. Int J Environ Res Public Health 2012;9(8):2728-41.
24. Dąbrowska-Galas M, Plinta R, Dąbrowska J, Skrzypulec-Plinta V. Physical activity in students of the Medical University of Silesia in Poland. Phys Ther 2013;93(3):384-92.
25. The IPAQ Group Guidelines for data processing and analysis of the International Physical Activity Questionnaire 2015. Available from: http://www.ipaq.ki.se
26. Norte Navarro AI, Ortiz Moncada R. Calidad de la dieta española según el índice de alimentación saludable. Nutr Hosp 2011;26(2):330-6.
27. Kennedy ET, Ohls J, Carlson S, Fleming K. The Healthy Eating Index: design and applications. J Am Diet Assoc 1995;95(10):1103-8.
28. Grupo Colaborativo de la Sociedad Española de Nutrición Comunitaria (SENC). Guías alimentarias para la población española (SENC, diciembre 2016); la nueva pirámide de la alimentación saludable. Nutr Hosp 2016;33(Supl. 8):1-48.
29. Fonseca Pedrero E, Paino Piñeiro M, Lemos Giráldez S, Muñiz Fernández J. Propiedades psicométricas de la Depresión Anxiety and Stress Scales-21 (DASS-21) en universitarios españoles. Ansiedad estrés 2010;16(2-3):215-26.
30. Sierra JC, Guillén-Serrano V, Santos-Iglesias P. Insomnia Severity Index: algunos indicadores acerca de su fiabilidad y validez en una muestra de personas mayores. Rev Neurol 2008;47(11):566-70.
31. Gellis LA, Arigo D, Elliott JC. Cognitive refocusing treatment for insomnia: a randomized controlled trial in university students. Behav Ther 2013;44(1):100-10.
32. Mairs L, Mullan B. Self-Monitoring vs. Implementation Intentions: a Comparison of Behaviour Change Techniques to Improve Sleep Hygiene and Sleep Outcomes in Students. Int J Behav Med 2015;22(5):635-44.
33. Gellis LA, Park A, Stotsky MT, Taylor DJ. Associations between sleep hygiene and insomnia severity in college students: cross-sectional and prospective analyses. Behav Ther 2014;45(6):806-16.
34. Aizpurua E, Caravaca-Sánchez F, Stephenson A. Victimization status of female and male college students in Spain: Prevalence and relation to mental distress. J Interpers Violence 2018;886260518802848.
35. Ibrahim AK, Kelly SJ, Adams CE, Glazebrook C. A systematic review of studies of depression prevalence in university students. J Psychiatr Res 2013;47(3):391-400.
36. Cervera Burriel F, Serrano Urrea R, Vico García C, Milla Tobarra M, García Meseguer MJ. Hábitos alimentarios y evaluación nutricional en una población Universitaria. Nutr Hosp 2013;28(2):438-46.
37. García-Meseguer MJ, Cervera Burriel F, Vico García C, Serrano-Urrea R. Adherence to Mediterranean diet in a Spanish university population. Appetite 2014;78:156-64.
38. Quehl R, Haines J, Lewis SP, Buchholz AC. Food and mood: Diet quality is inversely associated with depressive symptoms in female university students. Can J Diet Pract Res 2017;78(3):124-8.
39. Liu C, Xie B, Chou CP, Koprowski C, Zhou D, Palmer P, et al. Perceived stress, depression and food consumption frequency in the college students of China seven cities. Physiol Behav 2007;92(4):748-54.
40. Papier K, Ahmed F, Lee P, Wiseman J. Stress and dietary behaviour among first-year university students in Australia: sex differences. Nutrition 2015;31(2):324-30.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Epidemiología y dietética

Consumo de bebidas azucaradas y con azúcar añadida y su asociación con indicadores antropométricos en jóvenes de Medellín (Colombia)

Consumption of sugary drinks and sugar added to beverages and their relationship with anthropometric indicators in young people from Medellín (Colombia)

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Resumen

Introducción: a nivel mundial se reporta una alta prevalencia de sobrepeso y obesidad en los niños y jóvenes; la etiología es multicausal e influyen factores ambientales, culturales y de hábitos alimentarios, como es el consumo de bebidas azucaradas y azúcar añadido, que promueven el exceso de peso y el riesgo de enfermedades crónicas.

Objetivo: identificar la relación entre la cantidad ingerida de bebidas azucaradas (BA) o con azúcar añadido (AA) y el estado nutricional de los jóvenes.

Métodos: estudio transversal realizado en 596 individuos de entre 10 y 18 años de edad. La evaluación de la ingesta dietética se realizó por medio del Recordatorio de 24 horas (R24H); para cada uno de los individuos se consideró el mejor predictor lineal insesgado (MPLI) de energía y el %AMDR (*acceptable macronutrient distribution range*) de los carbohidratos (CHO) totales y los CHO simples; el estado nutricional se clasificó según el puntaje Z del índice de masa corporal (IMCz) y el porcentaje de grasa corporal (%GC). Se determinó la asociación con la correlación de Spearman, la U de Mann-Whitney, la prueba de Kruskal-Wallis y un modelo de regresión cuantílica.

Resultados: los jóvenes de estrato socioeconómico medio-bajo presentaron un mayor consumo de AA ($p \leq 0{,}0001$); los jóvenes con estado nutricional adecuado presentaron un mayor consumo de AA ($p = 0{,}011$) y de energía ($p \leq 0{,}0001$), y aquellos con estado nutricional excesivo ingerían una mayor cantidad de BA ($p = 0{,}025$) con un mayor %AMDR de CHO simples ($p = 0{,}045$).

Conclusiones: el desarrollo de sobrepeso no estaba relacionado con la ingesta excesiva de energía sino con el consumo de bebidas azucaradas y el aporte de carbohidratos simples a la energía total.

Palabras clave:

Consumo de bebidas azucaradas. Azúcar. Obesidad. Adolescentes. Estado nutricional.

Abstract

Introduction: worldwide, there is a high prevalence of overweight and obesity in children and young people; the etiology is multicausal and influences include environmental, cultural and eating habit factors such as the consumption of sugary drinks and added sugar, which promote excess weight and risk of chronic diseases.

Objective: to identify the relationship between the amount of ingested sugary drinks (BA) or added sugar (AA) and the nutritional status of young people.

Methods: cross-sectional study carried out in 596 individuals aged between 10 and 18 years; the evaluation of dietary intake was made using a Reminder 24 hours (R24H); for each subject the Best Linear Unbiased Predictor (BLUP) of energy, and %AMDR (Acceptable Macronutrient Distribution Range) for total carbohydrates (CHOs) and simple CHOs were considered; nutritional status was classified according to the Body Mass Index (BMI) Z-score and percentage of body fat (%BF). Association was determined using Spearman's correlation, Mann-Whitney U-test, Kruskal-Wallis test, and a quantile regression model.

Results: young people with medium-low socioeconomic status had higher AA consumption ($p \leq 0.0001$); young people with an adequate nutritional status had higher AA ($p = 0.011$) and energy consumption ($p \leq 0.0001$), and those with excess nutritional status ingested a greater amount of BA ($p = 0.025$) and had a greater %AMDR for CHOs ($p = 0.045$).

Conclusions: the development of overweight was not related to excessive energy intake but to consumption of sugary drinks and the contribution of simple carbohydrates to total energy.

Key words:

Sugary beverage consumption. Obesity. Adolescents. Nutritional status.

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INTRODUCCIÓN

Según la Organización Mundial de la Salud (OMS), en el mundo el exceso de peso se ha multiplicado. Datos de 2014 mostraron que más de 1900 millones de personas mayores de 18 años tenían sobrepeso; y de estos, 600 millones eran obesos. De continuar con esta tendencia para 2020, la cifra pasará a 2300 millones de adultos con sobrepeso y 700 millones con obesidad (1). Los adolescentes no son la excepción a este panorama: según el reporte de la OMS en 2016, cerca de 340 millones de niños y jóvenes (de 5 a 19 años) tenían exceso de peso, de los cuales 124 millones eran obesos (1).

La obesidad es un problema multicausal que se ha asociado a excesos o carencias nutricionales durante los primeros mil días de vida, a la genética, a los hábitos alimentarios, a los condicionantes culturales y sociales, a la actividad física y últimamente al consumo de bebidas azucaradas (BA) y de azúcar añadido (AA). En general, se considera que estos factores favorecen los procesos fisiológicos inherentes al almacenamiento de energía, lo cual no solo se evidencia en el aumento del índice de masa corporal (IMC) sino también en la grasa corporal (GC) (2,3). Sin embargo, estos indicadores evaluados de forma independiente pueden dar un diagnóstico errado al encontrar obesidad sin exceso de peso y exceso de peso sin exceso de grasa corporal, razón por la cual diversos autores recomiendan utilizarlos de forma conjunta (4,5).

Cada día es más común el consumo de BA y AA como se evidencia en el estudio "Los cambios en la ingesta de bebidas entre 1977 y 2001" llevado a cabo en Estados Unidos, donde el consumo de refrescos azucarados pasó del 2,8% al 7,0% por día, y el de gaseosas del 4,1% al 9,8%, siendo la variación superior en la población adulta (6). En Colombia, la Encuesta Nacional de la Situación Nutricional de 2005 (ENSIN 2005) encontró que el 58% de los jóvenes de 9 a 13 años consumían de promedio 20 g de azúcar añadido y el 22% consumían de promedio 330 mL de gaseosa al día; los jóvenes de 14 a 18 años tenían una ingesta similar de AA. Sin embargo, el porcentaje de jóvenes que ingerían BA fue del 26% y la cantidad aumentó a 400 mL. La ENSIN 2010 reportó una frecuencia diaria de consumo de bebidas azucaradas del 22,1% en la población de 5 a 64 años (7,8). El perfil de seguridad alimentaria de Medellín de 2015 encontró que el 32,4% de las personas habían consumido gaseosas el día anterior a la encuesta con un promedio de 224 mL/día (9); el 42% de los niños de 9 a 13 años y el 45% de los jóvenes de 14 a 18 años, con un promedio de 203 mL/día y 232 mL/día, respectivamente. Se ha demostrado una asociación entre el consumo de bebidas azucaradas y de azúcar añadido y el aumento del peso corporal; las razones que se exponen son múltiples, como el aumento de las calorías consumidas, la estimulación del apetito, los efectos metabólicos del jarabe de maíz alto en fructosa (endulzante base de las bebidas azucaradas), el desplazamiento de otras bebidas de mayor calidad nutricional y la baja capacidad de saciedad del azúcar en forma líquida (10-12).

Ni en Colombia ni en Medellín se encontraron publicaciones que demuestren la asociación entre ingesta de BA y de AA en las bebidas, y el IMC y la GC de niños y jóvenes, de forma que permitan plantear soluciones contextualizadas que contribuyan a disminuir el sobrepeso y la obesidad. Por esta razón, el objetivo de este estudio fue identificar la relación que existe entre la cantidad ingerida de BA y de AA en las bebidas con el estado nutricional de niños y jóvenes de 10 a 18 años de la ciudad de Medellín.

MÉTODOS

Se realizó un estudio analítico transversal de comparación de grupos para explorar la asociación entre el consumo de BA y AA con el estado nutricional. La selección de la muestra se hizo a partir de un estudio marco realizado como se detalla en la figura 1 (13,14).

EVALUACIÓN DE INGESTA DIETÉTICA

El estudio marco se realizó con el Recordatorio 24 horas (R24H), que se aplicó al 100% de los participantes distribuidos durante los 7 días de la semana; un segundo R24H se administró al 30% de los jóvenes, seleccionados de manera aleatoria, en días no consecutivos, garantizando así la independencia entre los datos. Esta información fue recolectada por estudiantes de nutrición previamente formados en la técnica.

Para la evaluación de consumo se visitó el hogar y se entrevistó al joven en presencia de la persona responsable de la preparación de los alimentos; para precisar la cantidad ingerida se emplearon modelos de alimentos, figuras geométricas y un álbum de fotografías en tamaño real (15). La conversión de alimentos en sus respectivos nutrientes se hizo con el programa de Evaluación de Ingesta Dietética Evindi v.5.0 de la Escuela de Nutrición y Dietética de la Universidad de Antioquia, que proporciona los gramos de alimentos ingeridos, los datos brutos de energía y los rangos de distribución aceptables de macronutrientes (%AMDR) correspondientes a los carbohidratos (CHO) totales y simples (16).

Para seleccionar las variables de interés en este estudio se siguió el siguiente procedimiento:

Consumo de bebidas azucaradas y azúcar añadido

A partir de los alimentos consumidos en el primer R24H se seleccionaron los productos de interés, con los cuales se conformaron dos grupos:

- Bebidas azucaradas, mL (BA): en este grupo se incluyeron las gaseosas azucaradas, la malta, los refrescos de fruta y los tés.
- Azúcar añadido, g (AA): grupo conformado por el azúcar blanco, el azúcar moreno, la miel, la panela y el jarabe de arce que se añade antes del consumo a las bebidas.

Ingesta de nutrientes

Para cada uno de los individuos se consideró el valor del "mejor predictor lineal insesgado" (MPLI) de energía, el %AMDR de

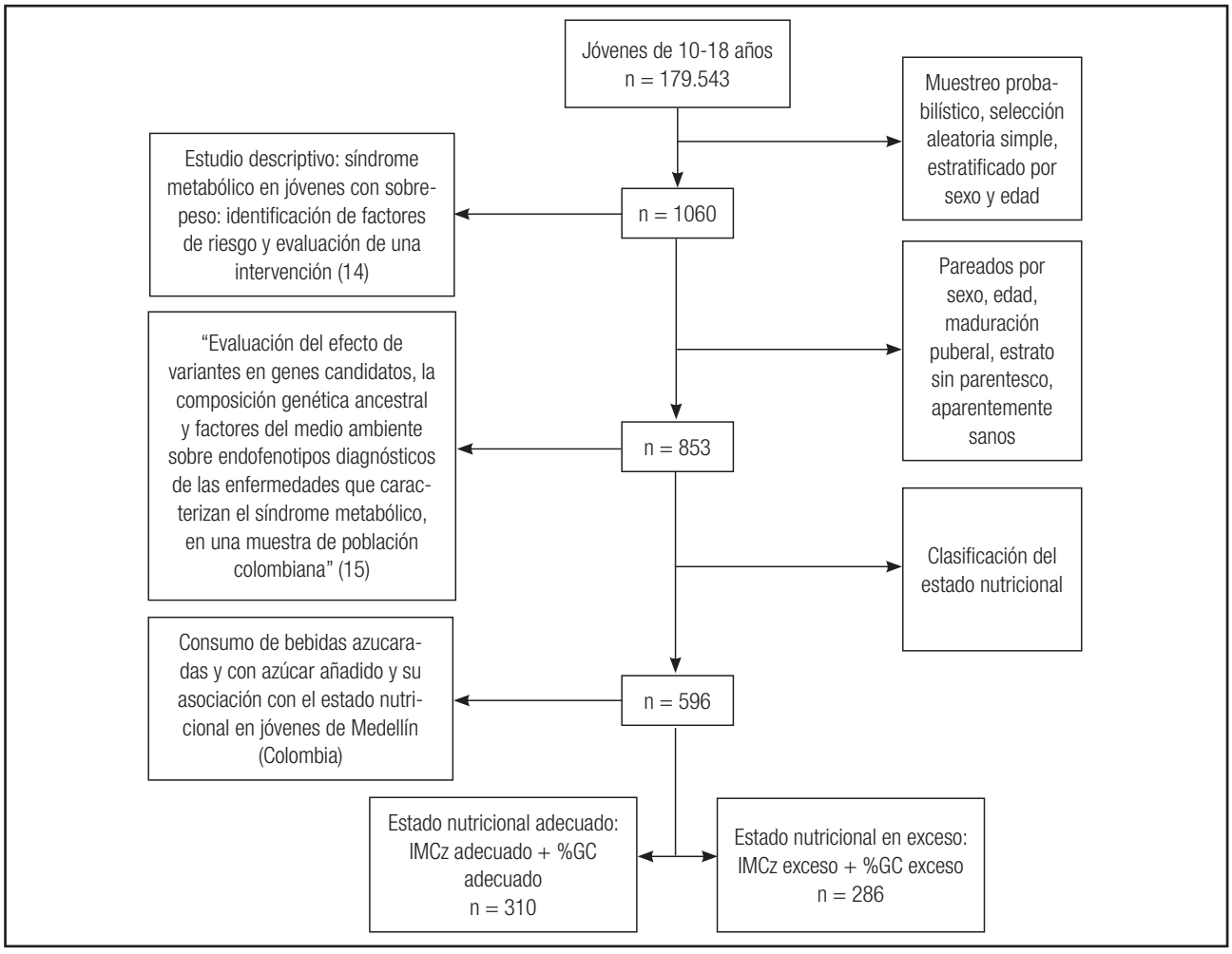

Figura 1.
Diagrama de flujo de la selección de la muestra del estudio.

los CHO totales y el %AMDR de los CHO simples, los cuales se obtuvieron de la base de datos del estudio marco, procedimiento que se realizó con el programa Personal Computer Software for Intake Distribution Estimation (PC-SIDE), versión 1.0 de junio de 2004 (17), desarrollado por el Departamento de Estadística de la Universidad del Estado de Iowa, Ames, IA, EE. UU., que estima el consumo habitual de nutrientes de cada individuo y su respectiva distribución en la población (17). El MPLI es un estimador que tiene buenas propiedades dado que combina la información de la ingesta de cada individuo con la del total de la muestra; de este modo se corrigen algunos errores de medición de la ingesta habitual y se minimiza el error de predicción.

EVALUACIÓN ANTROPOMÉTRICA

– *Puntaje Z del índice de masa corporal (IMCz):* para la toma de los datos antropométricos se usaron equipos y técnicas validados internacionalmente. Las personas encargadas de la recolección de la información fueron estandarizadas previamente; cada medida fue tomada y registrada dos veces, y se utilizó el promedio como dato definitivo (18-20); posteriormente, los datos de peso, talla y edad de cada participante se ingresaron al software Anthro Plus de la Organización Mundial de la Salud (OMS) (21). Los criterios de clasificación fueron los siguientes:
  - Exceso: ≥ +2 DE
  - Adecuado: < +2 DE a ≥ -1 DE
– *Porcentaje de grasa corporal (%GC):* se realizó con la sumatoria del pliegue de grasa subescapular y tricipital, y se aplicó la ecuación de Lohman (22), la cual tiene en cuenta el sexo, la raza y el estadio de maduración puberal para hombres y mujeres (23,24). Es de aclarar que la metodología de Tanner (23,24) plantea la clasificación según el desarrollo de los caracteres sexuales secundarios: en los niños, los genitales externos y la aparición de vello púbico; en las niñas, la menarquia, el desarrollo mamario y la aparición de vello púbico – prepúberes (estadios 1 y 2), púberes (estadio 3)

y pospúberes (estadios 4 y 5) (23,24). Una vez aplicada la ecuación de Lohman (22) se tuvieron en cuenta los siguientes criterios:

- Exceso: % de grasa > 25% en niños y > 32% en niñas.
- Adecuado: % grasa del 12-25% en niños y del 15-32% en niñas.

A partir de los datos anteriores se dividieron los jóvenes en dos grupos:

– *Estado nutricional adecuado:* participantes que tuvieron una clasificación adecuada tanto en IMCz como en %GC.
– *Estado nutricional en exceso:* individuos que tuvieron una clasificación en exceso tanto en IMCz como en %GC.

ACTIVIDAD FÍSICA

Se usó el método 3-Day Phisycal Activity Recall (3DPAR), que incluye las horas de sueño y la actividad física de tres días antes de su aplicación (dos de semana y uno de fin de semana). Los valores de múltiplos de la tasa metabólica basal (MET) se tomaron del compendio de actividad física establecido por el Colegio Americano de Medicina Deportiva (25). Con base en el promedio de MET minuto/día se clasificó la actividad física así: "Sedentario" cuando el valor estaba entre 1,0 y < 1,4; "Poco activo" cuando estaba entre 1,4 y < 1,6; "Activo" para los valores entre 1,6 y < 1,9, y "Muy activo" cuando estaba entre 1,9 y < 2,5.

A partir de los datos anteriores se reclasificó la variable en dos grupos:

– Poco activo: cuando el valor fue < 1,6 MET minuto/día.
– Activo: para valores ≥ 1,6 MET minuto/día.

ESTRATO SOCIOECONÓMICO

En el proyecto marco los participantes respondieron a un cuestionario con información general que incluía: estrato socioeconómico según el Departamento Administrativo Nacional de Estadística (DANE) (26), que establece seis categorías de acuerdo con la ubicación de la vivienda, siendo el estrato 1 el más bajo y el 6 el más alto. A efectos del análisis, los datos obtenidos se clasificaron en dos categorías:

– Medio-bajo: los estratos 1, 2, 3 y 4.
– Alto: los estratos 5 y 6.

ESCOLARIDAD DE LOS PADRES

A partir del cuestionario se clasificó el nivel de escolaridad de los padres en siete categorías: ninguno, primaria, secundaria, técnico, tecnológico, pregrado y posgrado. Estos datos se reclasificaron en dos categorías:

– Básica: ninguno, primaria y secundaria.
– Superior: técnico, tecnológico, pregrado y posgrado.

CONSIDERACIONES ÉTICAS

Según el Ministerio de Salud de Colombia, en la Resolución número 008430 de octubre de 1993, Artículo 11 (27), la investigación se clasificó con riesgo mínimo. El proyecto fue aprobado por el Comité de Bioética de la Sede de Investigación Universitaria (SIU) de la Universidad de Antioquia, certificado número 10-11-328.

ANÁLISIS ESTADÍSTICO

Para el análisis descriptivo de los aspectos sociodemográficos, antropométricos y de consumo se utilizaron distribuciones absolutas, relativas e indicadores de resumen como los cuartiles, el rango intercuartílico, el valor mínimo y el valor máximo. Para la correlación simple entre la cantidad ingerida (BA y AA) y las variables antropométricas según aspectos sociodemográficos se utilizó el coeficiente de correlación de Spearman.

Antes de definir las pruebas estadísticas se establecieron los criterios de normalidad y homocedasticidad con las pruebas de Kolmogorov-Smirnov y Levene, que mostraron que los datos no tenían distribución normal, por lo que se definió el uso de las pruebas no paramétricas U de Mann-Whitney y Kruskal-Wallis para establecer la relación entre la condición nutricional, los indicadores de consumo y los aspectos sociodemográficos.

Para establecer la magnitud del cambio de la relación entre los indicadores de consumo, el estado nutricional y los aspectos sociodemográficos se calculó el tamaño del efecto por medio de la probabilidad de superioridad (PS_{est}) con sus respectivos intervalos de confianza del 95% (IC 95%).

Para controlar el efecto de múltiples covariables frente a la relación entre los indicadores de consumo y el estado nutricional establecido por el IMCz y el %GC se aplicó un modelo de regresión cuantílica (regresión mediana); un valor de $p < 0,05$ se consideró estadísticamente significativo.

La sistematización, el procesamiento y el análisis de los datos se realizaron con los programas SPSS® versión 23 y R® versión 3.3.2.

RESULTADOS

La muestra estuvo constituida por 596 jóvenes, de los que el 82% pertenecían al estrato medio-bajo y el 56% al grupo de edad de 10 a 13 años; la mitad eran hombres, el 63% poco activos, y el 48% presentaban un estado nutricional en exceso. Con respecto a la escolaridad de los padres y de las madres, se encontró que el 62% tenían formación básica (Tabla I).

Además, se observó que el 75% de los participantes habían tomado 313 mL (RIC = 313) o menos de BA, con una cantidad máxima de 1480 mL, y consumido 50 g (RIC = 45) o menos de AA, con un máximo de 240 g. La mediana de la ingesta de energía era de 2263 kcal (RIC = 332), el %AMDR de los carbohidratos totales del 55% (RIC = 3,2) y el %AMDR de los carbohidratos simples del 11,1% (RIC = 3,1) (Tabla II).

Tabla I. Características generales de la muestra

Variable		n	%
Sexo	Hombre	279	46,8%
	Mujer	317	53,2%
Edad	10-13 años	334	56,0%
	14-18 años	262	44,0%
Estado nutricional	Adecuado	310	52,0%
	Exceso	286	48,0%
Actividad física	Poco activo	373	62,6%
	Activo	223	37,4%
Estrato	Medio-Bajo	491	82,4%
	Alto	105	17,6%
Escolaridad del padre	Básica	338	62,0%
	Superior	207	38,0%
Escolaridad de la madre	Básica	358	60,9%
	Superior	230	39,1%

Tabla II. Distribución de variables cuantitativas

Variables	Q1	Q2	Q3	RI	Mín	Máx
Mililitros de bebidas azucaradas	0,0	98,7	313,5	313,5	0,0	1480,0
Calorías de bebidas azucaradas	0,0	48,0	139,5	139,5	0,0	781,1
Gramos de azúcar añadido	4,5	20,1	49,6	45,1	0,0	240,0
Calorías de azúcar añadido	16,0	77,1	179,3	163,3	0,0	851,3
Calorías totales/día	2080	2263	2412	332	1517	2950
%AMDR de CHO totales	53,0	54,6	56,2	3,2	30,0	72,0
%AMDR de CHO simples	9,7	11,1	12,8	3,1	5,6	18,9

%AMDR: Rango de distribución aceptable de macronutrientes.

El resultado del análisis bivariado se presenta en la tabla III, donde se destaca que el consumo de energía fue mayor en el grupo de 14 a 18 años ($p = 0,029$), en los hombres y en los individuos con un estado nutricional adecuado ($p \leq 0,0001$), mientras que la ingesta de AA fue superior en el estrato medio-bajo ($p \leq 0,0001$) y en los jóvenes con estado nutricional adecuado ($p = 0,004$). La ingesta de BA fue mayor en el estrato alto y, si bien no hubo diferencias estadísticamente significativas, la magnitud del efecto fue alta y estadísticamente significativa ($PS_{est} = 2,820$; IC 95% = 2,606-3,034). Además, en los jóvenes cuyos padres tenían formación básica, el consumo AA y el %AMDR de los CHO totales fue mayor, y en ambos el cambio fue importante y estadísticamente significativo.

Los individuos con exceso de peso consumieron más BA y, si bien esto no fue estadísticamente significativo, el cambio en el consumo fue muy importante ($PS_{est} = 1.020$; IC 95% = 0,859 a 1,181); además, ellos presentaron un mayor %AMDR de CHO simples ($p = 0,017$) que fue estadísticamente significativo ($PS_{est} = 0.990$; IC 95% = 0,829 a 1,151).

Al realizar el análisis multivariado ajustando las variables intervinientes se encontró que las personas que pertenecían al estrato socioeconómico medio-bajo tenían un mayor consumo de AA ($p \leq 0,0001$) y los jóvenes con estado nutricional adecuado consumían más cantidad de AA ($p = 0,011$) y energía ($p \leq 0,0001$); pero los jóvenes con estado nutricional en exceso ingerían una mayor cantidad de BA ($p = 0,025$) y el %AMDR de los CHO simples era superior ($p = 0,045$).

Con relación a la actividad física no se encontraron diferencias estadísticamente significativas para ninguna de las variables seleccionadas.

DISCUSIÓN

Este estudio encontró una mediana en la ingesta de BA cercana a los 100 mL (aproximadamente, 44 calorías), cifra muy inferior a la de México, que en la Encuesta Nacional de Salud y Nutrición de 2006 (ENSANUT 2006) reportó que los adolescentes consumían 400 calorías provenientes de las BA, y a la de Chile, donde hallaron que los escolares presentaban cifras cercanas a los 300 cc diarios (132 calorías), similar a lo reportado en la encuesta de Ecuador. Estados Unidos era el país con mayor consumo de gaseosas en el mundo; en el año 2000, los adolescentes habían alcanzado un promedio de 570 mL/día, pero en los últimos años se reporta una disminución y EE. UU. se ve superado por países latinoamericanos como Argentina, Chile y México (28-30).

En este estudio, el azúcar añadido a las bebidas fue mayor en el estrato socioeconómico medio-bajo (Me = 26,5; RIC = 45,8) que en el alto (Me = 3,0; RIC = 16) ($p \leq 0,001$). Resultados similares se hallaron en Argentina, donde el consumo promedio de azúcar (33 g) en el país era superior en los quintiles con menores ingresos (28), y en el que realizó Araneda con escolares chilenos, que si bien no estimó la cantidad de AA agregado a las bebidas, sí reportó que la mediana de los líquidos a los que se añadió azúcar durante la preparación fue mayor en el estrato bajo (339 mL/día) que en el alto (247 mL/día) (3).

Tabla III. Consumo de azúcar añadido, bebidas azucaradas, kilocalorías totales, %AMDR de carbohidratos totales y %AMDR de carbohidratos simples

Variables		Gramos de azúcar añadido		p ajus R(Me)	Valor PS_{est} (r^2; r)	Gramos de bebidas azucaradas		p ajus R(Me)	Valor PS_{est} (r^2; r)	Kilocalorías		p ajus R(Me)	Valor PS_{est} (r^2; r)	%AMDR		p ajus R(Me)	Valor PS_{est} (r^2; r)	%AMDR		p ajus R(Me)	Valor PS_{est} (r^2; r)
														CHO	TOT			CHO	SIM		
		Me (RIC)	IC 95%			Me (RI)	IC 95%			Me (RI)	IC 95%			Me (RI)	IC 95%			Me (RIC)	IC 95%		
Actividad física	Poco activo (n = 373)	20,0 (43,8)	17,0-23,0	0,406	1,300	113 (309)	0,0-150,0	0,999	0,800	2254 (330)	2230-2284	0,808	1,310	54,5 (3,2)	54,3-54,8	0,572	1,320	11,1 (3,0)	10,8-11,4	0,538	1,320
	Activo (n = 223)	21,5 (48,1)	19,0-29,5			60 (316)	0,0-170,0			2274 (332)	2242-2312			54,6 (3,1)	54,2-54,9			11,2 (3,4)	10,8-11,5		
Grupo de edad	10-13 años (n = 334)	20,0 (46,1)	18,0-24,1	0,999	0,880	79,0 (327)	0,0-150,0	0,999	1,120	2248 (325)	2217-2270	0,168	1,080	54,5 (2,9)	54,2-54,8	0,964	1,120	11,3 (3,5)	11,0-11,6	0,074	0,840
	14-18 años (n = 262)	21,2 (45,0)	17,7-26,7			116,0 (304)	0,0-150,0			2290 (344)	2262-2317			54,8 (3,5)	54,2-54,9			10,9 (2,8)	10,6-11,3		
Sexo	Hombre (n = 279)	24,1 (47,0)	19,5-29,5	0,274	1,030	166,0 (350)	0,0-200,0	0,104	1,000	2319 (302)	2283-2349	< 0,0001	0,950	54,0 (2,5)	54,0-54,8	0,856	1,060	11,2 (3,4)	10,9-11,8	0,933	1,040
	Mujer (n = 317)	19,0 (42,5)	16,5-22,0			0,0 (250,0)	0,0-116,0			2231 (325)	2191-2254			54,0 (4,0)	54,3-54,8			11,1 (2,8)	10,8-11,3		
Estrato	Medio-Bajo (n = 491)	26,5 (45,8)	22,0-31,0	0,000	0,360	83,0 (300)	0,0-150,0	0,942	2,820	2268 (320)	2250-2294	0,538	0,550	54,7 (3,2)	54,5-54,9	0,152	0,500	11,2 (3,1)	10,9-11,4	0,461	0,560
	Alto (n = 105)	3,0 (16,0)	0,0-6,9			150,0 (350)	0,0-170,0			2230 (378)	2177-2305			53,7 (3,3)	53,4-54,2			10,9 (3,1)	10,3-11,3		
Escolaridad del padre	Básica (n = 338)	27,2 (48,0)	3,1-21,5	0,297	0,660	25,0 (316,0)	0,0-150	0,739	1,300	2271 (294)	2253-2308	0,060	0,750	54,7 (3,2)	54,5-55,0	0,969	0,730	11,3 (3,1)	10,8-11,5	0,082	0,790
	Superior (n = 207)	13,3 (29,0)	7,2-18,0			150,0 (340,0)	0,0-170,0			2228 (375)	2186-2282			54,2 (3,1)	53,8-54,6			11,1 (3,3)	10,7-11,3		
Escolaridad de la madre	Básica (n = 358)	27,9 (48,2)	22,2-33,0	0,547	0,680	0,0 (316,5)	0,0-150,0	0,999	1,260	2263 (312)	2238-2298	0,204	0,810	54,7 (3,3)	54,5-55,0	0,394	0,760	11,3 (2,9)	10,9-11,6	0,055	0,780
	Superior (n = 230)	12,0 (32,6)	7,5-19,0			116 (308,0)	0,0-170,0			2259 (375)	2214-2302			54,2 (3,3)	53,4-54,5			10,9 (3,5)	10,5-11,3		
Estado nutricional	Adecuado (n = 310)	25,5 (46,5)	20,0-30,7	0,011	0,900	0,0 (280)	0,0-125,0	0,025	1,02	2346 (230)	2320-2376	< 0,0001	0,690	54.6 (8,1)	53,7-55.4	0,728	0,950	10,9 (2,6)	10,7-11,2	0,045	0,990
	Exceso (n = 286)	18,5 (41,3)	14,0-21,0			150 (350)	0,0-166,0			2121 (360)	2068-2169			54,5 (1,8)	54,3-54,7			11,3 (3,6)	11,0-12,0		

Los valores presentados en la tabla son: mediana (rango intercuartílico), intervalo de confianza, p cruda (U de Mann- Whitney o Kruskal-Wallis), PS_{est} (tamaño del efecto) con escolaridad del padre, escolaridad de la madre y estado nutricional. %AMDR CHO TOT: % Rango de distribución aceptable de macronutrientes para los carbohidratos totales; %AMDR CHOS SIM: % Rango de distribución aceptable de macronutrientes para los carbohidratos simples. $p \leq 0,05$.

El consumo de azúcar añadido estuvo relacionado con la escolaridad de los padres pero, al ajustar las variables de interés, no fue estadísticamente significativo. Sin embargo, Grimm y cols. concluyeron que la calidad de la dieta en la etapa escolar dependía del nivel educativo, la estabilidad laboral de la madre, el nivel socioeconómico y la composición del hogar (31), lo cual lleva a pensar que la alimentación en las clases sociales menos favorecidas y con padres con menor escolaridad se compone de alimentos de alta densidad de energía y bajo aporte de nutrientes, como es el azúcar, lo que concuerda de alguna manera con nuestros hallazgos.

En cuanto a las BA, este estudio evidenció una mediana mayor en el estrato medio-alto (150 mL) frente al bajo (83 mL) y, a pesar de que no hubo significación estadística (p = 0,45), la magnitud del efecto fue muy importante (PS_{est} = 2,820; IC 95% = 2,606 a 3,034). Resultados similares se hallaron en Argentina, en donde se encontró que a la par con el aumento de los ingresos se incrementaba la cantidad de gaseosas (28), y en México, donde también se halló que el porcentaje de contribución de las bebidas azucaradas a las calorías totales era superior en los estratos socioeconómicos altos (32), lo cual lleva a suponer que la cantidad de BA ingeridas también es mayor.

Nuestros resultados mostraron que los jóvenes con estado nutricional adecuado presentaban un mayor consumo de AA y de energía; hallazgos similares encontraron diferentes estudios en Colombia, Chile, Perú y España, estudios en los que se compararon el consumo entre los niños o adolescentes con peso normal y con obesidad (33-36). Los resultados pueden estar indicando que la ingesta de energía no es el único factor que determina el estado nutricional.

En esta investigación se halló que los jóvenes con estado nutricional excesivo presentaban un mayor consumo de BA y de CHO simples. En la revisión bibliográfica se encontraron varios estudios que evidencian la asociación entre el IMC y las BA, dentro de los cuales se destacan el de Caravali y cols. (37), llevado a cabo en jóvenes mexicanos, en el cual se observó que quienes mantuvieron el consumo de BA durante 12 meses presentaron un 71% más de probabilidades de aumentar el IMC (RR = 1,71; IC 95%: 1,03-2,86, p = 0,039); en España, Esparza y cols. (38), después de un año de seguimiento a adolescentes, encontraron que la probabilidad de tener exceso de peso había aumentado un 55% (IC 95%: 32-82) entre los que habían tenido una mayor ingesta de BA, y un estudio chileno llevado a cabo por Araneda (3) asoció positivamente el consumo de BA con el aumento del IMCz en niños de 6 a 13 años, y concluyó que el aumento del consumo de una porción diaria de BA (250 mL) incrementaba el IMCz en 0,13; otro estudio aleatorizado realizado en adultos de Dinamarca halló que los individuos que consumieron BA incrementaron la ingesta de energía y a la vez el peso corporal, refiriendo que ello podría estar relacionado con la teoría de que la energía que proviene de las BA no genera sensación de saciedad ni compensación calórica, como sí sucede con los alimentos sólidos (39).

Con relación a la asociación entre el aporte porcentual de los CHO simples a la energía total y el estado nutricional en exceso, no se hallaron estudios específicos; sin embargo, existen estudios que han encontrado relación entre la calidad de la alimentación y la prevalencia del sobrepeso y la obesidad en adolescentes (40), aunque otras investigaciones difieren de esto, encontrando que no existen diferencias estadísticamente significativas entre la calidad de la dieta y el peso corporal de niños y adolescentes (41-43).

En conclusión, nuestro estudio aumenta la evidencia de la asociación entre el consumo de BA y el estado nutricional clasificado a partir del IMC y el porcentaje de grasa, pero además muestra la asociación entre la energía aportada por los azúcares simples a la dieta y el estado nutricional, lo cual respalda la recomendación de la OMS de disminuir el aporte de estos por debajo de un AMDR del 10% e idealmente hasta un AMDR del 5% (44).

Una de las limitaciones de este estudio es que las tablas de composición de alimentos no reportan datos del contenido de azúcar de los productos y preparaciones regionales, lo que dificulta precisar la cantidad consumida por la población, por lo que el total de CHO simples puede ser mayor de lo estimado.

Otra limitación es la imposibilidad de imputar una relación causa-efecto a los hallazgos obtenidos entre el estado nutricional y el consumo de BA y AA en los adolescentes, ya que corresponden a datos tomados de un estudio transversal y, además, los datos únicamente son válidos para este grupo de jóvenes.

No obstante, los resultados obtenidos son importantes porque son una aproximación a la relación positiva entre el consumo de BA y CHO simples y el estado nutricional en exceso, y por tanto nos invita a que realicemos acciones tales como educar a las personas sobre la disminución de dichos productos y estimular a la industria para que disminuya o elimine la cantidad de azúcar añadido a los productos.

También se considera importante desarrollar futuras investigaciones que permitan conocer el comportamiento en otros grupos de edad y que cuenten con una mayor población, además de conocer el efecto causal entre el consumo de carbohidratos simples y el IMC.

BIBLIOGRAFÍA

1. Organización Mundial de la Salud. Centro de prensa. Obesidad y sobrepeso. Nota descriptiva 311. [Internet]. 2016 [Citado 2017 Jun 4]. Disponible en: http://www.who.int/mediacentre/factsheets/fs311/es/.
2. American Academy of Child & Adolescent. Obesity in Children and Teens [Internet]. No.79.2016 [Citado 2017 Jun 4]. Disponible en: http://www.aacap.org/AACAP/Families_and_Youth/Facts_for_Families/FFF- Spanish/La-Obesidad-en-los-Niños-y-Adolescentes-079.aspx.
3. Araneda J, Bustos P, Cerecera F, Amigo H. Ingesta de bebidas azucaradas analcohólicas e índice de masa corporal en escolares chilenos. Salud Pública Mex 2015;57(2):128-34. DOI: 10.21149/spm.v57i2.7408.
4. Lisbona A, Palma S, Parra P, Gómez C. Obesidad y azúcar: Aliados o enemigos. Nutr Hosp 2013;28(4):81-7.
5. Vizmanos B, Hunot C, Capdevila F. Alimentación y obesidad. Investig en Salud 2006;VIII:79-85.
6. Nielsen SJ, Popkin BM. Changes in beverage intake between 1977 and 2001. Am J Prev Med 2004;27(3):205-10. DOI: 10.1016/j.amepre.2004.05.005.
7. Instituto Colombiano de Bienestar Familiar, Profamilia, Instituto Nacional De Salud, Escuela de Nutrición y Dietética, Universidad de Antioquia, Organización Panamericana de la Salud (OPS). Encuesta nacional de la situación alimentaria y nutricional de Colombia. ENSIN 2005. Panamericana; 2006.
8. Instituto Colombiano de Bienestar Familiar, Profamilia, Instituto Nacional De Salud, Ministerio de la protección Social. Encuesta nacional de la situación alimentaria y nutricional de Colombia. ENSIN 2010. Da Vinci Editores; 2011.

9. Hoyos M, Escobar M, Uscategui R. Perfil de Seguridad Alimentaria y nutricional de Medellín, 2015. 2015.
10. Silva P, Durán S. Bebidas azucaradas más que un simple refresco. Rev Chil Nutr 2014;41(13). DOI: 10.4067/S0717-75182014000100013.
11. Vartanian L, Schwartz M. Effects of soft drink consumption on nutrition and health: A systematic review and meta-analysis. Am J Public Heal 2007;97(4):667-75.
12. Schulze M, Manson J, Ludwing D, Colditz G, Stampfer M, Willet W, et al. Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women. JAMA 2004;292(8):927-34. DOI: 10.1001/jama.292.8.927.
13. Velásquez C, Bermúdez J. Síndrome metabólico en jóvenes con sobrepeso: identificación de factores de riesgo y evaluación de una intervención. Nutrients 2016;8(54):1-13.
14. Agudelo G, Bedoya G, Estrada A, Patiño F, Muñoz AM, Velásquez C. Evaluación del efecto de variantes en genes candidatos, la composición génetica ancestral y factores del medio ambiente sobre endofenotipos diagnósticos de las enfermedades que caracterizan el síndrome metabólico, en una muestra de población colombiana. Metab Syndr Relat Disord 2014;21(4):202-9. DOI: 10.1089/met.2013.0127.
15. Manjarrés LM. Métodos para precisar la recolección de la ingesta dietética en estudios poblacionales. Perspectivas en Nutrición Humana. Perspect Nutr Humana 2007;9:155-63.
16. Manjarrés L, Hérnandez J, Cárdenas D. Software de Evaluación de Ingesta Dietética - EVINDI V4. 2012.
17. Carriquiry A. PC-SIDE. 2003.
18. Onis M de, Onyango A, Borghi E, Siyam A, Nishida C, Sierkmann J. Development of a WHO growth reference for school-aged children and adolescents. Bull World Heal Organ 2007;85(9):660-7. DOI: 10.2471/BLT.07.043497.
19. Ministerio de Salud y de Protección Social. Resolución número 288 de 2008. 2008;2008:1-54. [Citado 2017 Jun 4]. Disponible en: https://www.invima.gov.co/normatividad.
20. Ministerio de salud y de Protección Social. Colombia. Resolución 2121 de 2010, por la cual se adoptan los Patrones de Crecimiento publicados por la Organización Mundial de la Salud, OMS, en el 2006 y 2007 para los niños, niñas y adolescentes de 0 a 18 años de edad.
21. Organización Mundial de la Salud. AnthroPlus. 2007.
22. Lohman T, Roche A. Anthropometric standardization reference manual. Champaign: Human Kinetics Books. 1998.
23. Marshall W, Tanner J. Variations in the pattern of pubertal changes in boys. Arch Dis Child 1970;45:13-23. DOI: 10.1136/adc.45.239.13.
24. Marshall W, Tanner J. Variations in pattern of pubertal changes in girls. Arch Dis Child 1969;44:291-303. DOI: 10.1136/adc.44.235.291.
25. American College of Sports Medicine [Internet]. 2010 [Citado 2017 Jun 4]. Disponible en: http://www.acsm.org/.
26. Departamento Administrativo Nacional de Estadistica (DANE). Estratificación socioeconómica para servicios públicos domiciliarios [Internet]. 1991 [Citado 2017 Jun 4]. Disponible en: http://www.dane.gov.co/index.php/servicios-al-ciudadano/servicios-de-informacion/estratificacion-socioeconomica.
27. Ministerio de Salud y Protección Social R de C. Resolución 008430 de 1993. 1993;(Octubre 4):1-19.
28. Zapata M. La mesa Argentina en las últimas decadas: cambios en el patrón de consumo de alimentos y nutrientes 1996-2012. Buenos Aires: CESNI; 2016. p. 204. DOI: 10.18294/sc.2016.936.
29. Araneda J, Bustos P, Cerecera F, Amigo H. Ingesta de bebidas azucaradas analcohólicas e índice de masa corporal en escolares chilenos TT - Intake of sugar-sweetened non-alcoholic beverages and body mass index: A national sample of Chilean school children. Salud Pública Mex [Internet]. 2015;57(2):128-34. [Citado 2017 Jun 4]. Disponible en: http://www.scielosp.org/scielo.php?script=sci%7B_%7Darttext%7B&%7Dpid=S0036-36342015000200007. DOI: 10.21149/spm.v57i2.7408.
30. Gómez-Miranda LM, Bacardi-Gascon M, Caravali-Meza NY, Jimenez-Cruz. Consumo de bebidas energéticas, alcohólicas y azucaradas en jóvenes universitarios de la frontera México-USA. Nutr Hosp 2015;31(1):191-5.
31. Grimm G, Harnack L, Story M. Factors associated with soft drink consumption in school-aged children. J Am Diet Assoc 2004;104:1244-9. DOI: 10.1016/j.jada.2004.05.206.
32. Ruvalcaba CG, Tucker KL, Morita K, Qiao N, Hannan MT, Cupples LA, et al. Consumo de refrescos y riesgo de obesidad en adolescentes de Guadalajara, México. Bol Med Hosp Infant Mex [Internet]. 2009;6(2):50-9. [Citado 2017 Jun 4]. Disponible en: http://www.scielo.org.mx/scielo.php?pid=S1665-11462009000600006&script=sci_arttext&tlng=pt.
33. Liberona ZY, Engler TV, Castillo VO, Villarroel Del PL, Rozowski Narkunska J. Ingesta de macronutrientes y prevalencia de malnutrición por exceso en escolares de 5° y 6° básico de distinto nivel socioeconómico de la región metropolitana. Rev Chil Nutr 2008;35(3):190-9. DOI: 10.4067/S0717-75182008000300004.
34. Liria MR, Mispireta mL, Lanata CF, Creed-Kanashiro HM. Perfil nutricional en escolares de Lima y Callao. 2008. p. 1-86.
35. Ledesma N, Sepúlveda D, Cárdenas D, Manjarrés LM. Ingesta de energía y nutrientes en niños de 2-4 años que asisten al programa "Buen Comienzo", Medellín (Colombia). Nutr Hosp 2016;33(3):644-8. DOI: 10.20960/nh.566.
36. Martín-Calvo N, Ochoa MC, Martí A, Ángel Martínez-González M, De Genoi M. Asociación entre los macronutrientes de la dieta y la obesidad en la infancia y la adolescencia; un estudio de casos y controles. Nutr Hosp 2013;28(5):1515-22.
37. Caravali-Meza NY, Jiménez-Cruz A, Bacardi-Gascón M. Estudio prospectivo sobre el efecto del consumo de bebidas azucaradas sobre la obesidad en un periodo de 12 meses en Mexicanos de 15 a 19 años. Nutr Hosp 2016;33(2):270-6. DOI: 10.20960/nh.102.
38. Esparza-Olcina M, González-Rodríguez M. El consumo de bebidas azucaradas se asocia a obesidad. Evis Pediatr 2013;9(29):2-5.
39. Raben A, Vasilaras T. Sucrose compared with artificial sweeteners: Different effects on adlibitum food intake and body weight after 10 wk of supplementation in overweight subjects. Am J Clin Nutr 2002;76(4):721-9. DOI: 10.1093/ajcn/76.4.721.
40. Kosti RI, Panagiotakos DB, Mariolis A, Zampelas A, Athanasopoulos P, Tountas Y. The diet-lifestyle Index evaluating the quality of eating and lifestyle behaviours in relation to the prevalence of overweight/obesity in adolescents. Int Food Sci Nutr 2009;60(Suppl 3):34-47. DOI: 10.1080/09637480802534525.
41. Janssen I, Katzmarzyk PT, Boyce WF, Vereecken C, Mulvihill C, Roberts C, et al. Comparison of overweight and obesity prevalence in school-aged youth from 34 countries and their relationships with physical activity and dietary patterns. Obes Rev 2005;6(2):123-32. DOI: 10.1111/j.1467-789X.2005.00176.x.
42. Rodríguez Cabrero M, García Aparicio A, Salinero Martín JJ, Pérez González B, Sánchez Fernández JJ, Gracia R, et al. Calidad de la dieta y su relación con el IMC y el sexo en adolescentes. Nutr clin diet hosp [Internet]. 2012;32(2):21-7. [Citado 2017 Jun 4]. Disponible en: http://dialnet.unirioja.es/servlet/articulo?codigo=4185624&info=resumen&idio ma=SPA.
43. Montaña Miguélez J, Cobas N, Rodríguez M, Míguez Bernárdez M, Castro Sobrino L. Adherencia a la dieta mediterránea y su relación con el índice de masa corporal en universiarios de Galicia. Nutr Hosp 2012;32(3):72-80.
44. Organización Mundial de la Salud (OMS). Directriz: Ingesta de azúcares para adultos y niños. 2015.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Otros

Folic acid-deficient diet during gestation and post-weaning alters *Pomc* gene and protein expression in rat offspring

La dieta deficiente en ácido fólico durante la gestación y el destete altera la expresión del gen Pomc *y de proteínas en la descendencia de ratas*

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Abstract

Background: folic acid participates in one-carbon metabolism, which supplies methyl groups to numerous reactions in the body. Impaired delivery of these methyl groups affects gene expression. We hypothesize that offspring exposed to less folic acid will express higher levels of *Pomc* (proopiomelanocortin) gene mRNA.

Aim: to investigate the *Pomc* gene and protein expression pattern in the female offspring of female rats receiving a folic acid-deficient diet during gestation, lactation, and post-weaning.

Methods: the study involved female rat offspring (n = 10) born from mothers subjected to a control (2.0 mg of folic acid/kg of food) or folic acid-deficient (0.5 mg of folic acid/kg of food) diet, and fed the same diet during post-weaning. Samples were collected from the arcuate nucleus of the hypothalamus of the female offspring for real-time PCR and Western blotting analyses.

Results: the female offspring in the folic acid-deficient diet group had significantly higher *Pomc* gene and protein expression than the female offspring in the control diet group (p = 0.03, p = 0.01, respectively).

Conclusion: a folic acid-deficient diet during gestation, lactation, and post-weaning increases *Pomc* gene and protein expression, but does not modify food intake or body weight of female rat offspring.

Key words:

Epigenetics.
Folic acid. Gene expression.
Proopiomelanocortin.
Protein expression.

Resumen

Antecedentes: el ácido fólico participa en el metabolismo de un solo carbono, que suministra grupos metilo a numerosas reacciones del cuerpo. La aportación alterada de estos grupos metilo afecta a la expresión génica. Nuestra hipótesis es que la descendencia expuesta a menos ácido fólico expresará niveles más altos de ARNm del gen *Pomc* (proopiomelanocortina).

Objetivo: investigar el patrón de expresión del gen *Pomc* y de sus proteínas en crías de ratas hembras que recibieron una dieta deficiente en ácido fólico durante la gestación, la lactancia y el destete.

Métodos: el estudio incluyó crías hembras (n = 10) nacidas de madres sometidas a una dieta control (2,0 mg de ácido fólico/kg de alimento) o deficiente en ácido fólico (0,5 mg de ácido fólico/kg de alimento) durante la gestación y la lactancia, y alimentadas con la misma dieta durante el destete. Se recolectaron muestras del núcleo arqueado del hipotálamo de las hembras para el análisis de la expresión génica (PCR en tiempo real) y de proteínas (inmunomanchado Western).

Resultados: las hembras pertenecientes al grupo de dieta deficiente en ácido fólico tuvieron una expresión del gen *Pomc* y sus proteínas significativamente mayor que la de las hembras pertenecientes al grupo con dieta de control (p = 0,03, p = 0,01, respectivamente).

Conclusión: la dieta deficiente en ácido fólico durante la gestación, la lactancia y el destete modifica la expresión del gen *Pomc* y sus proteínas pero no modifica la ingesta de alimentos ni el peso corporal de las ratas hembra.

Palabras clave:

Epigenética.
Ácido fólico.
Expresión génica.
Proopiomelanocortina.
Expresión de proteínas.

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BACKGROUND

Environmental effects on epigenetics are probably more important during the prenatal and early postnatal development, when epigenetic mechanisms are established. Error accumulation during epigenetic information maintenance contributes to inter-individual variation with age (1,2).

Nutriepigenomics (the study of epigenetic modifications including the interaction between nutrients and DNA) with an appropriate nutritional management through healthy, balanced, and personalized nutrition can prevent certain diseases and related complications (3).

Maternal nutrition around the time of conception and during gestation determines proper fetal development and reflects on the long-term health of the offspring. Indeed, placental development and function heavily depend on the mother's diet (4). In addition to maternal diet, the diet consumed by the offspring during the post-weaning period also influences their health in later life significantly (5).

Folic acid is one of the vitamins that women consume the most during gestation. Folate, the synthetic form of this vitamin, participates in one-carbon (1C) metabolism. 1C metabolism involves a network of interrelated biochemical reactions that include the methionine and folate cycles. These cycles are central to cell function and provide 1C units (methyl groups) for nucleotide biosynthesis, which in turn are essential for DNA and RNA synthesis. Folate is a generic term for compounds with activity that resemble the activity of pteroylglutamic acid, a water-soluble vitamin that has tetrahydrofolic acid (THF) as the biologically active form and therefore enters the folate cycle. THF is then converted to 5,10-methylene-tetrahydrofolate (5,10-CH2-THF) and irreversibly reduced to 5-mTHF. Alternatively, 5-mTHF can be converted to 10-formyl-tetrahydrofolate (10-f-THF) through a series of reactions catalyzed by methylenetetrahydrofolate dehydrogenases. 5-mTHF demethylation completes the folate cycle as 1C is donated for homocysteine (HCY) remethylation to methionine (6,7).

Nutrients such as folic acid, vitamins B_{12} and B_6, riboflavin, choline, betaine, and methionine have crucial roles in this biochemical pathway (8,9). Micronutrient deficiency or supplementation can disrupt 1C metabolism and directly affect genome integrity through inadequate uracil insertions into DNA, which changes DNA methylation and gene expression patterns (10).

Folic acid intake influences DNA methylation patterns and gene expression, and takes part in mechanisms that potentially impact chronic disease development. Therefore, adequate folic acid consumption helps organisms to develop healthily (11). According to the Dietary Reference Intakes (DRI) (12), the recommended folic acid intake by adults and pregnant women is 400 and 600 µg/day, respectively.

Animal studies have shown that maternal folic acid and vitamin B_{12} deficiency or supplementation in the peri-conceptional period may influence the establishment of DNA methylation patterns and thus alter gene expression and phenotype in the offspring (13,14). Huot et al. (15) showed that offspring that consumed the same diet supplemented with folic acid during gestation and post-weaning could have altered gene expression.

Environmental factors, like diet, physical activity, stress, and exposure to alcohol and tobacco during gestation can greatly impact the health of the offspring through changes in epigenetic mechanisms such as DNA methylation and histone modification. Therefore, environmental factors may play a critical part in determining the risk of an individual developing metabolic diseases during adulthood, including heart disease, allergies, neurodegenerative diseases, obesity, and some cancers (16,17).

Investigations into obesity have identified some genes that are involved in this disease, like the proopiomelanocortin (*Pomc*, an anorectic peptide) gene (18). The *Pomc* gene is expressed in the arcuate nucleus of the hypothalamus, in the anterior and intermediate lobes of the pituitary gland, as well as in several other tissues such as the placenta, gastrointestinal tract, reproductive tract, lungs, and lymphocytes (19,20). This gene has been mapped to chromosome 2p23.3 and 6q14 in humans and mice, respectively (21,22).

Pomc deficiency in the arcuate nucleus of the hypothalamus increases food intake and reduces energy expenditure, which culminates in obesity and metabolic and endocrine disorders. Zhan et al. (23) verified that *Pomc* neurons have different functions in the arcuate nucleus of the hypothalamus and in the nucleus of the solitary tract, which suggests that these neurons regulate energy feeding and homeostasis by integrating long-term hypothalamus adiposity signs and short-term brainstem satiety signs.

In humans, the first evidence that melanocortins (originating in *Pomc* proteolytic cleavage) participate in food intake control emerged from the description of two patients who developed very early obesity, and who had mutations in the *Pomc* gene. Similarly, *Pomc*-knockout mice were obese and hyperphagic, and had impaired pigmentation and adrenal gland function (24).

Because the *Pomc* gene bears a promoter region, it is rich in CpG islands and is methylated. These features are relevant during experiments involving folic acid manipulation: this vitamin takes part in 1C metabolism, enabling reactions with methyl groups and consequently altering gene expression.

The present study aims to investigate *Pomc* gene and protein expression in female rat offspring subjected to a folic acid-deficient diet.

METHODS

This study followed the Ethical Principles on Animal Experimentation and was approved by the National Council of Animal Experimentation Control (CONCEA) of Ribeirão Preto Medical School, University of São Paulo, under protocol number 005/2014-1.

Wistar rats obtained from the University of São Paulo Central Animal Housing Facility at Ribeirão Preto were used in this research. At the Animal Housing Facility, Department of Medical Clinics, Ribeirão Preto Medical School, University of São Paulo, the rats remained in individual plastic boxes (width = 44 cm, length = 50 cm, and height = 27 cm) at controlled temperature (22 °C) and under a 12-hour dark/light cycle with food and water *ad libitum*. Throughout the treatment, rat weight and food intake were measured three times a week. First, the rats received com-

mercial food for three days, which allowed them to adjust to the new site. Then, they were fed the modified diets (Table I), which were based on AIN 93G (American Institute of Nutrition) (25). To this end, the rats were separated into two distinct treatment groups: the control group (2.0 mg of folic acid/kg of food; two females and one male) and the folic acid-deficient group (0.5 mg of folic acid/kg of food; two females and one male). Within the corresponding group, the rats remained together for mating for approximately one week. They were separated after pregnancy was confirmed.

During gestation and lactation, which lasted a total of approximately 42 days (21 days for each period), the mothers remained on the modified diets. After weaning, the offspring also started being fed the modified diet corresponding to their mothers' treatment group for three months. Figure 1 depicts the treatment protocol.

A total of 10 female offspring, five per treatment group, were analyzed (n = 5/group). After treatment, all the female offspring were euthanized with 300 mg of ketamine/kg and 30 mg of xylazine/kg and decapitated. The rat brain was removed. All the procedures abode by the guidelines of the Ethics Committee on Animal Experimentation of Ribeirão Preto Medical School, University of São Paulo. The brain was weighed on an analytical balance (Mettler®, Ae200), wrapped in autoclaved aluminum foil, and immediately frozen in dry ice and stored in a freezer at -80 °C.

The arcuate nucleus (ARC) of the hypothalamus was extracted at the Laboratory of Histology, Department of Physiology, Ribeirão Preto Medical School, University of São Paulo.

To perform this step, the cryostat (Microm International/HM 500 OM) was used so that the brain tissue was manually sliced at low temperature (-18 °C) and the ARC sample mRNA was not degraded.

Table I. Amount of ingredients used to prepare the control diet and the folic acid-deficient diet

Ingredients	Quantity (g/kg of food)
L-cysteine	1.8
Choline bitartrate	2.5
Mix of vitamins containing folic acid	10 (providing 2 mg of folic acid/kg of food – control diet – and 0.5 mg of folic acid/kg of food – folic acid-deficient diet)
Mineral mix	35
Microfine cellulose	50
Sucrose	100
Casein	140
Dextrinized starch	155
Corn starch	465.69
Di-tert butylhydroquinone	0.008
Soy oil	40
Water	1,750 mL

To localize the ARC correctly, reference points in the Atlas Brain Maps, Structure of the Rat Brain (26), were employed. The frozen brains were initially cut into 30 µm coronal sections. The tissue was cut until the hippocampus became visible and the optic tract became smaller and began to lateralize, which left the lower part of the brain irregular. Thereafter, a 1500 µm-thick cut containing the ARC was made. This slice was then transferred to a pre-cooled sterile glass slide where the ARC was withdrawn with a 1.5 mm autoclaved punch needle. The ARC was placed in a 1.5 mL sterile microtube containing RNAlater® Solution (Ambion®, Foster City, CA, USA) and stored in a freezer at -80 °C until it was processed.

RNA was extracted from the collected tissue with the TRIzol® Reagent (Life Technologies™, Carlsbad, CA, USA) according to the manufacturer's protocol. The extracted RNA was quantified on the Nanodrop 2000 apparatus (Thermo Fisher Scientific, Waltham, MA, USA), and its purity was evaluated by A260/A280 (1.8-2.0) and A260/A230 (2.0-2.2) ratios. The RNA was then treated with the enzyme RQ1 RNase-Free DNase® (Promega™, Fitchburg, USA) according to the manufacturer's protocol. The amount of treated RNA was 1500 ng. The reaction was carried out in the Thermal Cycler Veriti® 96-well Thermal Cycler (Applied Biosystem®, Foster City, CA, USA). cDNA was synthesized according to the SuperScript® VILO™ MasterMix (Life Technologies Inc., Carlsbad, CA, USA) manufacturer's protocol. The reaction was conducted in the Thermal Cycler Veriti® 96-well Thermal Cycler (Appied Biosystem®, Foster City, CA, USA). The following cycle was accomplished: incubation at 25 °C for 10 min, incubation at 42 °C for 60 min, and incubation at 85 °C for 5 min, when the reaction was terminated.

The relative *Pomc* gene expression (Pomc-Rn00595020_m1) was quantified by real-time PCR in a 7500 Fast Thermal Cycler apparatus (Applied Biosystem®, Foster City, CA, USA). TaqMan® Array Fast Plates (Life Technologies Inc., Carlsbad, CA, USA) were used, and the manufacturer's protocol was followed. The samples were analyzed by the $2^{-\Delta\Delta Ct}$ method (27), in triplicate; the Expression Suite Software v1.0.3 (Thermo Scientific™) was employed. Beta-actin (Actb-Rn00667869_m1) and hypoxanthine phosphoribosyltransferase-1 (Hprt1-Rn01527840_m1) were used as the reference genes. The appropriate cDNA concentration was 50 ng for a final reaction volume of 20 µL.

The protein was extracted by using a modification of the TRIzol® Reagent (Life Technologies Inc., Carlsbad, CA, USA) protocol. The protein was re-suspended in 100 µL of 1% SDS (sodium dodecyl sulfate). To solubilize the protein completely, the sonicator Virtis Virsonic 100 Ultrasonic Cell Disruptor (five cycles that

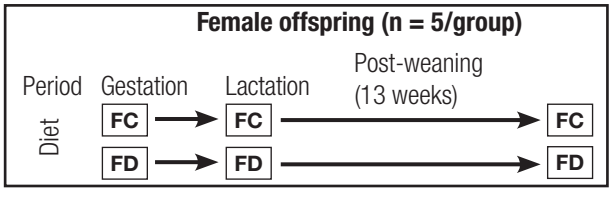

Figure 1.
Protocol for female offspring treatment during the study (FC: female offspring in the control diet group; FD: female offspring in the folic acid-deficient diet group).

included 15 sec in the sonicator and 30 sec of incubation on ice) was employed. Then, the samples were taken to a water bath (ALB 800s; INBRAS™) at 100 °C for 3 min and centrifuged at 8,700 rpm and 4 °C for 10 min.

The protein was quantified in each sample by means of the Pierce™ BCA Protein Assay Kit (Thermo Scientific™, Rockford, USA) protocol. Absorbance at 562 nm was read on the spectrophotometer SpectraMax® M3 (Molecular Devices, Sunnyvale, CA, USA) after the samples had been incubated at 37 °C for 30 min.

For electrophoresis, 4-15% Mini-PROTEAN® TGX™ Precast Protein Gels (Bio-Rad, Hercules, CA, USA) were used. Tris-Glycine-SDS was the run buffer for protein separation. The molecular weight marker PageRuler™ Prestained Protein Ladder (Thermo Scientific™, 5 µL) was added to the first well of the gel, whereas 20 µL of the sample containing the protein extract (3 µg of protein per well) was added to each of the other wells. The race started at 80 V for 10 min. The voltage was increased to 100 V and maintained at this value for 1 h 20 min.

Subsequently, the gel was transferred to a TransBlot® Turbo™ Mini Nitrocellulose Transfer Packs (Bio-Rad, Hercules, CA, USA) nitrocellulose membrane with the Trans-Blot® Turbo™ (Bio-Rad, Hercules, CA, USA).

After being blocked with 5 mL of 5% BSA in TBS for 1 h, the membrane was incubated with the primary antibodies at 4 °C overnight (16 h). The primary antibodies were as follows: 1 µL of anti-β-actin (mouse, monoclonal, 1:10,000, Sigma 5441) for the endogenous antibody, and 6.25 µL of anti-POMC (Rabbit, polyclonal, 1:800, ab94446) for the reference gene. Next, the membrane was washed with TBS-T, placed in 5 mL of 5% BSA and 1 µL of anti-mouse IgG HRP conjugated secondary antibody (Goat, 1:5000, sc2302) for the endogenous antibody (anti-β-actin), and incubated for 1 h. For the reference antibody (anti-POMC), 1 µL of anti-Rabbit IgG HRP conjugated secondary antibody (Goat, 1:10,000, ab97051) in 10 mL of 5% BSA was used for 1 h. Soon after that, the membranes were washed with TBS-T, and the Amersham™ ECL™ Select Western Blotting Detection Reagent (GE Healthcare Life Sciences, Marlborough, MA, USA) developer was added for analysis on an ImageQuant LAS 4000 (GE Healthcare Life Sciences, Marlborough, MA, USA).

The final protein quantification, based on the bands, was performed with the Image Studio Lite software v.3.3.1 (LI-COR® Biosciences, Lincoln, Nebraska, USA).

Descriptive statistics based on the mean and standard deviation were used. The Shapiro-Wilk test helped to verify data normality. The t-test was used to compare weight and gene and protein expression values. The Mann-Whitney test helped to analyze consumption data. All the statistical analyses were performed with the Statistical Package for Social Science (SPSS version 20); a significance level of 5% ($p < 0.05$) was adopted.

RESULTS

The body weight and food intake measured for the female offspring in the control diet group and the female offspring in the folic acid-deficient group were not statistically different ($p > 0.05$; Fig. 2).

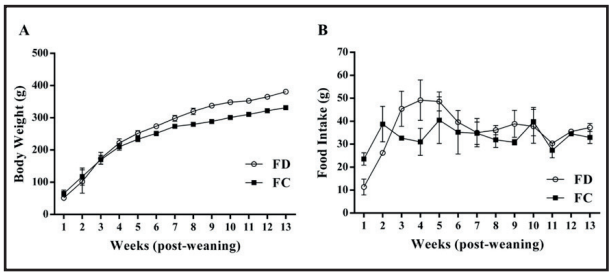

Figure 2.
Body weight and food intake. A. Body weight of female offspring from 0 to 13 weeks post-weaning, in grams. FC: female offspring in the control diet group; FD: female offspring belonging to the folic acid-deficient diet group. Data represented as mean ± SD (standard deviation), n = 5 per group. The t-test was used. B. Food intake of female offspring from 0 to 13 weeks post-weaning, in grams. FC: female offspring in the control diet group; FD: female offspring in the folic acid-deficient diet group). Data represented as mean ± SD (standard deviation), n = 5 per group. The Mann-Whitney test was used.

The *Pomc* gene mRNA expression in the ARC of the female offspring in the folic acid-deficient diet group was significantly higher than the *Pomc* gene mRNA expression in the ARC of the female offspring in the control diet group ($p = 0.03$; Fig. 3).

The Pomc protein expression in the ARC of the female offspring in the folic acid-deficient diet group was significantly higher than the Pomc protein expression in the ARC of the female offspring in the control diet group ($p = 0.01$; Fig. 4).

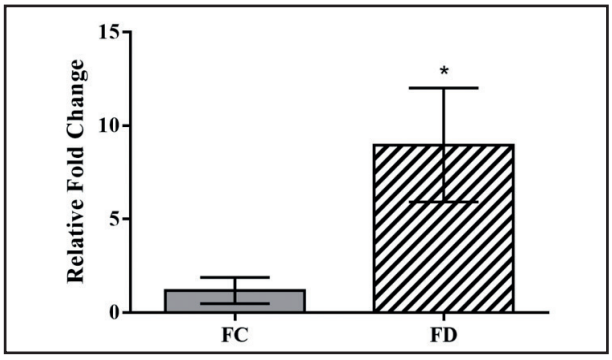

Figure 3.
Relative Pomc gene mRNA expression in the arcuate nucleus of the hypothalamus (FC: female offspring belonging to the control diet group; FD: female offspring belonging to the folic acid-deficient diet group). Data represented as mean and ± SD (standard deviation), n = 5 per group. *p = 0.03. The t-test was used.

DISCUSSION

The study involved female rat offspring born from mothers receiving a control or folic acid-deficient diet and fed the same diet during post-weaning for thirteen weeks. Samples were collected from the arcuate nucleus of the hypothalamus of the female offspring for *Pomc* gene and protein expression analyses.

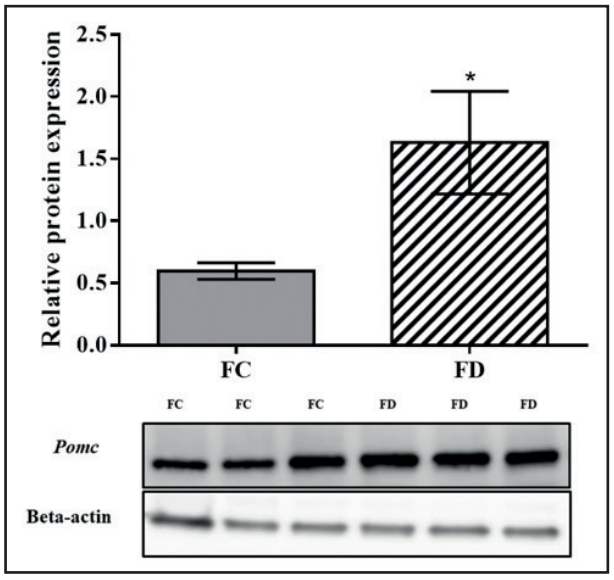

Figure 4.
Relative Pomc protein expression in the arcuate nucleus of the hypothalamus (FC: female offspring in the control diet group; FD: female offspring in the folic acid-deficient diet group). Data represented as mean ± SD (standard deviation), n = 4 per group. *p = 0.01. The t-test was used.

Changing the amount of folic acid (0.5 mg/kg of food) that was consumed during gestation, lactation, and post-weaning significantly altered the *Pomc* gene and protein expression even though the dietary intake and weight gain did not differ significantly between the offspring in the folic acid-deficient diet group and the control diet group.

Folic acid is a vitamin that plays key roles in many cellular reactions: it participates in purine and pyrimidine biosynthesis (for DNA and RNA synthesis), amino acid metabolism, and primary methylating agent (namely S-adenosyl methionine, or SAM) formation (28).

Given the countless folic acid functions during the embryonic period and because clinical practice has shown that folic acid deficiency is no longer common among individuals (29), we decided not to remove all of this micronutrient from the animal food. The absence of folic acid in the diet of pregnant rats causes congenital defects, such as neural tube defects (NTDs) in the offspring, or may even produce non-viable offspring (30). In fact, Maloney et al. (31) observed that the administration of a folic acid-free diet with low methionine and choline concentrations during gestation resulted in smaller offspring.

Several studies have demonstrated that the amount of folic acid in the maternal diet can modify the expression of various genes in the offspring. Mckay et al. (32) conducted a nutrigenomics investigation of liver samples obtained from adult offspring born from mothers that had been subjected to a folic acid-deficient diet (0.4 mg/kg of food). These authors identified 1,859 differentially expressed genes, 920 of which showed increased gene expression.

In contrast, Bermingham et al. (33) analyzed gene expression in colon samples obtained from female offspring subjected to a diet containing selenium and folate (0.6 and 1.8 mg/kg of food, respectively) and verified that 23 genes had higher expression ($p < 0.01$) during post-weaning. It is noteworthy that Bermingham et al. (33) used a 3.6 times greater amount of folic acid as compared to the present study. These authors also noted that this same diet elevated *Dmbx1*, *Errfi1*, *Plce1*, and *Fpr-rs2* gene mRNA expression in liver tissue. However, they did not find any correlations between gene and protein expression in hepatic tissue samples. On the other hand, here we observed a correlation between *Pomc* gene and protein expression in brain tissue samples.

Diets deficient in vitamin B (folic acid and vitamin B_6) influence gene expression in the central nervous system. Herein, a folic acid-deficient diet raised *Pomc* gene and protein expression in the female rat offspring brain tissue. Almeida et al. (34) treated Wistar rats with vitamin B_6-deficient diet during gestation and lactation, and detected significantly higher glutamate decarboxylase-1 (*Gad1*) gene and protein expression in the offspring hippocampus.

Meher et al. (35) analyzed the hepatic tissue of male and female Wistar rat offspring exposed to different diets during gestation and lactation, and confirmed an altered mRNA expression of hepatic transcription factors. The offspring that received vitamin B_{12}-deficient diet supplemented with omega-3 fatty acids presented a significantly greater PPARα expression, whereas the offspring that received folic acid- and vitamin B_{12}-deficient diet supplemented with omega-3s exhibited a significantly higher PPARγ expression.

Cho et al. (36) reported that folic acid supplementation during pregnancy and after weaning increased *Pomc* mRNA expression in the hypothalamus of male offspring. These data resembled the results obtained in another study by Cho et al. (37), in which male offspring born from rats that received a multivitamin-rich diet (10 times the amount recommended by AIN-93G) containing folic acid during pregnancy and weaned with the same diet also displayed increased *Pomc* gene and protein expression in the hypothalamus.

Nevertheless, folic acid supplementation or deficiency may afford divergent results regarding the *Pomc* gene in male and female rats. Huot et al. (15) verified discrepant results when they fed Sprague-Dawley rat offspring a diet supplemented with folic acid (5 mg/kg of food) during gestation and post-weaning: male offspring on this diet had higher *Pomc* mRNA expression than male offspring on the control diet, whilst *Pomc* mRNA expression in female offspring did not depend on the diet. In other words, the same treatment may furnish opposite results in females and males. The mechanisms underlying gender differences upon exposure to a folic acid-deficient diet or folic acid supplementation are not yet clear in the literature.

Gene expression is also a consequence of epigenetic events, which are essential for mammalian development and have a major part in fetal programming (38) and throughout life (4). Some studies have shown that, depending on the amount of folic acid consumed during pregnancy, *Pomc* mRNA expression may increase and result in lower food consumption and weight gain in the offspring (35-37). This happens because the *Pomc* gene acts as

the central regulator of energy homeostasis in the arcuate nucleus of the hypothalamus (39). In hypothalamic neurons, numerous hormones, nutrients, and cytokines regulate *Pomc* expression. Adipocytes secrete leptin, which mediates *Pomc* and both cocaine- and amphetamine-regulated transcript (CART) expression regulation (39). Briefly, leptin released by adipocytes stimulates Pomc and CART synthesis, thereby promoting alpha-MSH release by melanocortinergic neurons in the hypothalamus. Alpha-MSH acts on the MC4R and MC3R expressed in these neurons, inhibiting food intake and raising energy expenditure (40). Besides that, leptin also exerts an anorexigenic effect via inhibition of neuropeptide Y (NPY) and agouti-related peptide (AgRP) neurons (41).

Here, offspring belonging to the folic acid-deficient diet group presented higher *Pomc* gene and protein expression than the offspring belonging to the control diet group, but food consumption and weight in these groups were not statistically different. There are possible explanations for these findings. First, other genes involved in the food consumption cascade may also have had their expression pattern altered, compensating for the increased *Pomc* expression, as previously explained, and maintaining food consumption and weight unaltered. A second reason for our results may have been the reduced sample size and short intervention period. In contrast, Moloney et al. (31) evaluated 25-week-old female offspring (n = 7) (a relatively longer period as compared to the 21-week-old female offspring assessed here) and found that the folic acid-deficient diet with low choline and methionine concentrations reduced body weight. As for Jadavji et al., (42) they observed that male offspring (n = 14) born from mothers that received a folic acid-deficient diet (0.3 mg/kg of food), but which did not receive this same diet after weaning, weighed significantly more than the male offspring born from mothers that received a control diet (2 mg of folic acid/kg of food).

Cho et al. (36) revealed that a diet supplemented with folic acid during gestation and post-weaning lowered food intake and body weight by 7% and 9%, respectively, in male offspring (n = 12) at 29 weeks. In another study, these authors also demonstrated that male offspring (n = 13) born from mothers that received a multivitamin diet (10 times the amount recommenced by AIN-93G) containing folic acid during gestation, and weaned with a high-fat diet, had a 5% and 4% lower dietary intake and body weight, respectively (37). In their studies, Cho et al. (36) and Cho et al. (37) provided male offspring with a diet supplemented with folic acid at different periods. However, in both cases, the feeding intervention increased *Pomc* mRNA expression and decreased food consumption and weight gain.

Although the limitations of the study were a reduced sample size, the specific sex of the animals studied, and that the analyses were performed with only one hypothalamic gene, our results show that environmental factors, such as the presence of smaller folic acid amounts in the maternal diet during gestation and lactation, and in the diet that the offspring was fed during post-weaning, significantly modifies *Pomc* gene and protein expression, although offspring food consumption and body weight remain unaffected.

REFERENCES

1. Waterland RA, Michels KB. Epigenetic epidemiology of the developmental origins hypothesis. Annu Rev Nutr 2007;27:363-88. DOI: 10.1146/annurev.nutr.27.061406.093705.
2. Eriksson JG. Developmental Origins of Health and Disease - from a small body size at birth to epigenetics. Ann Med 2016;48:456-67. DOI: 10.1080/07853890.2016.1193786.
3. Remely M, Stefanska B, Lovrecic L, Magnet U, Haslberger AG. Nutriepigenomics: the role of nutrition in epigenetic control of human diseases. Curr Opin Clin Nutr Metab Care 2015;18:328-33. DOI: 10.1097/mco.0000000000000180.
4. King JCA. Summary of Pathways or Mechanisms Linking Preconception Maternal Nutrition with Birth Outcomes. J Nutr 2016;146:1437s-44s. DOI: 10.3945/jn.115.223479.
5. Zheng J, Xiao X, Zhang Q, Yu M. Maternal and post-weaning high-fat, high-sucrose diet modulates glucose homeostasis and hypothalamic POMC promoter methylation in mouse offspring. Metab Brain Dis 2015;30:1129-37. DOI: 10.1007/s11011-015-9678-9.
6. Clare CE, Brassington AH, Kwong WY, Sinclair KD. One-Carbon Metabolism: Linking Nutritional Biochemistry to Epigenetic Programming of Long-Term Development. Annu Rev Anim Biosci 2019;7:263-287. DOI: 10.1146/annurev-animal-020518-115206.
7. Zeisel SH. Importance of methyl donors during reproduction. Am J Clin Nutr 2009; 89:673s-7s. DOI: 10.3945/ajcn.2008.26811D.
8. Millian NS, Garrow TA. Human betaine-homocysteine methyltransferase is a zinc metalloenzyme. Arch Biochem Biophys 1998;356:93-98. DOI: 10.1006/abbi.1998.0757.
9. Zeisel SH. The fetal origins of memory: the role of dietary choline in optimal brain development. J Pediatr 2006;149:S131-6. DOI: 10.1016/j.jpeds.2006.06.065.
10. Choi SW, Friso S, Ghandour H, Bagley PJ, Selhub J, Mason JB. Vitamina B-12 deficiency induces anomalies of base substitution and methylation in the DNA of rat colonic epithelium. J Nutr 2004;134:750-5. DOI: 10.1093/jn/134.4.750.
11. Crider KS, Yang TP, Berry RJ, Bailey LB. Folate and DNA Methylation: A Review of Molecular Mechanisms and the Evidence for Folate's Role. Adv Nutr 2012;3:21-38.
12. Padovani RM, Amaya-Farfán J, Colugnati FAB, Domene SMA. Dietary reference intakes: application of tables in nutritional studies. Rev. Nutr 2006;19:741-60. DOI: 10.1590/S1415-52732006000600010.
13. Waterland RA, Jirtle RL. Transposable elements: targets for early nutritional effects on epigenetic gene regulation. Mol Cell Biol 2003;23:5293-300.
14. Sinclair KD, Allegrucci C, Singh R, Gardner DS, Sebastian S, Bispham J et. al. DNA methylation, insulin resistance, and blood pressure in offspring determined by maternal periconceptional B vitamin and methionine status. Proc Natl Acad Sci U S A 2007;104:19351-6. DOI: 10.1073/pnas.0707258104.
15. Huot PS, Ly A, Szeto IM, Reza-Lopez SA, Cho D, Kim YI, Anderson GH. Maternal and postweaning folic acid supplementation interact to influence body weight, insulin resistance, and food intake regulatory gene expression in rat offspring in a sex-specific manner. Appl Physiol Nutr Metab 2016;41:411-20. DOI: 10.1139/apnm-2015-0503.
16. Alegría-Torres JA, Baccarelli A, Bollati V. Epigenetics and lifestyle. Epigenomics 2011;3:267-77. DOI: 10.2217/epi.11.22.
17. Smith CJ, Ryckman KK. Epigenetic and developmental influences on the risk of obesity, diabetes, and metabolic syndrome. Diabetes Metab Syndr Obes 2015;8:295-302. DOI: 10.2147/dmso.s61296.
18. Martínez JA, Parra MD, Santos JL, Moreno-Aliaga MJ, Martí A, Martínez-González MA. Genotype-dependent response to energy-restricted diets in obese subjects: towards personalized nutrition. Asia Pac J Clin Nutr 2008;17:119-22.
19. Levitov AB, Dallas AP, Slonim AD (Eds.), Harper's Illustrated Biochemistry, AMGH; 2013.
20. Mountjoy KG. Pro-Opiomelanocortin (POMC) Neurones, POMC-Derived Peptides, Melanocortin Receptors and Obesity: How Understanding of this System has Changed Over the Last Decade. J Neuroendocrinol 2015;27:406-18. DOI: 10.1111/jne.12285.
21. Marques-Lopes I, Marti A, Moreno-Aliaga MJ, Martínez A. Genetic aspects of obesity. Rev. Nutr 2004;17:327-38. DOI: 10.1590/S1415-52732004000300006.
22. Kohl I. Research of genes and / or chromosomal segments in patients with obesity and / or hyperphagia, delayed neuropsychomotor development and

learning difficulties and behavioral disorders. 2010. 162 f. Thesis (PhD in Biology / Genetics) - Institute of Biosciences, University of São Paulo, São Paulo, 2010.
23. Zhan C, Zhou J, Feng Q, Zhang JE, Lin S, Bao J, et al. Acute and long-term suppression of feeding behavior by POMC neurons in the brainstem and hypothalamus, respectively. J Neurosci 2013;33:3624-32. DOI: 10.1523/jneurosci.2742-12.2013.
24. Krude H, Biebermann H, Luck W, Horn R, Brabant G, Gruters A. Severe early-onset obesity, adrenal insufficiency and red hair pigmentation caused by POMC mutations in humans. Nat Genet 1998;19:155-7. DOI: 10.1038/509.
25. Reeves PG, Nielsen FH, Fahey GCJ. AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-76A rodent diet. J Nutr 1993;123:1939-51. DOI: 10.1093/jn/123.11.1939.
26. Swanson LW (Eds.). Atlas Brain Maps, Structure of the Rat Brain, Elsevier, Amsterdam; 1992.
27. Livak KJ, Schmittgen TD. Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. Methods 2001;25:402-8. DOI: 10.1006/meth.2001.1262.
28. Ebara S. The Nutritional Role of Folate. Congenit Anom (Kyoto) 2017;57:138-41. DOI: 10.1111/cga.12233.
29. Castaño E, Piñuñuri R, Hirscha S, Roncoa AM. Folate and Pregnancy, current concepts. It is required folic acid supplementation? Rev Chil Pediatr 2017;88:199-206. DOI: 10.4067/s0370-41062017000200001.
30. Wallingford JB, Niswander LA, Shaw GM, Finnell RH. The continuing challenge of understanding, preventing, and treating neural tube defects. Science 2013;339:1222002. DOI: 10.1126/science.1222002.
31. Maloney CA, Hay SM, Ree WD. The effects of feeding rats diets deficient in folic acid and related methyl donors on the blood pressure and glucose tolerance of the offspring. Br J Nutr 2009;101:1333-40. DOI: 10.1017/s0007114508066798.
32. Mckay JA, Xie L, Adriaens M, Evelo CT, Ford D, Mathers JC. Maternal folate depletion during early development and high fat feeding from weaning elicit similar changes in gene expression, but not in DNA methylation, in adult offspring. Mol Nutr Food Res 2016;61. DOI: 10.1002/mnfr.201600713.
33. Bermingham EN, Bassett SA, Young W, Roy NC, McNabb WC, Cooney JM et al. Post-weaning selenium and folate supplementation affects gene and protein expression and global DNA methylation in mice fed high-fat diets. BMC Med Genomics 2013;5:6-7. DOI: 10.1186/1755-8794-6-7.
34. Almeida MR, Mabasa L, Crane C, Park CS, Venâncio VP, Bianchi mL et al. Maternal vitamin B6 deficient or supplemented diets on expression of genes related to GABAergic, serotonergic, or glutamatergic pathways in hippocampus of rat dams and their offspring. Mol Nutr Food Res 2016;60:1615-24. DOI: 10.1002/mnfr.201500950.
35. Meher A, Joshi A, Joshi S. Differential regulation of hepatic transcription factors in the Wistar rat offspring born to dams fed folic acid, vitamin B12 deficient diets and supplemented with omega-3 fatty acids. PLoS One 2014;9:e90209. DOI: 10.1371/journal.pone.0090209.
36. Cho CE, Sánchez-Hernández D, Reza-lópez SA, Huot PS, Kim YI, Anderson GH. High folate gestational and post-weaning diets alter hypothalamic feeding pathways by DNA methylation in Wistar rat offspring. Epigenetics 2013;8:710-9. DOI: 10.4161/epi.24948.
37. Cho CE, Pannia E, Huot PS, Sánchez-Hernández D, Kubant R, Dodington DW, et al. Methyl vitamins contribute to obesogenic effects of a high multivitamin gestational diet and epigenetic alterations in hypothalamic feeding pathways in Wistar rat offspring. Mol Nutr Food Res 2015;59:476-89. DOI: 10.1002/mnfr.201400663.
38. Bernal AJ, Jirtle RL. Epigenomic disruption: the effects of early developmental exposures. Birth Defects Res A Clin Mol Teratol 2010;88:938-44. DOI: 10.1002/bdra.20685.
39. Gali Ramamoorthy T, Begum G, Harno E, White A. Developmental programming of hypothalamic neuronal circuits: impact on energy balance control. Front. Neurosci 2015;9:126. DOI: 10.3389/fnins.2015.00126.
40. Cowley MA, Smart JL. Rubinstein M, et al. Leptin activates anorexigenic POMC neurons through a neural network in the arcuate nucleus. Nature 2001;411:480-4. DOI: 10.1038/35078085.
41. Nicoletti CF, Delfino HBP, Ferreira FC, et al. Role of eating disorders-related polymorphisms in obesity pathophysiology. Rev Endocr Metab Disord 2019. ISSN 1389-9155. Available at: http://dx.doi.org/10.1007/s11154-019-09489-w.
42. Jadavji NM, Deng L, Malysheva O, Caudill MA, Rozen R. MTHFR deficiency or reduced intake of folate or choline in pregnant mice results in impaired short-term memory and increased apoptosis in the hippocampus of wild-type offspring. Neuroscience 2015;300:1-9. DOI: 10.1016/j.neuroscience.2015.04.067.

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Trabajo Original

Otros

The inflammatory potential of Argentinian diet and oral squamous cell carcinoma

Potencial inflamatorio de la dieta argentina y carcinoma oral de células escamosas

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Abstract

Introduction: the goal of this study was to evaluate whether an association exists between dietary components related to inflammation and oral squamous cell carcinoma (OSCC) in Argentina.

Methods: a case-control study was carried out with 3 controls for each case and participants of both genders who were between 24 and 85 years of age, who were recruited at the outpatient clinic, Odontology School, Universidad Nacional de Córdoba, between 2012 and 2015. Dietary information was collected using a semi-quantitative food frequency questionnaire from which energy-adjusted Dietary Inflammatory Index (E-DII™) scores were computed. Logistic regression models were fit to assess the association between E-DII and OSCC.

Results: significantly higher intakes of macronutrients such as fat, protein and cholesterol, and of micronutrients such as iron, riboflavin, monounsaturated, polyunsaturated, omega-6 and omega-3 fatty acids, and vitamin B6 were observed in cases as compared to controls (all $p < 0.05$). We also observed a significant 69% increase in OSCC for each point on the E-DII scale (OR 1.69, 95% CI [1.18-2.43]) after adjusting for alcohol and tobacco consumption.

Conclusion: we found an association between diet-associated inflammation, as represented by the E-DII, and risk of OSCC. Future research should be directed at deepening our understanding of this association in other populations, and should include studies utilizing prospective designs.

Key words:

Diet. Inflammation. Oral cancer. Case-control study. Dietary inflammatory index. Argentina.

Resumen

Introducción: el objetivo de este estudio fue evaluar la asociación entre los componentes de la dieta relacionados con la inflamación y el carcinoma oral de células escamosas (OSCC) en Argentina.

Métodos: estudio de casos y controles con 3 controles para cada caso y participantes de ambos sexos, con edades comprendidas entre 24 y 85 años, que fueron atendidos por demanda espontánea en los Consultorios Externos de la Facultad de Odontología de la Universidad Nacional de Córdoba entre 2012 y 2015. La información sobre la dieta se recopiló mediante un cuestionario semicuantitativo de frecuencia alimentaria, a partir del cual se calcularon las puntuaciones del Índice Inflamatorio Dietético (E-DII®), ajustado por energía. Se utilizó un modelo de regresión logística para evaluar la asociación entre el E-DII y el OSCC.

Resultados: en los casos se observaron ingestas de macronutrientes como grasas, proteínas y colesterol, y de micronutrientes como hierro, riboflavina, ácidos grasos monoinsaturados, poliinsaturados, omega-6 y omega-3, y vitamina B6 significativamente más altas que en los controles ($p < 0,05$). También observamos un aumento significativo del 69% en el OSCC por cada punto en la escala E-DII (OR 1,69, IC 95% [1,18-2,43]) después de ajustar el consumo de alcohol y tabaco.

Conclusión: nuestros resultados mostraron una asociación entre la inflamación asociada a la dieta, representada por el E-DII, y el riesgo de OSCC. La investigación futura deberá dirigirse a profundizar en la comprensión de esta asociación en otras poblaciones, incluyendo estudios que utilicen diseños prospectivos.

Palabras clave:

Dieta. Inflamación. Cáncer oral. Estudio de casos y controles. Índice dietario inflamatorio. Argentina.

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INTRODUCTION

Oral cancer (OC) is the sixth most prevalent human cancer in the world and in Latin America (1,2). Globally, the vast majority of these are oral squamous cell carcinomas (OSCC) (1). OC is associated with high morbidity and low survival rates. Most cancers, including OC, have complex pathologies, and their incidence and survival are closely related to the social, cultural and socio-economic determinants of health (3,4). Some of these factors, such as diet, are modifiable (5).

Controversies abound in epidemiological studies on the relationship of diet and oral carcinogenesis (5,6). Many studies indicate that red meat intake or a diet poor in fruit and vegetables could increase the risk of different cancers such as OSCC (6), probably because certain dietary components are related to inflammatory processes (7). Chronic local inflammation is known to disturb homeostatic control in cell signaling pathways, which may transform normal cells to become premalignant or malignant. In some kinds of cancer, an inflammatory environment is present before malignant change occurs (8). However, in other kinds of cancer, malignant change induces an inflammatory environment around a primary lesion and promotes tumor development (9). Inflammatory processes are known to play a major role at different stages of tumorigenesis (9), and chronic inflammation predisposes to develop cancer (10). There is evidence that various dietary components could lead to chronic inflammation (11). For this reason, it is interesting to evaluate the association between dietary inflammatory potential and OSCC.

Researchers at the University of South Carolina's Cancer Prevention and Control Program have developed a tool called the Dietary Inflammatory Index (DII®) to measure the overall inflammatory potential of any individual's diet (12). The DII has been validated in numerous studies and has been shown to be associated with different kinds of cancers and other diseases (12-15). However, there are few studies on the association between DII and OC (16), and this relation has not yet been studied in Argentinian people with OSCC. Hence, the aim of this study was to evaluate if there is an association between dietary inflammatory potential and OSCC in adult patients. The results of this study could have direct applicability in programs to prevent OSCC.

MATERIAL AND METHODS

A case-control study with controls in a 3:1 ratio to cases and representing both genders was carried out between 2012 and 2015. The clinical examination of the oral cavity was performed by previously trained dentists. Lifestyle habits were assessed using the criteria by Secchi et al. 2015 (6). The medical, dental characteristics and dietary intake data were collected in a unique clinical record.

All cases (n = 27) were ≤ 85 years old at diagnosis (age range, 23-83 years; mean, 59 years) and were recruited at the outpatient clinic, Odontology School, Universidad Nacional de Córdoba, Argentina. A total of 27 patients, newly diagnosed by histopathological analysis and classified by the International Classification of Diseases (ICD-10) codes C00 to C14, were considered eligible for the study. Controls (n = 86) were enrolled in the same period and at the same clinic as cases. They presented at the time of the survey with a mean age of 59 years and an age range between 21 and 86 years. They did not have any neoplastic diseases, and they did not report changes in their dietary habits or other relevant habits such as smoking and drinking for a period of no less than 5 years. They were matched by gender and age (± 5-years) with cases.

Additional risk factors were assessed according to the following criteria: s*moker*: current consumption of at least one cigarette/day over a 1-year minimal period; *alcohol*: current consumption of 2 drinks/week over a 1-year minimal period. The workplace (e.g., occupational exposure to carcinogens) presents possible risks in industries such as textiles, rubber, coal, dyes, leather, herbicides, automotive, plastics and chemicals. Age was categorized as < 45 years and ≥ 45 years. The E-DII score was considered a continuous variable or categorized into tertiles based on cutpoints among controls. Age was fit as a continuous variable. Body mass index, calculated as BMI = weight (kg)/height (m)^2 was categorized into < 25 or ≥ 25 kg/m^2 according to World Health Organization criteria (https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight). Education was classified as primary, secondary, tertiary, and university.

DIETARY ASSESSMENT

A 127-item food frequency questionnaire (FFQ), validated by Navarro et al., 2001 (17), was administered to cases and controls by trained nutritionists at the stomatology clinic after clinical examination and histopathological confirmation of clinical diagnosis.

This questionnaire includes two sections: a) bio-socio-cultural characteristics, anthropometric measurements, and lifestyle; b) food intake, evaluating dietary exposure in the 5 years prior to diagnosis for cases, and before interview for controls. Additionally, a photographic food atlas, also validated by Navarro et al., 2000 (18), was used, and nutritional composition was estimated using the Nutrio 1.2 sofware package (19).

DIETARY INFLAMMATORY INDEX ASSESSMENT

Details of the steps involved in the DII calculation are described elsewhere (20,21). In order to compute the DII score, the dietary information for each study participant was first linked to the regionally representative database, which provided a robust estimate of a mean and standard deviation for each of the 45 parameters (i.e., foods, nutrients, and other food components) considered in the DII definition (20,21). These parameters were then used to derive the subject's exposure relative to a standard global mean as a z-score, by subtracting the mean of the regionally representative database from the amount reported, and dividing this value by the parameter's standard deviation. To minimize the effect of "right skewing", this value was converted to a centred percentile score, which was computed by doubling the raw percentile score and then subtracting 1. This score was then multiplied by the respective food

parameter effect score (derived from a literature review of 1943 articles) (21). All of these food parameter-specific DII scores were then summed to create the overall DII score for every subject in the study. The energy adjusted-DII (E-DII) was calculated per 1000 kcal using methods paralleling those of the DII, but relied on an energy-adjusted global database. A higher E-DII score indicates a pro-inflammatory diet rich in calorie-dense nutrients such as saturated fat and total cholesterol; a lower E-DII score indicates that the diet is more anti-inflammatory, rich in nutrients such as vitamins, minerals, and a variety of other antioxidant compounds (16,22).

ETHICAL ASPECTS

This study was approved by the Research and Ethics Committee of the Ministry of Health of the Province of Córdoba (No. 1378), and all subjects signed informed consent forms. Patients who were under therapeutic medication such as corticosteroids or chemotherapy drugs that modify or alter the clinical behavior of malignant oral lesions were excluded. Patients diagnosed with other cancers, systemic diseases, chronic alcoholism or drug addictions were also excluded.

STATISTICAL ANALYSIS

Quantitative data were statistically described using mean ± standard error and median values. Qualitative variables were described as relative/absolute frequencies. The Mann-Whitney test for testing the hypothesis that median consumption is equal between cases and controls was performed because continuous data were not normally distributed. The measures of association, the odds ratio (OR) and its 95% confidence interval (95% CI), were estimated by fitting the logistic regression model between the presence of disease and the E-DII score, while controlling for potential confounders. For all tests, statistical significance was set at $p < 0.05$ (2-sided). The Stata Statistical Software package, version 13 (Stata Corp LP -2014- College Station, TX 77845, USA), was used for all analyses.

RESULTS

Patients with OSCC presented with lesions in various oral cavity sites: tongue (42.1%), palate (6.3%), lip (9.6%), oral mucosa (16.2%), gum (16.2%), and floor of the mouth (9.6%). Most of the patients were diagnosed within one year of the first symptoms appearing (80%). Cases and controls showed similar distributions of bio-demographic characteristics such as BMI. They were matched on age and gender (Table I).

Cases had a significantly higher intake of fat and protein as compared to controls (Table II). Other dietary components such as cholesterol, iron, monosaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), omega-6 fatty acids, omega-3 fatty acids, selenium, vitamin B6, and vitamin E were significantly higher in

Table I. Bio-demographic and risk factor characteristics studied. Absolute and relative % frequencies (RF calculated over total of controls or cases)

Characteristics		Categories	Control (n = 86) FA (FR%)	Case (n = 27) FA (FR%)	95% CI			p (Fisher test)
					OR	LB	UB	
Bio-demography	Gender	Male	46 (53.5)	15 (55.5)	Reference category			
		Female	40 (46.5)	12 (44.4)	1.32	0.45	3.87	0.62
	Age	< 45 years	16 (18.6)	4 (14.8)	Reference category			
		≥ 45 years	69 (81.4)	23 (85.2)	1.36	0.32	5.81	0.67
	Education	Primary	36 (41.8)	13 (48.1)	Reference category			
		Secondary	24 (27.9)	7 (25.9)	0.95	0.27	3.33	0.93
		Tertiary	12 (13.9)	2 (7.4)	0.43	0.06	3.21	0.41
		University	14 (16.3)	5 (18.5)	0.81	0.21	3.1	0.76
	BMI[1]	< 25	28 (32.6)	11 (40.7)	Reference category			
		≥ 25	53 (61.6)	16 (59.3)	1.30	0.54	3.14	0.57
Risk factors	Smoker[2]	Never/ex	56 (65.1)	17 (63.0)	Reference category			
		Current	30 (34.9)	10 (37.0)	0.64	0.19	2.15	0.47
	Alcohol consumption[3]	Never/ex	56 (65.1)	15 (55.5)	Reference category			
		Current	30 (34.9)	12 (44.4)	1.21	0.37	3.9	0.75
	Work[4]	Never	73 (84.9)	20 (74.1)	Reference category			
		Current and at least more than 5 years	13 (15.1)	7 (25.9)	2.38	0.68	8.35	0.18

[1]Body mass index (BMI): weight (kg)/height (m)[2]. [2]Smoker: current consumption of at least one cigarette/day over a 1-year minimal period. [3]Alcohol: current consumption of 2 drinks/week over a 1-year minimal period. [4]Work: one or more years of exposure to carcinogens considered a risk factor at work in industries such as textiles, rubber, leather, herbicides, automotive, plastic, and chemicals by IARC. p-values < 0.05 indicate statistical significance.

Table II. Macronutrients and micronutrients including estimation of energy-adjusted dietary inflammatory index (E-DII) scores in cases and controls

Dietary components included in the E-DII (n = 113)	Control (n = 86)			Case (n = 27)			p (Mann-Whitney)[a]
	Mean	SE	Median	Mean	SE	Median	
Carbohydrates (g/day)	305.3	133.7	280.9	343.2	109.9	334.4	0.09
Proteins (g/day)	*107.9*	*43.00*	*96.30*	*129.42*	*47.85*	*118.1*	*0.03*
Fat (g/day)	*112.3*	*62.89*	*94.90*	*167.22*	*103.39*	*141.4*	*0.006*
Energy (cal/day)	*2766.9*	*1165.92*	*2462.74*	*3476.72*	*1305.84*	*3515.9*	*0.006*
Cholesterol (mg/day)	*415.3*	*207.56*	*376.75*	*529.75*	*235.88*	*520.41*	*0.02*
Iron (mg/day)	*18.65*	*7.87*	*17.58*	*23.2*	*9.63*	*21.04*	*0.02*
Vitamin A (µg/day)	1404	1043	1039	1672	927.1	1735	0.11
Riboflavin (mg/day)	2.11	0.93	1.94	2.39	1.02	2.04	0.23
Vitamin B6 (mg/day)	*1.29*	*0.6*	*1.25*	*1.57*	*0.59*	*1.35*	*0.02*
Vitamin C (mg/day)	187.3	132.9	156.1	197.9	176.3	124.4	0.88
Vitamin E (mg/day)	*6.21*	*4.14*	*4.85*	*10.66*	*8.06*	*8.43*	*0.002*
Selenium (µg/day)	*106.6*	*51.88*	*95.87*	*142.98*	*47.34*	*145.7*	*0.001*
Zinc (mg/day)	11500	6546	8849	13506	6958	11616	0.08
Ethanol (g/day)	13.13	23.62	1.99	32.32	56.47	0.9	0.98
Fiber (g/day)	15.41	6.58	15.5	17.53	6.06	16.62	0.089
Tea (cc/day)	66.28	127.41	0.00	62.35	115.6	0	0.67
Omega-3 (g/day)	*1.54*	*0.89*	*1.26*	*2.32*	*1.43*	*1.59*	*0.01*
Omega-6 (g/day)	*12.11*	*6.51*	*10.51*	*23.91*	*21.47*	*16.85*	*0.001*
Saturated fat (g/day)	*47.31*	*28.91*	*39.04*	*60.56*	*33.12*	*55.33*	*0.02*
Garlic (g/day)	0.03	0.14	0	0.04	0.17	0	0.94
Onion (g/day)	10.7	10.46	7.14	11.23	14	3.57	0.26
MUFA (g/day)	*42.81*	*25.26*	*35*	*59.99*	*36.61*	*48.33*	*0.007*
PUFA (g/day)	*13.64*	*7.18*	*12.12*	*26.23*	*22.56*	*17.9*	*0.0007*
Caffeine (mg/day)	162.2	137.1	115.2	154.8	196.5	86.25	0.19
Omega-6/omega-3 ratio	*8.49*	*3.9*	*7.47*	*10.44*	*4.87*	*8.94*	*0.03*

MUFA: monosaturated fatty acid; PUFA: polyunsaturated fatty acid. [a]Mann-Whitney U-test for proving Ho: median values are equal between cases and controls. Bold letters indicate statistical significance at $p < 0.05$.

Table III. The relationship between E-DII scores and oral squamous cell carcinoma from a logistic regression model

E-DII	Population	Crude OR	(95% CI)	p-value	Adjusted[a] OR	(95% CI)	p-value
Continuous	113	1.68	(1.20-2.35)	0.003*	1.69	(1.18-2.43)	0.0029*
T1 (< 0.37)	48/113	1 (Ref.)			1 (Ref.)		
T2 (0.37-1.69)	34/113	2.53	(0.92-6.96)	0.07	2.74	(0.97-3.60)	0.06
T3 (≥ 1.69)	31/113	19.66	(2.47-56.50)	0.005*	18.46	(2.28-149.72)	0.003*

*OR: odds ratio; CI: confidence interval. aT1: DII values lower than the 1st tertile; T2: E-DII values between 2nd and 3rd tertile; T3: E-DII values higher than 3rd tertile. Categories based on E-DII tertiles of controls. Adjusted by alcohol and tobacco consumption. *Indicates statistical significance at $p < 0.05$.*

cases than in the control group (Table II). The ratio of omega-6/omega-3 fatty acids in controls (average, 8.49 ± 3.9) was significantly lower than in cases (average, 10.44 ± 4.9) ($p = 0.025$, Mann Whitney test) (Table II).

The median E-DII score was 0.81, with a range of -2.24 to +3.72 across the entire population. A significant association was observed between E-DII (continuous) and OSCC by logistic regression (OR 1.69, 95% CI [1.18-2.43]) after adjusting for alcohol and tobacco consumption, the two main parameters recognized as risk factors for oral cancer (Table III). A similar result was observed with E-DII categories based on tertiles (Table III).

DISCUSSION

The results of this study showed that OSCC cases had significantly higher daily intakes of fat and protein than control subjects. It has previously been shown that factors such as growth hormones and estrogen can modify metabolic factors, adipocytokine, low-grade inflammation, and cellular oxidative stress levels, and can also result in alterations of the microbiome, which may eventually lead to carcinogenesis (23). It has been demonstrated that NFκB signaling and expression of COX-2, TNFα and IL-1β are all increased in the mammary glands and visceral fat of obese female mice obtained through genetic and diet-induced obesity models; these molecules participate in processes associated with chronic inflammation and have been linked to various epithelial malignancies (24).

A significantly higher intake of iron was observed in cases with OSCC *vs.* controls in this study. This observation matches other studies, demonstrating a relationship between this micronutrient and the presence of multiple cancer types, such as lung cancer, breast cancer, prostate cancer, colorectal cancer, hepatocellular cancer, pancreatic cancer, hematological cancer, renal cell carcinoma, and melanoma (6,25). One explanation is that iron has important functions in mammalian cells, such as cell proliferation, metabolism and growth (6,25). Iron- and heme-containing proteins, including the enzymes involved in DNA stability and cell cycle progression, the mitochondrial enzymes implicated in respiratory complexes, and detoxifying enzymes such as peroxidase and catalase, control these processes (25). For example, heme-iron can promote endogenous production of nitrous compounds and catalyze free radical formation, leading to oxidative cell damage (25). Iron is one of the pro-inflammatory components in the DII.

A high intake of omega-6 and PUFA was observed in this study in patients with OSCC compared with control subjects. Omega-6 metabolism produces arachidonic acid (AA), which makes inflammatory prostaglandins and lipoxins by oxidation. In contrast, sources of omega-3 have anti-inflammatory activities (26). There is evidence that food components such as α-linolenic acid, omega-3 and omega-6 PUFAs, conjugated linoleic acid, butyrate, curcumin, resveratrol, genistein, vitamin A, vitamin D, etc., can regulate inflammatory processes (26,27).

Our results showed a higher ratio of omega-6 to omega-3 fatty acids in oral cancer patients. Our previous experimental work showed that tumors of DMBA-induced mice fed chia oil (enriched omega-3) reduced the ω-6/ω-3 ratio and decreased tumor development (28). The relationship between omega-6 and omega-3 could modify the action of carcinogenic factors and decrease the risk of oral cancer development (28). In Western populations the ω-6/ω-3 ratio varies from 10:1 to 20-25:1, while in populations such as the Japanese this ratio is much lower, i.e., around 4:1 (29). *In vivo* and *in vitro* animal studies have shown that the balance between ω-6 and ω-3 PUFAs has an impact on the development of cancers such as prostate cancer (29). In human feeding studies with fish or fish oil, EPA and DHA partially replace ω-6 PUFAs, especially AA, probably in the membranes of all cells (27). Given that in Western diets the amount of ω-6 is greater than in other populations, eicosanoids obtained from the metabolic pathway of AA are present in greater quantities than those produced by ω-3 PUFAs (28). It is known that LA and ALA are not exchangeable compounds that compete for Δ6-desaturase, an enzyme that participates in the elongation of the hydrocarbon chains of PUFAs. In addition, it is known that the activity of desaturases Δ6 and Δ5 is the main factor controlling the conversion of dietary LA to AA (28).

In our study we also observed that selenium (Se) intake was increased in patients with OSCC. Experiments *in vivo*, *in vitro*, and in healthy persons have shown that Se is involved in the regulation of epigenetic mechanisms (30). These studies have determined that high exposure to Se leads to inhibition of DNA methyltransferase activity, and affects methylation of specific tumor suppressor genes, among other pathways studied (30).

Several of the dietary components observed in this study participate in epigenetic events. These include vitamin B6, omega-6 and omega-3 PUFAs, and Se, among others. The dietary modulation of the epigenome is related to the processes involving the metabolism of one-carbon moieties. Methylation reactions catalyzed by methyltransferases depend on a set of methyl-S-adenosylmethionine (SAM) amino acids in the human body. Methyl-tetrafolate is a methyl donor group that converts homocysteine to methionine (30). Methionine activates SAM by means of methionine-adenosyltransferase, adding a methylated cytosine group. This addition of the methyl group is a complex process that can be affected by several dietary factors including folate, methionine, and several B vitamins (B2, B6 and B12). This is why the factors consumed in the diet that are related to the methyl group can participate in epigenetic changes (31,32).

Our study showed a relationship between E-DII and risk of OSCC. Other cancers such as gastric, prostate and colorectal cancer also have evinced this relationship (33-35). It is known that inflammation is associated with the development of most cancers; and the inflammatory tumor microenvironment is related to several factors such as infections, tobacco smoking, and excessive alcohol consumption, all of which increase cancer risk and encourage malignant progression (1,6,8). In a study conducted in Japan a positive association was observed between increasing E-DII scores and overall upper aerodigestive tract cancers, as well as across anatomic subsites. For upper aerodigestive tract cancers the OR_{Q4vsQ1} was 1.73 (95% CI: 1.37-2.20); for head and neck cancer the OR_{Q4vsQ1} was 1.92 (95% CI: 1.42-2.59); and for esophageal cancer the OR_{Q4vsQ1} was 1.71 (95% CI: 1.54-1.90). The risks for hypopharyngeal and nasopharyngeal cancers were greatly elevated: OR_{Q4vsQ1} = 4.05 (95% CI: 1.24-13.25) for hypopharyngeal cancer and OR_{Q4vsQ1} = 4.99 (95% CI: 1.14-21.79) for nasopharyngeal cancer (36).

The limitations of the present study include a small number of cases. The small sample size might result in unstable risk estimates with wide confidence intervals. In addition, the range of E-DII scores was much narrower than seen in other studies (i.e., ≈6 compared to ≈11) (37). Another limitation includes the retrospective character of the case-control design, which is prone to both selection and information biases (38,39).

In conclusion, our results are inconsistent with the null hypothesis of no association between DII and OSCC, suggesting that the inflammatory components of daily diet could be involved in the development of OSCC. These results are consistent with the biological mechanisms described in both experimental and observational studies in OSCC and other types of cancers. There is a need for future research on this topic, including larger studies, especially those with prospective design, to explore the association between dietary inflammatory potential and oral premalignant and malignant lesions.

REFERENCES

1. Brunotto M, Zarate AM, Bono A, Barra JL, Berra S. Risk genes in head and neck cancer: a systematic review and meta-analysis of last 5 years. Oral Oncol 2014;50(3):178-88. DOI: 10.1016/j.oraloncology.2013.12.007
2. Shield KD, Ferlay J, Jemal A, Sankaranarayanan R, Chaturvedi AK, et al. The global incidence of lip, oral cavity, and pharyngeal cancers by subsite in 2012. CA Cancer J Clin 2017;67(1):51-64. DOI: 10.3322/caac.21384
3. Marchioni DML, Fisberg RM, de Góis Filhol JF, Kowalskil LP, de Carvalho MB, et al. Dietary patterns and risk of oral cancer: a case-control study in São Paulo, Brazil. Rev Saúde Pública 2007;41(1):19-26. DOI: 10.1590/S0034-89102007000100004
4. Díaz M, García F, Caro P, Díaz MP. Modelos Mixtos Generalizados para el Estudio de los Determinantes Socioeconómicos del cáncer en Córdoba, Argentina. Estadística Int Stat Educ Institute 2009;135-46.
5. Pou SA, Díaz MD, Osella AR. Applying multilevel model to the relationship of dietary patterns and colorectal cancer: an ongoing case control study in Córdoba, Argentina. Eur J Nutr 2012;51(6):755-64. DOI: 10.1007/s00394-011-0255-7
6. Secchi DG, Aballay LR, Galíndez MF, Piccini D, Lanfranchi H, Brunotto M. Red Meat, Micronutrients and Oral Squamous Cell Carcinoma of Argentine Adult Patients. Nutr Hosp 2015;32(3):1214-21.
7. Perloy A, Maasland DHE, van den Brandt PA, Kremer B, Schouten LJ. Intake of meat and fish and risk of head-neck cancer subtypes in the Netherlands Cohort Study. Cancer Causes Control 2017;28(6):647-56. DOI: 10.1007/s10552-017-0892-0
8. Piemonte E, Lazos J, Belardinelli P, Secchi D, Brunotto M, Lanfranchi-Tizeira H. Oral cancer associated with chronic mechanical irritation of the oral mucosa. Med Oral Patol Oral Cir Bucal 2018;23(2):e151-e160. DOI: 10.4317/medoral.22017
9. Kundu JK, Surh YJ. Emerging avenues linking inflammation and cancer. Free Radic Biol Med 2012;52(9):2013-23. DOI: 10.1016/j.freeradbiomed.2012.02.035
10. Crusz SM, Balkwill FR. Inflammation and cancer: advances and new agents. Nat Rev Clin Oncol 2015;12(10):584-96. DOI: 10.1038/nrclinonc.2015.105
11. Iyengar NM, Gucalp a, Dannenberg AJ, Hudis CA. Obesity and cancer mechanisms: tumor microenvironment and inflammation. J Clin Oncol 2016;34(35):4270-6. DOI: 10.1200/JCO.2016.67.4283
12. Shivappa N, Steck SE, Hurley TG, Hussey JR, Ma Y, Ockene IS, Tabung F, Hébert JR. A population-based dietary inflammatory index predicts levels of C-reactive protein in the Seasonal Variation of Blood Cholesterol Study (SEASONS). Public Health Nutr 2014;17(8):1825-33. DOI: 10.1017/S1368980013002565
13. Vahid F, Shivappa N, Faghfoori Z, Khodabakhshi A, Zayeri F, Hebert JR, Davoodi SH. Validation of a Dietary Inflammatory Index (DII) and Association with Risk of Gastric Cancer: a Case-Control Study. Asian Pac J Cancer Prev 2018;19(6):1471-7.
14. Niclis C, Pou SA, Shivappa N, Hébert JR, Steck SE, Díaz MDP. Proinflammatory Dietary Intake is associated with Increased Risk of Colorectal Cancer: Results of a Case-Control Study in Argentina Using a Multilevel Modeling Approach. Nutr Cancer 2018;70(1):61-8. DOI: 10.1080/01635581.2018.1397710
15. Shivappa N, Niclis C, Coquet JB, Román MD, Hébert JR, Diaz MDP. Increased inflammatory potential of diet is associated with increased odds of prostate cancer in Argentinian men. Cancer Causes & Control 2018;29(9):803-13. DOI: 10.1007/s10552-018-1056-6
16. Shivappa N, Hebert JR, Rosato V, Garavello W, Serraino D, La Vecchia C. Inflammatory potential of diet and risk of oral and pharyngeal cancer in a large case-control study from Italy. Int J Cancer 2017;141(3):471-9. DOI: 10.1002/ijc.30711
17. Navarro A, Osella AR, Guerra V, Muñoz SE, et al. Reproducibility and Validity of a Food-Frequency Questionnaire in Assessing Dietary Intakes and Food Habits in Epidemiological Cancer Studies in Argentina. J Exp Clin Cancer Res 2001;20:203-8.
18. Navarro A, Cristaldo P, Díaz MP, Eynard A. Atlas fotográfico para cuantificar el consumo de alimentos y nutrientes en estudios nutricionales epidemiológicos en Córdoba, Argentina. Rev Fac Cienc Med 2000;57:67-74.
19. Peyrano M, Gigena J, Muñoz SA. A computer software system for the analysis of dietary data in cancer epidemiological research. In: Moraes M. Brentani R, Bevilaqcua R, eds. International proceedings division. Bologna: Monduzzi Editore, 1998, pp.381-4.
20. Shivappa N, Steck SE, Hurley TG, Hussey JR, Hebert JR. Designing and developing a literature-derived, population-based dietary inflammatory index. Public Health Nutr 2014;17(8):1689-96. DOI: 10.1017/S1368980013002115
21. Cavicchia PP, Steck SE, Hurley TG, Hussey JR, Ma Y, et al. A new dietary inflammatory index predicts interval changes in serum high-sensitivity C-reactive protein. J Nutr 2009;139(12):2365-72. DOI: 10.3945/jn.109.114025
22. Kim HS, Sohn C, Kwon M, Na W, Shivappa N, Hébert JR, Kim MK. Positive Association between Dietary Inflammatory Index and the Risk of Osteoporosis: Results from the KoGES_Health Examinee (HEXA) Cohort Study. Nutrients 2018;17:10(12). DOI: 10.3390/nu10121999

23. Berger NA. Obesity and cancer pathogenesis. Ann N Y Acad Sci 2014;1311:57-76. DOI: 10.1111/nyas.12416
24. Schottenfeld D, Beebe-Dimmer J. Chronic inflammation: a common and important factor in the pathogenesis of neoplasia. CA Cancer J Clin 2008;56(2):69-83. DOI: 10.3322/canjclin.56.2.69
25. Zhang C, Zhang F. Iron homeostasis and tumorigenesis: molecular mechanisms and therapeutic opportunities. Protein Cell 2015;6(2):88-100. DOI: 10.1007/s13238-014-0119-z
26. Dinarello CA. Anti-inflammatory Agents: Present and Future Cell 2010;140(6):935-50. DOI: 10.1016/j.cell.2010.02.043
27. Nosrati N, Bakovic M, Paliyath G. Molecular Mechanisms and Pathways as Targets for Cancer Prevention and Progression with Dietary Compounds. Int J Mol Sci 2017;25:18(10). DOI: 10.3390/ijms18102050
28. Scherma ME, Madzzuduli G, Silva RA, Garay MI, Repossi G, et al. The effects of ω-6 and ω-3 fatty-acids on early stages of mice DMBA submandibular glands tumorigenesis. Prostaglandins Leukot Essent Fatty Acids 2017;125:48-55. DOI: 10.1016/j.plefa.2017.08.004
29. Kobayashi N, Barnard JR, Hennings SM, Elashoff D, Reddy ST, et al. Effect of altering dietary ω6/ω3 fatty acid ratios on prostate cancer membrane composition cycloxygenase2 and prostaglandin E2. Clin Cancer Res 2006;12(15):4662-70. DOI: 10.1158/1078-0432.CCR-06-0459
30. Jabłonska E, Reszka E. Selenium and Epigenetics in Cancer: Focus on DNA Methylation. Adv Cancer Res 2017;136:193-234. DOI: 10.1016/bs.acr.2017.07.002
31. Feller L, Altini M, Lemmer J. Inflammation in the context of oral cancer. Oral Oncology 2013;49:887–92. DOI: 10.1016/j.oraloncology.2013.07.003
32. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. Cell 2010;140(6):883-99. DOI: 10.1016/j.cell.2010.01.025
33. Shivappa N, Hébert JR, Ferraroni M, La Vecchia C, Rossi M. Association between Dietary Inflammatory Index and Gastric Cancer Risk in an Italian Case-Control Study. Nutr Cancer 2016;16:1-7. DOI: 10.1080/01635581.2016.1224367
34. Zucchetto A, Gini A, Shivappa N, Hébert JR, Stocco C et al. Dietary inflammatory index and prostate cancer survival. Int J Cancer 2016;139(11):2398-404. DOI: 10.1002/ijc.30208
35. Shivappa N, Zucchetto A, Montella M, Serraino D, Steck SE, et al. Inflammatory potential of diet and risk of colorectal cancer: a case-control study from Italy. Br J Nutr 2015;14114(1): 152-8. DOI: 10.1017/S0007114515001828
36. Abe M, Shivappa N, Ito H, Oze I, Abe T, et al. Dietary inflammatory index and risk of upper aerodigestive tract cancer in Japanese adults. Oncotarget 2018;(35):24028-40. DOI: 10.18632/oncotarget.25288
37. Hebert JR, Shivappa N, Wirth MD, Hussey JR, Hurley TG. Perspective: The Dietary Inflammatory Index (DII®): Lessons Learned, Improvements Made and Future Directions. Adv Nutr 2019;10(2):185-95. DOI: 10.1093/advances/nmy071
38. Austin H, Flanders WD, Rothman KJ. Bias arising in case-control studies from selection of controls from overlapping groups. Int J Epidemiol 1989;18(3):713-6. DOI: 10.1093/ije/18.3.713
39. Ge I, Rudolph A, Shivappa N, Flesch-Janys D, Hebert JR, Chang-Claude J. Dietary inflammation potential and postmenopausal breast cancer risk in a German case-control study. Breast 2015;24(4):491-6. DOI: 10.1016/j.breast.2015.04.012

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ARÁN

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Trabajo Original

Otros

Calidad de vida relacionada con la salud, variables psicosociales y rendimiento académico en mujeres de edad escolar practicantes de danza. Un estudio comparativo

Health-related quality of life, psychosocial variables, and academic performance in school-age girls who practice dancing. A comparative study

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Resumen

Introducción: el desarrollo psicosocial afecta a la calidad de vida relacionada con la salud (CVRS) y el rendimiento académico (RA).

Objetivo: determinar si existen diferencias en cuanto a niveles de autoestima, insatisfacción con la imagen corporal y CVRS entre niñas practicantes de danza, niñas practicantes de deportes y niñas que no realizan actividad física y determinar la asociación entre estas variables y el RA.

Método: participaron 252 niñas de entre 9 y 14 años, divididas en tres grupos: no practicantes de actividad física (NAF, n = 99, 10,25 ± 1,10 años, IMC = 21,97 ± 11,69 kg/m^2), practicantes de deporte (DEP, n = 82, 10,54 ± 1,19 años, IMC = 21,36 ± 3,99 kg/m^2) y practicantes de danza (DAN, n = 71, 10,51 ± 1,2 años, IMC= 20,08 ± 3,68 kg/m^2), y se realizaron mediciones antropométricas, psicosociales, de la CVRS y del RA.

Resultados: el puntaje de CVRS ($p < 0,001$) y de autoestima global ($p = 0.001$) fue mayor en las niñas practicantes de danza. En relación a las preguntas sobre calidad de vida; ¿Te has sentido bien y en buen estado físico? (38,0%, $p = 0,007$); ¿Te ha ido bien en el colegio? (31,0%, $p = 0,010$); ¿Has sido capaz de poner atención? (39,4%, $p = 0,023$) las escolares practicantes de danza eligieron la respuesta "muchísimo" en mayor proporción. Los resultados del análisis de regresión lineal mostraron que la CVRS (B = 0,023, $p = 0,001$) y la autoestima escolar (B = 0,054, $p = 0,010$) presentan asociación con el RA.

Conclusión: las escolares practicantes de danza presentaron mayor autoestima, CVRS y percepción de bienestar físico y escolar. Esto indica que la práctica de la danza es una actividad que puede favorecer el desarrollo psicosocial y la adaptación escolar.

Palabras clave:

Calidad de vida relacionada con la salud. Autoestima. Imagen corporal. Rendimiento académico.

Abstract

Introduction: psychosocial development affects health-related quality of life (HRQoL) and academic performance (AP).

Objective: to determine differences in self-esteem, body image dissatisfaction, and HRQoL between girls who practice dancing, girls who play sports, and girls who perform no physical activity and to determine the association between these variables and AP.

Method: 252 girls between 9 and 14 years of age were enrolled into three groups: no physical activity (NAF, n = 99, 10.25 ± 1.10 years, BMI = 21.97 ± 11.69 kg/m^2), sports (DEP, n = 82, 10.54 ± 1.19 years, BMI = 21.36 ± 3.99 kg/m^2), and dancing (DAN, n = 71, 10.51 ± 1.2 years, BMI = 20.08 ± 3.68 kg/m^2), and anthropometric parameters, psychosocial variables, HRQoL, and AP were measured.

Results: HRQoL scores ($p < 0.001$) and global self-esteem ($p = 0.001$) were higher for girls who practiced dancing. Regarding HRQoL-related questions; Have you felt well and in good physical condition? (38.0%, $p = 0.007$); Are you doing well in school? (31.0%, $p = 0.010$); have you been able to pay attention? (39.4%, $p = 0.023$), girls who practiced dancing reported the highest proportion of "very much" responses. The results of a multiple regression analysis showed that HRQoL (B = 0.023, $p = 0.001$) and school self-esteem (B = 0.054, $p = 0.010$) were associated with AP.

Conclusion: girls who practice dancing have greater self-esteem, HRQoL, and physical and school well-being. This suggests that practicing dancing is an activity that may potentially improve psychosocial well-being and school adaptation.

Key words:

Health-related quality of life. Self-esteem. Body image. Academic performance.

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INTRODUCCIÓN

La calidad de vida relacionada con la salud (CVRS) se define como la evaluación de la percepción individual sobre la posición en la vida. Se presenta en niños y adolescentes como un concepto multidimensional que abarca elementos de bienestar físico, cognitivo, social, emocional y conductual (1,2). En este sentido, la actividad física (AF) se ha relacionado con una mejor CVRS, presentándose como un factor protector (3) y se ha demostrado que una mayor frecuencia de AF en los programas escolares se asocia a una mejor CVRS (4,5).

El rendimiento académico (RA), por su parte, está condicionado por diversos factores, destacándose la autoestima como un factor de gran influencia (6) que potencia la seguridad del estudiante y media en la motivación por el logro, presentándose como indicador de éxito influyente en la CVRS. En este sentido, la autoestima se define como un componente afectivo y evaluativo que se otorga a la percepción de uno mismo y que afecta al aspecto físico, emocional, social y cognitivo (7), siendo un propósito fundamental favorecer su desarrollo en las etapas tempranas. Por otro lado, la imagen corporal es una representación mental y valoración del cuerpo (8); se construye desde la infancia y su alteración limita el desarrollo integral en los adolescentes (9), registrándose en las mujeres un mayor riesgo de insatisfacción con la imagen corporal (8,10) y de baja autoestima (11) en comparación con los varones.

Hoy en día, la evidencia señala que los mayores niveles de AF se asocian a mejores resultados en las variables psicosociales (12), mejorando de esta manera el desarrollo integral de los escolares. Además, la AF se ha asociado a mejor funcionamiento cerebral, concentración y atención (13), consiguiendo mejores resultados en las diversas etapas educativas (14). Se recomienda que los niños acumulen diariamente al menos 60 minutos de AF de intensidad moderada a vigorosa, pudiendo esta abarcar distintos tipos de actividades recreativas (15). En este sentido, en los escolares, la práctica de la danza se ha asociado a una adecuada imagen corporal, autoestima (16) y educación emocional (17). Sin embargo, los estudios que incorporan la CVRS y realizan comparaciones con otros tipos de AF, como la práctica deportiva, han sido más escasos. Por ello, el propósito de este estudio fue determinar si existen diferencias en los niveles de autoestima, insatisfacción con la imagen corporal y CVRS entre niñas practicantes de danza, niñas que practican deportes y niñas que no realizan AF. Además, el segundo objetivo fue determinar la asociación entre estas variables y el RA.

MATERIAL Y MÉTODOS

PARTICIPANTES

En este estudio de tipo transversal comparativo, con muestreo intencionado no probabilístico, participaron de forma voluntaria 252 niñas de entre 9 y 14 años de edad, pertenecientes a un establecimiento educativo de la ciudad de Temuco (Chile).

Una vez establecida la muestra (n = 252), se formaron tres grupos de acuerdo con la modalidad y frecuencia de la AF según las recomendaciones de la OMS (15): en el primer grupo, las participantes no realizan ningún tipo de AF fuera del horario escolar (NAF, n = 99, 10,25 ± 1,10 años, IMC = 21,97 ± 11,69 kg/m^2); el segundo grupo lo integran participantes en talleres deportivos que realizan AF 3-5 horas semanales, 2-3 veces/semana (DEP, n = 82, 10,54 ± 1,19 años, IMC = 21,36 ± 3,99 kg/m^2), en disciplinas tales como patinaje, básquetbol, fútbol, gimnasia artística, voleibol y artes marciales; finalmente, el tercer grupo lo forman practicantes de danza que realizan esta actividad 2-5 horas semanales, 1-3 veces/semana (DAN, n = 71, 10,51 ± 1,2 años, IMC = 20,08 ± 3,68 kg/m^2), en las variantes de danza contemporánea, ballet y folklore.

Los criterios de inclusión utilizados fueron: a) tener entre 9 y 14 años de edad; b) consentimiento informado del progenitor/tutor; c) asentimiento de la participante; y d) estar matriculada en el establecimiento del estudio. Como criterios de exclusión se establecieron: a) padecer de alguna discapacidad física, sensorial y/o mental; b) estar ausente el día de la evaluación; y c) actividades extracurriculares el mismo día. Del total de las participantes iniciales (n = 261) 9 fueron excluidas según los criterios de inclusión y exclusión, obteniéndose finalmente una muestra de 252 niñas (Fig. 1).

Todas las escolares evaluadas contaban con al menos un semestre de práctica en el grupo asignado; la información fue dada por las escolares en el momento de recibir los documentos de autorización y corroborada por los datos del registro de asistencia entregados por el coordinador de actividades extracurriculares del establecimiento.

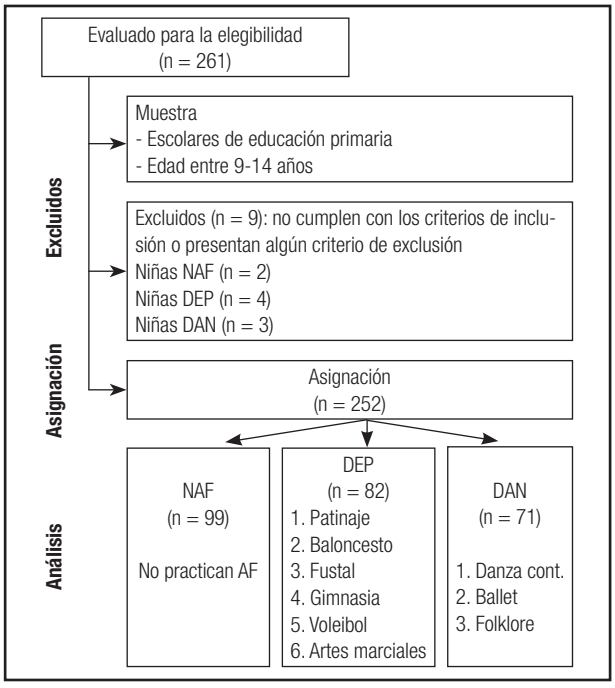

Figura 1.
Diseño del estudio.

La investigación respetó los acuerdos de la declaración de Helsinki del año 2013 y fue aprobada por el comité de ética de la Universidad de La Frontera. Todos los participantes recibieron explicaciones verbales del programa y de las pruebas antes del inicio de este estudio.

INSTRUMENTOS

Antropometría

Para evaluar masa corporal (kg) se utilizó una balanza digital OMROM (modelo HN-289LA, Kyoto, Japón), con una precisión de 0,1 kg y una capacidad máxima de 150 kg. La talla (cm) se midió con un estadiómetro SECA (modelo 206, Hamburgo, Alemania). El índice de masa corporal (IMC) se determinó mediante la fórmula: masa corporal/talla^2 (kg/m^2) (18).

Autoestima

Para la medición de la variable autoestima se utilizó el inventario de autoestima de Coopersmith para escolares, validado en niños chilenos (19). El mayor puntaje indica un nivel más alto de autoestima. Consta de la valoración de la autoestima global, que comprende cuatro subescalas:

- Autoestima general (AG): rango de aceptación con que se estiman las conductas autodescriptivas (26 ítems).
- Autoestima social (AS): hace referencia a la relación con los pares, valorando el modo de actuar en las interacciones de acuerdo con el contexto (8 ítems).
- Autoestima familiar (AF): autopercepción de la relación con los familiares directos (8 ítems).
- Autoestima escolar (AE): nivel de conformidad con que se valora la relación con los compañeros y docentes en el medio escolar, enfocándose en la satisfacción que le otorgan sus habilidades como estudiante, como compañera y en cada rol que desempeñe en el contexto escolar (8 ítems) (19).

Calidad de vida relacionada con la salud

La evaluación de la CVRS se realizó mediante el cuestionario autocumplimentado Kidscreen 10 (20), creado para niños y adolescentes de 8 a 18 años, que es una versión abreviada del Kidscreen 27. Mide la CVRS desde lo multidimensional, evaluando el punto de vista del niño con respecto a su bienestar físico y psicológico, su autonomía y su relación con padres, amigos, entorno social y entorno escolar. Posee 12 preguntas evaluables con una escala de cantidad y frecuencia de tipo Likert, puntuada de 0 a 4 (0: nada/nunca; 1: un poco/casi nunca; 2: moderadamente/algunas veces; 3: mucho/casi siempre; 4: muchísimo/siempre).

Imagen corporal

La insatisfacción con la imagen corporal se evaluó mediante el cuestionario *Body Shape Questionnaire* (BSQ), creado por Cooper, Taylor, Cooper y Fairburn en 1987. Identifica la insatisfacción con la imagen corporal, indicando los puntajes más altos mayor insatisfacción (21). Comprende 34 preguntas evaluadas con escala Likert de frecuencia: 1: nunca; 2: raramente; 3: a veces; 4: a menudo; 5: muy a menudo; 6: siempre. La puntuación fluctúa entre 34 y 204.

Rendimiento académico

La medición del nivel de RA se realizó mediante el reporte del promedio de calificaciones escolares como criterio válido de medición, siendo esta variable muy utilizada en el ámbito educativo y de la investigación para aproximarse al RA (22). Se empleó el reporte semestral obtenido del promedio de todas las asignaturas cursadas en el primer semestre lectivo de 2018 (marzo a julio), accediéndose al mismo a través de la plataforma de registro de notas del establecimiento.

PROCEDIMIENTO

La recolección de datos se realizó durante el periodo de agosto-octubre de 2018 en el establecimiento escolar donde se encontraban matriculadas las participantes. En primera instancia se evaluaron las variables psicosociales y antropométricas; posteriormente se accedió al reporte de notas del primer semestre del año escolar en curso. Los cuestionarios se aplicaron en una sala reservada y acondicionada especialmente para la evaluación, con horarios y fechas diferidas durante la jornada escolar en el periodo de agosto a octubre, sujeto todo ello a las condiciones del establecimiento en lo que respecta a horarios y actividades internas. La evaluación de los datos antropométricos se realizó con las participantes descalzas, vestidas con short o falda y camiseta. Finalmente, para la obtención de datos referentes al desempeño académico, se accedió a la plataforma de registro de notas con la previa autorización de la Unidad Técnico-Pedagógica del establecimiento. El proceso de recolección de datos estuvo a cargo de un profesional docente y un asistente educativo, capacitados antes de la evaluación. Los grupos de evaluación oscilaron entre 15 y 25 estudiantes, organizados por edad y curso/nivel.

ANÁLISIS ESTADÍSTICO

Para el análisis de datos se utilizó el programa SPSS v.23.0 (SPSS™, IBM Corporation, NY, EE. UU.). En primera instancia se analizó la distribución de los datos mediante la prueba de Kolmogorov-Smirnov. Los datos se reportaron como media ± desviación estándar (DE). La diferencia entre grupos se determinó mediante un análisis de la varianza (ANOVA) con el *post hoc* de Bonferroni.

La relación entre variables se determinó a través de la correlación de Pearson y el respectivo modelo de regresión lineal; se aplicó la prueba del χ^2 en preguntas específicas de las dimensiones del cuestionario de CVRS (KIDSCREEN 10). Se consideraron estadísticamente significativos los resultados con $p < 0,05$.

RESULTADOS

En la tabla I se muestran las comparaciones de las variables del estudio según al tipo de AF (NAF *vs*. DEP *vs*. DAN). Se hallaron diferencias significativas en el nivel de autoestima global (NAF: 29,40 ± 6,72; DEP: 31,28 ± 5,90; DAN: 34,51 ± 6,67, $p < 0,001$) y en sus subescalas, siendo mejores los resultados del grupo DAN: AG (18,15 ± 3,99, $p < 0,001$), AS (5,46 ± 1,53, $p = 0,009$), AF (5,49 ± 1,77, $p = 0,001$), AE escolar (5,39 ± 1,64, $p = 0,004$). El grupo NAF muestra la AS más baja (4,79 ± 1,26, $p = 0,009$). La CVRS muestra diferencias significativas (NAF: 37,33 ± 4,95; DEP: 38,77 ± 5,22; DAN: 40,41 ± 5,07, $p = 0,001$), registrando el grupo DAN los mejores resultados. No hubo diferencias en la insatisfacción por la imagen corporal (NAF: 75,14 ± 36,79; DEP: 74,52 ± 31,98; DAN: 64,86 ± 28,59, $p = 0,099$). De igual modo, el RA no mostró diferencias significativas (NAF: 5,82 ± 0,44; DEP: 5,81 ± 0,52; DAN: 5,97 ± 0,49; $p = 0,080$) (Tabla I).

La tabla II muestra los resultados de bienestar físico de la CVRS en aquellas preguntas en que se produjeron diferencias significativas según el KIDSCREEN-10. En el análisis de las preguntas "¿Te has sentido bien y en buen estado físico?" (38,0%, $p = 0,007$), "¿Te ha ido bien en el colegio?" (31,0%, $p = 0,010$) y "¿Has sido capaz de poner atención?" (39,4%, $p = 0,023$), el grupo DAN obtuvo la mayor proporción de respuestas "muchísimo".

La tabla III muestra los grados de correlación entre la CVRS y las subescalas de autoestima. La correlación más alta fue la de la CVRS con la AG ($r = 0,59$, $p < 0,001$). El RA presentó las correlaciones más altas con la autoestima escolar ($r = 0,30$, $p < 0,001$) y la CVRS ($r = 0,326$, $p < 0,001$). La insatisfacción con la imagen corporal mostró distintos grados de correlación negativa con las subescalas de autoestima, siendo la más alta la obtenida con la autoestima global ($r = -0,35$, $p < 0,001$); también presentó correlación con la CVRS ($r = -0,38$, $P < 0,001$).

Los resultados del análisis de regresión múltiple mostraron que la CVRS ($B = 0,023$, $P = 0,001$) y la AE ($B = 0,054$, $p = 0,010$) presentan asociación con el RA (Tabla IV).

DISCUSIÓN

El propósito del estudio fue determinar si existen diferencias en los niveles de autoestima, insatisfacción con la imagen corporal y CVRS entre niñas practicantes de danza, niñas practicantes de deportes y niñas que no realizan AF.

Tabla I. Comparación de las variables del estudio según la categoría de actividad física

	NAF (n = 99) A	DEP (n = 82) B	DAN (n = 71) C	Valor p	*Post hoc*
Parámetros antropométricos					
Edad (años)	10,25 ± 1,10	10,54 ± 1,19	10,51 ± 1,22	0,197	-
Peso (kg)	44,31 ± 10,89	47,07 ± 11,93	43,44 ± 10,47	0,101	-
Talla (cm)	142,75 ± 19,07	148,04 ± 10,03	147,35 ± 8,01	0,222	-
IMC (kg/m^2)	21,97 ± 11,69	21,36 ± 3,99	20,08 ± 3,68	0,305	-
Variables psicosociales					
Autoestima general (pts.)	15,61 ± 4,34	16,34 ± 3,58	18,15 ± 3,99	< 0,001	A,B<C
Autoestima social (pts.)	4,79 ± 1,26	5,10 ± 1,46	5,46 ± 1,53	0,009	A<B<C
Autoestima familiar (pts.)	4,45 ± 1,87	5,05 ± 1,69	5,49 ± 1,77	0,001	A<B<C
Autoestima escolar (pts.)	4,56 ± 1,53	4,79 ± 1,71	5,39 ± 1,64	0,004	A,B<C
Autoestima global (pts.)	29,40 ± 6,72	31,28 ± 5,90	34,51 ± 6,67	< 0,001	A<B<C
Insatisfacción corporal (pts.)	75,14 ± 36,79	74,52 ± 31,98	64,86 ± 28,59	0,099	-
Rendimiento académico					
RA (media)	5,82 ± 0,44	5.81 ± 0,52	5,97 ± 0,49	0,080	-
Calidad de vida					
CVRS (pts.)	37,33 ± 4,95	38,77 ± 5,22	40,41 ± 5,07	0,001	A,B<C

Datos presentados como media ± DE. Los valores de $p < 0,05$ se consideran estadísticamente significativos. NAF: sin actividad física; DEP: participan en talleres deportivos; DAN: practican danza; A: grupo de niñas NAF, B: grupo de niñas DEP, C: grupo de niñas DAN, para el análisis post hoc; IMC: índice de masa corporal; RA: rendimiento académico; CVRS: calidad de vida relacionada con la salud.

Tabla II. Comparación de proporciones en las preguntas de calidad de vida KIDSCREEN-10

	NAF (n = 99)		DEP (n = 82)		DAN (n = 71)		Valor p
¿Te has sentido bien y en buen estado físico?							
	n	**%**	**n**	**%**	**n**	**%**	
Nada	3	3,10%	4	4,90%	0	0,00%	0,007
Un poco	18	18,40%	14	17,10%	5	7,00%	
Moderadamente	31	31,60%	15	18,30%	16	22,50%	
Mucho	30	30,60%	33	40,20%	23	32,40%	
Muchísimo	16	16,30%	16	19,50%	27	38,00%	
Total	98	100,00%	82	100,00%	71	100,00%	
¿Te ha ido bien en el colegio?							
Nada	0	0,00%	1	1,20%	0	0,00%	0,010
Un poco	12	12,10%	9	11,00%	1	1,40%	
Moderadamente	47	47,50%	31	37,80%	24	33,80%	
Mucho	30	30,30%	26	31,70%	24	33,80%	
Muchísimo	10	10,10%	15	18,30%	22	31,00%	
Total	99	100,00%	82	100,00%	71	100,00%	
¿Has sido capaz de poner atención?							
Nada	0	0,00%	2	2,40%	0	0,00%	0,023
Un poco	3	3,00%	3	3,70%	0	0,00%	
Moderadamente	26	26,30%	18	22,00%	6	8,50%	
Mucho	47	47,50%	36	43,90%	37	52,10%	
Muchísimo	23	23,20%	23	28,00%	28	39,40%	
Total	99	100,00%	82	100,00%	71	100,00%	

Datos presentados como n (%). Prueba chi², una p < 0,05 representa una diferencia significativa. NAF: sin actividad física; DEP: participan en talleres deportivos; DAN: practican danza.

Tabla III. Correlación lineal entre autoestima, imagen corporal, rendimiento académico y calidad de vida

	AG	AS	AF	AE	A global	IIC	RA	CVRS
Autoestima general	1	0,220**	0,467**	0,404**	0,883**	-0,328**	0,137*	0,476**
Autoestima social		1	0,298**	0,245**	0,487**	-0,119	0,131*	0,228**
Autoestima familiar			1	0,423**	0,723**	0,273**	0,241**	0,508**
Autoestima escolar				1	0,658**	-0,222**	0,300**	0,480**
Autoestima global					1	-0,354**	0,250**	0,594**
Insatisfacción con imagen corporal						1	-0,084	-0,377**
Rendimiento académico							1	0,326**

*Valor presentado como r. **Representa una p < 0,01; *Representa una p < 0,05; una p < 0,05 se considera estadísticamente significativa. AG: autoestima general; AS: autoestima social; AF: autoestima familiar; AE: autoestima escolar; A global: autoestima global; IIC: insatisfacción con imagen corporal; RA: rendimiento académico.*

Tabla IV. Modelo de regresión lineal múltiple del rendimiento académico

	B	IC 95,0%	Valor p
(Constante)	4,661	(4,114-5,208)	< 0,001
Autoestima general	-0,010	(-0,027-0,007)	0,247
Autoestima social	0,010	(-0,032-0,052)	0,644
Autoestima familiar	0,021	(-0,017-0,060)	0,275
Autoestima escolar	0,054	(0,013-0,094)	0,010
Insatisfacción imagen corporal	0,001	(-0,001-0,003)	0,452
Calidad de vida	0,023	(0,009-0,037)	0,001

Valores presentados como B (IC 95,0%), valor de p; una p < 0,05 se considera estadísticamente significativa; IC: intervalo de confianza.

Además, como segundo objetivo, se determinó la asociación entre estas variables y el RA. Los principales hallazgos fueron: a) las escolares que practican danza presentan mejor CVRS y autoestima; b) tienen también una mejor percepción del nivel de bienestar físico y en el entorno escolar; y c) el RA se asocia significativamente a la CVRS y la AE.

En el presente estudio, la CVRS fue mayor en las practicantes de danza que en sus compañeras, lo que coincide con estudios que revelan que la práctica de la danza aumenta el nivel de CVRS en todas sus dimensiones (23). Por ejemplo, en los bailarines profesionales se reporta una CVRS superior a la de los "no bailarines" (24). Asimismo, existen estudios que avalan la práctica de la danza como terapia, reportando positivos resultados en la CVRS (25). En línea con lo anterior, frente a la pregunta "¿Te has sentido bien y en buen estado físico?", las niñas practicantes de danza presentan un mayor % de respuestas positivas; en este sentido, la danza contribuye a mejorar la salud física y mental (26) y el bienestar físico en general (23).

Respecto del entorno escolar de la CVRS, la pregunta "¿Te ha ido bien en el colegio?" revela un mayor % de respuestas positivas entre las practicantes de danza. En relación a lo anterior, se han encontrado resultados similares en grupos de bailarines, que han presentado una mayor CVRS en la dimensión escolar (27). En Grecia, por ejemplo, un programa basado en la danza logra un mayor nivel de CVRS escolar (23). Asimismo, ocho semanas de danza creativa y "danza cerebral" mejoran significativamente la CVRS escolar (28).

En relación con el análisis de la pregunta "¿Has sido capaz de poner atención?", las niñas practicantes de danza reportan mejores resultados. En este sentido, la AF regular contribuye a los procesos de atención de los adolescentes (13), afirmándose que el trabajo coreográfico implica un mayor flujo sanguíneo cerebral que favorece la concentración y la memoria. Por ejemplo, un estudio realizado con bailarines mexicanos evidencia niveles de atención y concentración mayores (29).

En esta línea, en el presente estudio, las niñas practicantes de danza reportaron una mayor autoestima global; sin embargo, en relación con la insatisfacción por la imagen corporal no existieron diferencias con sus compañeras. En este sentido, la evidencia muestra un efecto positivo de la danza sobre la autoestima en las niñas con sobrepeso (16); además, las intervenciones en niños y adolescentes con programas de danza evidencian un aumento significativo de la autoestima (30,31). Por el contrario, un estudio realizado en niñas de edad escolar, practicantes de danza en formación, muestra que estas presentan una imagen corporal alterada que no corresponde con la realidad, siendo estos resultados negativos para su salud mental (32). De igual forma, otro estudio ha reportado que las bailarinas de cursos iniciales y menor edad se ven más gruesas de como están, quieren ser más delgadas de como se ven, pero están más delgadas de lo que les gustaría estar (33). Esto podría favorecer la aparición de trastornos de insatisfacción corporal y es un punto importante a considerar en las actividades relacionadas con la danza infantil.

En el presente estudio, el RA presentó asociación con la CVRS y la AE. En este sentido se han encontrado resultados similares entre la autoestima, la CVRS y el RA (34). Asimismo, algunos estudios donde han participado escolares de América y Europa reportan que las calificaciones más altas se relacionan con una mejor CVRS (2). Del mismo modo se establece que la autoestima y la AF son las más relacionadas con el RA y las que más lo afectan , por lo que deben ser una prioridad en el sistema escolar.

LIMITACIONES

Entre las limitaciones que encontramos en el estudio está su diseño transversal, que no permite extrapolar los resultados y generalizarlos. Sin embargo, como fortaleza encontramos que los resultados permiten aportar algunas variables novedosas sobre los beneficios de la danza en edad escolar, variables que se asocian al RA.

CONCLUSIÓN

En conclusión, en este estudio, las escolares que practican danza presentaron mayor CVRS, autoestima y una mejor percepción de bienestar físico y escolar. Esto indica que la práctica de la danza es una actividad que puede favorecer el desarrollo de las aptitudes psicosociales, la adaptación escolar y el logro académico. Lo anterior plantea la posibilidad de revisar los programas de AF en relación con la danza, con la finalidad de ampliar las experiencias y posibilidades de autovalidarse, potenciando un adecuado desarrollo.

BIBLIOGRAFÍA

1. Degoy E, Berra S. Differences in health-related quality of life by academic performance in children of the city of Cordoba-Argentina. Qual Life Res 2018;27(6):1463-71.
2. Degoy E, Berra S. Differences in health-related quality of life by academic performance in children of the city of Cordoba-Argentina. Qual Life Res 2018;27(6):1463-71
3. Lima-Serrano M, Martínez-Montilla J, Guerra-Martín M, Vargas-Martínez A, Lima-Rodriguez JS. Quality-of-life-related factors in adolescents. Gaceta sanitaria 2018;32(1):68-71.

4. Salvini M, Gall S, Müller I, Walter C, du Randt R, Steinmann P, et al. Physical activity and health-related quality of life among schoolchildren from disadvantaged neighbourhoods in Port Elizabeth, South Africa. Qual Life Res 2018;27(1):205-16.
5. Ra JS, Gang M. Depression moderates between physical activity and quality of life in low-income children. Appl Nurs Res 2016;29:e18-e22.
6. Wang F, Veugelers P. Self–esteem and cognitive development in the era of the childhood obesity epidemic. Obes Rev 2008;9(6):615-23.
7. Wang F, Wild T, Kipp W, Kuhle S, Veugelers P. The influence of childhood obesity on the development of self-esteem. Health Rep 2009;20(2):21-7.
8. Vaquero Cristóbal R, Alacid F, Muyor JM, López Miñarro PA. Imagen corporal; revisión bibliográfica. Nutr Hosp 2013;28(1).
9. Delgado-Floody P, Martínez-Salazar C, Caamaño-Navarrete F, Jerez-Mayorga D, Osorio-Poblete A, García-Pinillos F, et al. Insatisfacción con la imagen corporal y su relación con el estado nutricional, riesgo cardiometabólico y capacidad cardiorrespiratoria en niños pertenecientes a centros educativos públicos. Nutr Hosp 2017;34:1044-9.
10. Jiménez-Flores P, Jiménez-Cruz A, Bacardí-Gascón M. Insatisfacción con la imagen corporal en niños y adolescentes: revisión sistemática. Nutr Hosp 2017;34(2):479-89.
11. Moksnes UK, Espnes GA. Self-esteem and emotional health in adolescents–gender and age as potential moderators. Scand J Psychol 2012;53(6):483-9.
12. Stiglic N, Viner RM. Effects of screentime on the health and well-being of children and adolescents: a systematic review of reviews. BMJ open 2019;9(1):e023191.
13. Pérez-Lobato R, Garrido R, Enrique R, Hernández-Mendo A. Relaciones entre la práctica física, condición física y atención en una muestra adolescente. Revista de psicología del deporte 2016;25(1):179-186.
14. Leandro CR, Monteiro E, Melo F. Interdisciplinary working practices: can creative dance improve math? Research in Dance Education 2018;19(1):74-90.
15. Organization WH. Global recommendations on physical activity for health: World Health Organization; 2010.
16. Monteiro LA, Novaes JS, Santos mL, Fernandes HM. Body dissatisfaction and self-esteem in female students aged 9-15: the effects of age, family income, body mass index levels and dance practice. J Hum Kinet 2014;43(1):25-32.
17. Requena-Pérez CM, Martín-Cuadrado AM, Lago-Marín BS. Imagen corporal, autoestima, motivación y rendimiento en practicantes de danza. Revista de psicología del deporte 2015;24(1).
18. Pizarro T, Rodríguez L, Benavides X. Technical norm for the nutritional evaluation of children aged 6 to 18 years old. Year 2003. Rev chil nutr 2004;31:11-30.
19. Brinkmann H, Segure T, Solar M. Adaptación, estandarización y elaboración de normas para el inventario de autoestima de Coopersmith. Revista Chilena de Psicología 1989;10(1):63-71.
20. Ravens-Sieberer U, Erhart M, Rajmil L, Herdman M, Auquier P, Bruil J, et al. Reliability, construct and criterion validity of the KIDSCREEN-10 score: a short measure for children and adolescents' well-being and health-related quality of life. Qual Life Res 2010;19(10):1487-500.
21. Cooper PJ, Taylor MJ, Cooper Z, Fairbum CG. The development and validation of the Body Shape Questionnaire. International Journal of eating disorders 1987;6(4):485-94. DOI: 10.1002/1098-108X(198707)6:4<485::AID-EAT2260060405>3.0.CO;2-O
22. Edel Navarro R. El rendimiento académico: concepto, investigación y desarrollo. REICE: Revista electrónica Iberoamericana sobre calidad, eficacia y cambio en educación 2003.
23. Lykesas G, Giosos I, Theocharidou O, Chatzopoulos D, Koutsouba M. The Effect of a Traditional Dance Program on Health-Related Quality of Life as Perceived by Primary School Students. J Educ Train Stud 2017;6(1):96-103. DOI: 10.11114/jets.v6i1.2878
24. Kapur N, Rawat MV. Professional Dance in Relation to Quality of Life, Emotional Intelligence and Self Concept. The International Journal of Indian Psychology 2016;3(2):90.
25. Serrano-Guzmán M, Valenza-Peña CM, Serrano-Guzmán C, Aguilar-Ferrándiz E, Valenza-Demet G, Villaverde-Gutiérrez C. Efectos de un programa de terapia de baile en la calidad de vida, el sueño y la presión arterial en mujeres de mediana edad: un ensayo controlado aleatorizado. Med Clin 2016;147(8):334-9. DOI: 10.1016/j.medcli.2016.06.030
26. Sivvas G, Batsiou S, Vasoglou Z, Filippou D-A. Dance contribution in health promotion. Journal of Physical Education and Sport 2015;15(3):484.
27. Nicholson LL, Adams RD, Tofts L, Pacey V. Physical and Psychosocial Characteristics of Current Child Dancers and Nondancers With Systemic Joint Hypermobility: A Descriptive Analysis. J Orthop Sports Phys Ther 2017;47(10):782-91. DOI: 10.2519/jospt.2017.7331
28. Theocharidou O, Lykesas G, Giossos I, Chatzopoulos D, Koutsouba M. The Positive Effects of a Combined Program of Creative Dance and BrainDance on Health-Related Ouality of Life as Perceived by Primary School Students. Physical Culture and Sport Studies and Research 2018;79(1):42-52. DOI: 10.2478/pcssr-2018-0019
29. Orozco-Calderón G, Gil-Alvarado KR. Beneficios cognitivos cerebrales de la práctica de la danza. Ciencia & Futuro 2018;8(3):142-60.
30. Domínguez Cacho C, Castillo Vera E. Relación entre la danza libre-creativa y autoestima en la etapa de educación primaria. Cuadernos de Psicología del Deporte 2017;17(1).
31. Connolly MK, Quin E, Redding E. dance 4 your life: exploring the health and well-being implications of a contemporary dance intervention for female adolescents. Research in Dance Education 2011;12(1):53-66. DOI: 10.1080/14647893.2011.561306
32. Vaquero-Cristóbal R, Kazarez M, Esparza-Ros F. Influence of the dance discipline on body image distortion and dissatisfaction in preadolescents, adolescents and young women dancersInfluencia de la modalidad de danza en la distorsión e insatisfacción de la imagen corporal en bailarinas preadolescentes, adolescentes y jóvenes. Nutr Hosp 2017;34(5):1442-7.
33. Kazarez M, Vaquero-Cristóbal R, Esparza-Ros F. Percepción y distorsión de la imagen corporal en bailarinas españolas en función del curso académico y de la edad. Nutr Hosp 2018;35(3):661-8.
34. Karatzias A, Power KG, Swanson V. Quality of school life: Development and preliminary standardisation of an instrument based on performance indicators in Scottish secondary schools. School Effectiveness and School Improvement 2001;12(3):265-84. DOI: 10.1076/sesi.12.3.265.3449

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Otros

Consumption of meat, eggs and dairy products is associated with aerobic and anaerobic performance in Brazilian athletes – A cross-sectional study

El consumo de carne, huevos y productos lácteos se asocia al rendimiento aeróbico y anaeróbico en los deportistas brasileños: un estudio transversal

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Abstract

Objective: to associate food consumption according to the groups that make up the food pyramid with the aerobic and anaerobic performance of Brazilian athletes.

Method: a cross-sectional study of 168 athletes with a mean age and BMI of 20.84 ± 7.74 years and 22.88 ± 3.1 kg/m², respectively.

Results: maximum power output was significantly associated with the meat and eggs groups ($\beta = 0.31$; $p < 0.05$). VO_{2max} exhibited a positive relationship with the fruit group ($\beta = 0.29$; $p < 0.05$). A significant inverse relation between VO_{2max} and the legumes group was observed ($\beta = -0.76$; $p < 0.05$). The meat and eggs group and the dairy products group had an inverse and significant association with VO_{2max} ($\beta = -0.43$; $p < 0.01$).

Conclusions: consumption of meat and eggs showed a positive association with anaerobic performance, whereas the same group and the dairy products group had a negative association with aerobic performance.

Key words:

Food groups. VO_{2max}. Diet. Food pyramid.

Resumen

Objectivo: asociar el consumo de alimentos según los grupos que componen la pirámide de alimentos con el rendimiento aeróbico y anaeróbico de deportistas brasileños.

Método: estudio transversal de 168 deportistas con una media de edad e IMC de 20,84 ± 7,74 años y 22,88 ± 3,1 kg/m², respectivamente.

Resultados: la potencia máxima se asoció significativamente con el consumo de los grupos de carne y huevos ($\beta = 0,31$; $p < 0,05$). El VO_{2max} mostró una relación positiva con el grupo de la fruta ($\beta = 0,29$; $p < 0,05$). Se observó una relación inversa significativa entre el VO_{2max} y el grupo de las leguminosas ($\beta = -0,76$; $p < 0,05$). El grupo de carnes y huevos y el grupo de productos lácteos tuvieron una asociación inversa y significativa con el VO_{2max} ($\beta = -0,43$; $p < 0,01$).

Conclusiones: el consumo de carne y huevos mostró una asociación positiva con el rendimiento anaeróbico, mientras que el mismo grupo y los productos lácteos se asociaron de forma negativa al rendimiento aeróbico.

Palabras clave:

Grupos de alimentos. VO_{2max}. Dieta. Pirámide alimenticia.

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INTRODUCTION

Proper diet to the amount of physical work should be the starting point for maximum performance for high-performance athletes (1). The adequacy of energy and nutrient consumption is essential to maintaining performance, body composition and health in these individuals (2,3). Nutrition, when well targeted, can reduce fatigue, allowing the athlete to train longer or to recover better between workouts; reduce or assist in recovery from injury; increase energy deposits for competition; and finally help the general health of the athlete (4).

Qualitative food consumption, that is, the consumption seen in portions of the various food groups can affect both the nutritional status and the dietary nutrient supply (5). One of the common behaviors among athletes is the partial or total restriction of certain food groups, resulting in a consumption below that recommended for some nutrients (6) responsible for the regulation of energy metabolism, glucose and oxidative and muscle contraction, thus affecting performance (3,7).

A number of studies involving athletes are concerned with the quantitative consumption of nutrients and their effects on physical performance (8-10), but as far as we know, there are no studies that use food consumption by food groups for this same purpose and population. In 2013, Radavelli-Bagatini et al. (11) showed the association of milk consumption and milk products with performance (gripstrength, timed up and go, slow timed up and go, and self-reported falls) in the elderly. A similar study with adolescents showed that fruit and vegetable consumption was positively associated with muscle strength and potency (12). The results of this type of research may point to both the performance and the health of the population studied, suggesting the adequacy of food consumption to maintain good performance and health maintenance (13,14).

Thus, the objective of this study was to evaluate the association between the intake of the foods in the Brazilian food pyramid groups and the physical aerobic and anaerobic performance of Brazilian athletes. The present study will allow the establishment of relationships among food groups and performance in terms of potency, fatigue index and oxygen volume (VO_2), and will make it possible in the future to establish dietary guidelines specifically formulated for athletes needs.

METHODS

PARTICIPANTS

This was a cross-sectional study carried out at the *Núcleo de Aptidão Física, Informática, Metabolismo, Esporte e Saúde* (Nafimes, Center for Physical Fitness, Informatics, Metabolism, Sports, and Health) from 2014 to 2016. The sample was composed of 168 athletes of both genders, who competed in fifteen different sports (athletics, cycling, bodybuilding, soccer, American football, futsal, Brazilian jiu-jitsu, judo, karate, kung fu, mixed martial arts (MMA), swimming, taekwondo, triathlon and volleyball).

Athletes were contacted directly via phone calls or e-mail, and through indications from coaches or sporting federations. Convenience sampling was used, i.e., the participant athletes were selected based on availability and accessibility after contacting sports federations, clubs and coaches. Individuals who trained with competitive objectives, participated in regional and international events, or had a weekly training load equal to or greater than 6 hours were considered athletes (15). Athletes who did not respond to two 24-hour recalls (R24h) were excluded. All athletes (adults and under 18) and those responsible for athletes under the age of 18 years were informed of the study objectives and signed an informed consent form. Demographic (age and sex) and training (type of sport, volume, training phase) information was obtained through a questionnaire. This investigation was conducted according to the Declaration of Helsinki and was approved by the local University Ethics Committee (no. 488.198).

BODY COMPOSITION

Body mass was measured to the nearest 0.1 kg using a calibrated electronic scale, and height was measured using a stadiometer to the nearest 0.1 cm. The participants wore light clothing without shoes. Body mass index (BMI) was calculated as the body mass in kilograms divided by the square of the height in meters.

DIETARY INTAKE

Food intake was assessed by the 24-hour dietary recall method applied on two non-consecutive days of the week, with the aid of a photographic record taken during an interview (16). The homemade measurements of the nutritional values of foods and supplementations were converted into grams and milliliters by the online software Virtual Nutri Plus (Keeple®, Rio de Janeiro, Brazil). Some foods were not found in the program database and therefore items were added from food tables (17). Participants who used dietary supplements were instructed to report the brand and quantity consumed in order to ensure a higher accuracy of the macronutrient values present in each product. For the determination of food portions, the criterion of the Brazilian food pyramid was used (18). Foods are distributed in the food pyramid within eight groups, and each food group has a portion with a certain amount of calories. In this way, the foods consumed were quantified as total calories and later transformed into portions according to their characteristics. For supplements, the source of the nutrient with the highest prevalence in these was used to identify which group they belonged to, and to account for the caloric equivalent of their respective group.

AEROBIC AND ANAEROBIC PERFORMANCE

Anaerobic performance (maximum power) was obtained by using the Running Anaerobic Sprint Test (RAST), consisting of maximum sprints of 35 meters with 10 seconds of recovery between each sprint. The time recording was performed by photocells at each effort to determine the power generated at each run (HIDROFIT model PTL-BM 2 SK-D, software Multisprint full version 3.5.7, Brazil) (19). The RAST results provide an estimate of the

neuromuscular and energetic determinants of maximal anaerobic performance (19).

Power produced in each sprint was calculated by the formula (19):

$$\text{Power (watts)} = (\text{body mass} \times \text{distance}^2)/\text{time}^3$$

$$\text{Maximum power (w.kg}^{-1}) = \text{highest power produced in the six races.}$$

The aerobic performance (VO_{2max}) was obtained by means of the 20-m shuttlerun test consisting of one-minute continuous run steps, with increased velocity during the test. It is requested that the individual run in an area of 20 meters marked in two points, maintaining the pace of running with a sound signal that is emitted. The test stops when the participant fails and cannot pass by a 20-meter point before the beep occurs twice in a row (20).

The maximum volume of expired oxygen was estimated in mL.kg^{-1}.min^{-1} using the equations proposed by Léger et al. (1988) (21), as described below:

- From 6 to 18 years: VO_{2max} (mL.kg^{-1}.min^{-1}) = 31.025 + (3.238 x speed in km.h^{-1} in the last completed stage) - (3.248 x age in years rounded down) + (0.1536 x speed in km.h^{-1} in the last stage completed x age in years rounded down).
- Over 18 years: VO_{2max} (mL.kg^{-1}.min^{-1}) = -27.4 + (6.0 x speed in km.h^{-1} in the last completed stage).

STATISTICAL ANALYSIS

The Kolmogorov-Smirnov test was used to verify data distribution. Descriptive statistics are presented as mean and standard deviation. Differences in general characteristics, eating habits, and average training time according to sex were determined using the Mann-Whitney U-test, and the Kruskal-Wallis test was performed to evaluate the other analyses. For all statistical analyses, significance was accepted at $p < 0.05$. The data were analyzed using the SPSS software, version 20.0 (SPSS, Inc., Chicago, IL, USA). Differences in general according to sex and modalities were determined using the Mann-Whitney U-test or Student's t-test for independent samples. The values of maximum power and VO_{2max} were separated into tertiles and compared using the Kruskal-Wallis test.

For verification of the crude relationship between consumption of food groups and personal and training characteristics (independent variables) and maximum power and VO_{2max} (dependent variables) a linear regression (bivariate analyses) was performed. A multiple regression analysis was conducted to further test whether food groups (independent variables) were related to performance parameters (dependent variables), after adjusting for potential covariates such as hours of training, sex, BMI, and food intake (total calorie consumption/kg, g/kg of protein, g/kg of carbohydrates, and g/kg of lipids). For all statistical analyses significance was accepted at $p < 0.05$. The data were analyzed using the statistical package "R", version 3.4.2 (New Zealand).

RESULTS

The main characteristics of the athletes are presented in table I. When compared to women, men showed higher values in the variables age ($p = 0.000$), weight ($p = 0.000$), height ($p = 0.000$), BMI ($p = 0.000$), training hours ($p = 0.004$), consumption ($p = 0.000$), maximum power ($p = 0.000$), and VO_{2max} ($p = 0.000$). Table II

Table I. Descriptive characteristics of athletes by sex

	Total (n = 168)	Male (n = 131)	Female (n = 37)
Age (years)	20.84 ± 7.74	22.1 ± 8.1*	16.4 ± 3.88
Weight (kg)	68.28 ± 13.48	72.57 ± 11.65*	53.08 ± 7
Height (m)	1.72 ± 0.09	1.76 ± 0.07*	1.6 ± 0.07
BMI (kg/m^2)	22.88 ± 3.1	23.49 ± 3.05*	20.73 ± 2.27
Hours of training/week	18.45 ± 12.93	20.13 ± 13.86*	12.51 ± 5.98
Proteins (g/kg/d)	1.73 ± 0.89	1.79 ± 0.95	1.56 ± 0.63
Carbohydrates (g/kg/d)	5.27 ± 2.82	5.39 ± 2.99	4.88 ± 2.16
Lipids (g/kg/d)	1.3 ± 0.7	1.31 ± 0.75	1.32 ± 0.56
Kcal (kcal/kg/d)	40.29 ± 17.96	40.91 ± 18.93	38.12 ± 14.03
Cereals (portions/d)	5.96 ± 3.6	6.42 ± 3.78*	4.33 ± 2.20
Vegetables (portions/d)	1.55 ± 1.98	1.62 ± 2.16	1.30 ± 1.17
Fruits (portions/d)	5.98 ± 5.65	6.52 ± 6.06	4.11 ± 3.38
Legumes (portions/d)	1.66 ± 1.42	1.80 ± 1.50*	1.18 ± 1
Meat & eggs (portions/d)	3.85 ± 2.15	4.15 ± 2.27*	2.83 ± 1.21
Dairy products (portions/d)	1.52 ± 1.81	1.67 ± 1.97	1.00 ± 0.94
Oils (portions/d)	1.49 ± 2.05	1.59 ± 2.19	1.12 ± 1.43
Sugars (portions/d)	3.98 ± 5.38	4.21 ± 5.88	3.17 ± 2.9
Maximum power (w/kg)	7.41 ± 1.97	8.09 ± 1.54*	5.04 ± 1.42
VO_{2max} (mL O_2.kg^{-1}.min^{-1})	43.98 ± 6.93	45.62 ± 6.56*	38.2 ± 4.86

Values presented as mean ± standard deviation. BMI: body mass index; VO_{2max}: maximum oxygen consumption.

presents the characteristics of the athletes according to sports modalities.

Table III shows the values for the portions of food consumed according to their respective food groups, and the contribution of nutritional supplements to the adequacy of the groups according to the recommendations proposed in the food pyramid. There was no significant difference between the "with supplements" and "without supplements" diets for all the food groups analyzed.

When analyzing food intake by food groups regarding maximum power (Table IV), as was expected,t weight and height differed between groups (T1 < T2 < T3). Regarding hours of training and age, we noticed that participants in tertiles T2 and T3 presented higher scores when compared with T1. It can also be seen that the meats and eggs (T1 < T2 and T3) and legumes (T1 < T3) groups presented significant differences between their respective tertiles.

Table V shows the tertiles obtained for VO_{2max}. Height differed between groups (T1 < T2 < T3). Regarding hours of training, we noticed that participants in tertiles T1 and T2 presented lower scores when compared with T3. It has also been observed that in calorie intake the participants of tertiles T2 and T3 presented higher scores when compared with T1. As regards protein intake, T2 differed from T1 and T3 (T1 = T3 < T2).

Table VI shows the linear regression model between maximum power and food groups. Maximum power was significantly associated with consumption of foods in the meat and eggs groups in the last model, adjusted for other possible confounding variables (Model 06).

Table VII displays the linear regression model between aerobic performance and food groups. VO_{2max} exhibited a positive relationship with the fruit group ($\beta = 0.29$; $p < 0.05$). These relationships remained significant after adjustment for the covariables hours of training, sex, and BMI ($\beta = 0.19$; $p < 0.05$). A significant inverse relation between VO_{2max} and the legumes group was observed after adjusting for hours of training, gender, BMI, and consumption of kcal/kg of body weight ($\beta = -0.76$; $p < 0.05$). The group of meats and eggs and the group of dairy products had an inverse and significant association with VO_{2max} after adjusting for hours of training, gender, BMI, consumption of kcal/kg of body weight, carbohydrate intake (g/kg/d), protein intake (g/kg/d), and lipid intake (g/kg/d) ($\beta = -0.76$, $p < 0.05$; $\beta = -0.44$, $p < 0.05$; and $\beta = -0.43$, $p < 0.01$, respectively).

DISCUSSION

According to the findings of the present investigation, the highest consumption of meat, eggs and legumes was observed in the upper tertiles of potency, and fruits were ingested in greater quantity in the higher tertiles of VO_{2max}. After adjusting for confounding factors, meat and egg consumption was positively associated with anaerobic performance, whereas the same group and dairy products were negatively associated with aerobic performance.

To the authors' knowledge, to date, this is the first study to investigate the association between dietary intake and physical perfor-

Table II. Characteristics of participants of the study by modality

Modality	n	Age (years)	Weight (kg)	Height (m)	BMI (kg/m²)	Hours of training / week	Maximum power (w/kg)	VO_{2max} (mL O_2.kg^{-1}.min^{-1})
Athletics	15	26 ± 14.94	65.57 ± 12.08	1.71 ± 0.10	22.14 ± 2.07	18.1 ± 10.99	8.04 ± 2.14	37.32 ± 7.02
Cycling*	1	45	71	1.69	25	12	5.45	26.6
Bodybuilding	5	27 ± 3.57	88 ± 7.59	1.72 ± 0.05	29.86 ± 2.88	10.8 ± 7.82	6.92 ± 1.39	41 ± 5.37
Soccer	69	21 ± 4.62	72.99 ± 9.58	1.76 ± 0.08	23.38 ± 2.21	23.88 ± 15.63	8.61 ± 1.16*	46.01 ± 5.45
American football*	1	31	94	1.86	27	9	8.78	44.6
Futsal*	1	17	70	1.74	23	10	7.91	42.47
Brazilian jiu-jitsu	7	23 ± 3.59	79.44 ± 10.52	1.76 ± 0.04	25.59 ± 2.42	20.86 ± 14.96	7.69 ± 1.08	50.78 ± 9.7
Judo	13	20 ± 9.57	59.12 ± 15.99	1.63 ± 0.09	21.94 ± 4.10	16.24 ± 11.82	5.25 ± 1.55	44.64 ± 5.47
Karate	10	21 ± 8.56	60.69 ± 23.64	1.61 ± 0.13	22.78 ± 5.37	12.6 ± 4.09	5.4 ± 1.64	39.02 ± 3.93
Kung fu	3	20 ± 0.64	58.77 ± 5.20	1.67 ± 0.07	21.16 ± 0.80	10.67 ± 4.16	6.26 ± 1.52	45.6 ± 17.58
MMA	2	27 ± 2.25	65.1 ± 6.93	1.65 ± 0.04	23.9 ± 1.36	18.5 ± 12.02	9.46 ± 1.03	41.6 ± 0
Swimming	19	16 ± 2.22	62.33 ± 11.54	1.69 ± 0.10	21.68 ± 2.42	16.47 ± 5.74	6.07 ± 1.34	46.62 ± 5.25
Taekwondo*	1	32	74	1.73	25	16	9.18	41.6
Triathlon*	1	48	71	1.71	24	36	6.62	62.6
Volleyball	20	15 ± 1.38	60.43 ± 9.09	1.71 ± 0.09	20.5 ± 1.93	8.95 ± 2.29	6.46 ± 2.34	40.03 ± 4.26

*Values presented as mean ± standard deviation. *The mean value was not calculated because there was only one subject.*

Table III. Consumption of food groups according to modality and contribution of dietary supplements

Modality	With supplements					Without supplements				
	Cereals	Vegetables	Fruits	Legumes	Meat and eggs	Cereals	Vegetables	Fruits	Legumes	Meat and eggs
Athletics	4.57 ± 1.31	-	1.86 ± 2.18	-	-	4.46 ± 1.4	2.05 ± 4.21	1.86 ± 2.19	2.2 ± 1.53	3.17 ± 1.79
Cycling*	-	-	-	-	-	4.83	0.76	11.09	0.56	1.58
Bodybuilding	12.06 ± 3.47	-	-	-	-	10.89 ± 3.55	1.14 ± 1.01	1.60 ± 3.58	0.48 ± 0.78	7.9 ± 4.16
Soccer	6.06 ± 3.54	-	-	-	-	5.98 ± 3.56	1.41 ± 1.85	7.55 ± 5.96	2.1 ± 1.43	4.18 ± 2.27
American football*	-	-	-	-	-	5.03	0.73	8.78	0.39	5.16
Futsal*	-	-	-	-	-	4.94	0.27	3.60	0.0	11.08
Brazilian jiu-jitsu	4.79 ± 2.37	1.70 ± 2.35	-	-	-	4.79 ± 2.36	1.69 ± 2.35	10.58 ± 7.8	1.57 ± 0.68	3.06 ± 0.55
Judo	5.46 ± 5.02	-	-	0.89 ± 0.51	-	5.32 ± 4.96	1.46 ± 1.05	6.32 ± 6.8	0.89 ± 0.52	3.01 ± 0.99
Karate	-	1.13 ± 0.93	-	-	-	5.06 ± 2.52	1.13 ± 0.94	3.54 ± 2.82	1.43 ± 1.36	3.07 ± 1.79
Kung fu	6.11 ± 3.19	-	-	-	-	6.11 ± 3.2	1.33 ± 0.68	5.84 ± 5.08	1.67 ± 1.57	3.32 ± 0.94
MMA	10.75 ± 2.58	3.01 ± 3.63	-	-	-	10.69 ± 2.67	3.01 ± 3.64	2.69 ± 3.8	0.0	2.71 ± 1.92
Swimming	6.88 ± 4.28	-	-	-	3.98 ± 1.43	6.85 ± 4.27	1.91 ± 1.47	6.15 ± 4.8	1.52 ± 1.81	3.98 ± 1.44
Taekwondo*	2.09	-	-	-	-	1.95	0.82	0.0	2.39	5.64
Triathlon*	-	-	-	-	-	8.69	3.27	17.27	0.87	2.39
Volleyball	-	-	-	-	-	5.19 ± 2.81	1.62 ± 1.53	3.85 ± 3.93	1.22 ± 1.21	3.24 ± 1.31
Total average	5.96 ± 3.6	1.55 ± 1.98	5.98 ± 5.65	1.66 ± 1.42	3.85 ± 2.15	5.87 ± 3.55	1.55 ± 1.98	5.98 ± 5.65	1.66 ± 1.42	3.85 ± 2.15

**The mean was not calculated because there was only one subject. With supplement: column with the supplement consumption counted in the diet; Without supplement: column without supplement consumption counted in the diet; -: there was no supplement consumed.*

mance in a population of athletes. The novelty of the study precludes a direct comparison with the literature. Overall, a proper diet is a key factor for adaptation and improved physical performance.

Meats are the best food sources of proteins with high biological value (22,23), are a good source of micronutrients such as zinc, iron, and vitamin B_{12} (24), and have better bioavailability when compared to plant sources of these nutrients (25). In addition, albumin has a high biological value, and contains amino acids that aid in the synthesis of creatine (26) and in pH control, favoring greater resistance to fatigue (27-29) and possibly the best anaerobic performance observed in our study.

In aerobic performance the consumption of meat, eggs and dairy products was inversely associated with VO_{2max} after adjustment for different confounding factors. Moreover, the athletes in the present study consumed carbohydrates in amounts inferior to the national recommendations for athletes (1), and cereal portions in the lower limit proposed in the Brazilian food pyramid (18). This dietary profile is similar to that observed in an earlier study by our study group in another cohort of athletes (30), who consumed protein-rich diets neglecting carbohydrate intake and total calories. This possibly affected the aerobic performance of the athletes in our study, justifying the negative association obtained for the food groups of meat and eggs and dairy products, whose main nutrient is protein.

In the group of milk and dairy products 11 modalities were below the proposed recommendation (athletics, cycling, futsal, soccer, Brazilian jiu-jitsu, judo, karate, kung fu, MMA, swimming, and volleyball) and 4 modalities were above (bodybuilding, American football, taekwondo, and triathlon). The values corresponding to the group of sugars and sweets were: 2 modalities as recommended (American football, kung fu) and 13 above recommendations (athletics, cycling, bodybuilding, soccer, futsal, Brazilian jiu-jitsu, judo, karate, MMA, swimming, taekwondo, triathlon, and volleyball).

Regarding oils 03 modalities were below recommendations (athletics, MMA, and taekwondo), 07 were within recommendations (bodybuilding, soccer, Brazilian jiu-jitsu, judo, swimming, triathlon, and volleyball) and 05 were above the recommended values (cycling, soccer, futsal, karate, kung fu). When supplements were removed from the calculation of portions, the only food group that obtained a change in the classification as related to the food pyramid was that of dairy products, where the modality of bodybuilding entered the classification below recommended values.

The consumption of legumes was negatively associated with VO_{2max} in the Model 5 of adjustment. This inverse association was a significant one and could be based on the assumption that legumes have an antinutritional factor called phytic acid. Phytic acid may be related to reduced bioavailability and absorption of some micronutrients (31), especially calcium and zinc (32). Calcium is closely related to energy metabolism and muscle contraction (33), while zinc is required for the activity of more than 300 enzymes and, if consumed in low amounts, can alter the individual's eating behavior and compromise aerobic fitness (34).

In addition, legumes are important sources of protein in the diet of vegetarians (35). In the present study the foods that mostly represented the legume group were beans.

Table IV. Consumption of nutrients and portions of food groups according to tertiles of maximum power output for the athletes

Characteristic	Total	T1 (< 6.67)	T2 (6.67 to 8.45)	T3 (> 8.45)	p-value
n	168 (131 M, 37 F)	56	56	56	
Maximum power (w/kg)	7.42 ± 1.97	5.08 ± 1.09 a	7.69 ± 0.50 b	9.46 ± 0.68 c	< 0.0001
Hours of training/week	18.45 ± 12.93	13.28 ± 7.62 b	18.55 ± 12.27 a	23.52 ± 15.70 a	0.0014
Age (years)	21 ± 7.74	20.75 ± 11.46 b	20.41 ± 5.31 a	21.35 ± 4.68 a	0.0003
Weight (kg)	68.28 ± 13.49	61.16 ± 15.75 a	69.30 ± 11.47 b	74.36 ± 9.18 c	< 0.0001
Height (m)	1.72 ± 0.10	1.65 ± 0.097 a	1.73 ± 0.079 b	1.78 ± 0.068 c	< 0.0001
BMI (kg/m²)	23 ± 3.11	22.13 ± 3.89	23.03 ± 2.88	23.47 ± 2.21	0.0669
Kcal (kcal/kg/d)	40.3 ± 17.96	38.98 ± 14.74	44.57 ± 20.86	37.33 ± 17.25	0.056
Proteins (g/kg/d)	1.74 ± 0.89	1.82 ± 0.95	1.84 ± 1.07	1.54 ± 0.54	0.359
Carbohydrates (g/kg/d)	5.28 ± 2.83	4.96 ± 2.10	5.78 ± 2.90	5.08 ± 3.31	0.124
Lipids (g/kg/d)	1.31 ± 0.71	1.28 ± 0.55	1.42 ± 0.94	1.21 ± 0.54	0.657
Cereals (portions/d)	5.96 ± 3.6	5.35 ± 3.43	6.69 ± 4.12	5.56 ± 2.90	0.059
Fruits (portions/d)	5.98 ± 5.65	4.77 ± 4.72	6.81 ± 6.03	6.42 ± 5.96	0.138
Vegetables (portions/d)	1.55 ± 1.98	1.66 ± 2.43	1.42 ± 1.52	1.55 ± 1.91	0.895
Meat and eggs (portions/d)	3.85 ± 2.15	3.23 ± 2.04 b	4.37 ± 2.40 a	3.97 ± 1.84 a	0.003
Legumes (portions/d)	1.66 ± 1.42	1.46 ± 1.64 b	1.66 ± 1.45 ab	1.84 ± 1.11 a	0.008
Dairy products (portions/d)	1.52 ± 1.81	1.47 ± 1.68	1.21 ± 1.18	1.40 ± 2.05	0.556
Sugars (portions/d)	3.98 ± 5.38	2.98 ± 3.04	4.82 ± 5.55	4.14 ± 6.78	0.289
Oils (portions/d)	1.49 ± 2.05	1.23 ± 1.45	1.92 ± 2.95	1.24 ± 1.30	0.545

Values expressed as mean ± standard deviation. kg: kilograms; m: meters; kg/m²: kilograms divided by meters squared; g/kg/d: grams per kilogram of weight per day; w/kg: watts per kilogram of weight. Means followed by the same letter do not differ at the 5% level (p < 0.05) of significance by the Kruskal-Wallis test.

Table V. Consumption of food groups according to tertiles of VO_{2max} for the athletes

Characteristics	Total	T1 (< 41.6)	T2 (41.6 to 46.57)	T3 (> 46.57)	p-value
n	168 (131 M, 37 F)	56	56	56	-
VO_{2max} (mL O_2 .kg^{-1}.min^{-1})	43.98 ± 6.93	36.72 ± 3.60 a	43.74 ± 1.32 b	51.48 ± 4.51 c	< 0.0001
Hours of training/week	18.45 ± 12.93	15.89 ± 11.50a	17.08 ± 11.85 a	22.37 ± 14.52 b	0.025
Age (years)	21 ± 7.74	21.43 ± 10.17 a	19.34 ± 5.49 a	21.74 ± 6.68 a	0.060
Weight (kg)	68.28 ± 13.49	65.84 ± 16.16 a	68.66 ± 12.99 a	70.33 ± 10.57 a	0.052
Height (m)	1.72 ± 0.10	1.69 ± 0.10 a	1.72 ± 0.09 b	1.75 ± 0.07 c	0.003
BMI (kg/m²)	23 ± 3.11	22.81 ± 3.87 a	23.05 ± 2.93 a	22.76 ± 2.39 a	0.771
Kcal (kcal/kg/d)	40.3 ± 17.96	36.85 ± 14.39 a	40.36 ± 13.43 b	43.67 ± 23.84 b	0.043
Proteins (g/kg/d)	1.74 ± 0.89	1.57 ± 0.92 a	1.83 ± 0.77 b	1.79 ± 0.96 ab	0.036
Carbohydrates (g/kg/d)	5.28 ± 2.83	4.74 ± 2.14	5.23 ± 2.50	5.84 ± 3.56	0.163
Lipids (g/kg/d)	1.31 ± 0.71	1.20 ± 0.50	1.34 ± 0.65	1.38 ± 0.90	0.514
Cereals (portions/d)	5.96 ± 3.6	5.43 ± 3.73	5.90 ± 3.01	6.27 ± 3.86	0.121
Fruits (portions/d)	5.98 ± 5.65	4.36 ± 4.85b	6.24 ± 5.30a	7.35 ± 6.39a	0.019
Vegetables (portions/d)	1.55 ± 1.98	1.38 ± 2.35	1.61 ± 1.86	1.64 ± 1.70	0.508
Meat and eggs (portions/d)	3.85 ± 2.15	3.46 ± 2.16	3.94 ± 1.88	4.16 ± 2.35	0.113
Legumes (portions/d)	1.66 ± 1.42	1.69 ± 1.63	1.45 ± 1.15	1.84 ± 1.44	0.207
Dairy products (portions/d)	1.52 ± 1.81	1.07 ± 1.57	1.60 ± 2.12	1.42 ± 1.15	0.117
Sugars (portions/d)	3.98 ± 5.38	3.33 ± 2.80	3.41 ± 4.37	5.20 ± 7.65	0.454
Oils (portions/d)	1.49 ± 2.05	1.24 ± 1.59	1.86 ± 2.79	1.29 ± 1.50	0.263

Values presented as mean ± standard deviation. m = meters; kg/m²: kilograms divided by meters squared; g/kg/d: grams per kilogram of weight per day; w/kg: watts per kilogram of weight. Means followed by the same letter do not differ from each other at the level of 5% (p < 0.05) of significance by the Kruskal-Wallis test.

Table VI. Value of beta (β) and p-value for maximum power output (w/kg) according to the food groups

Relative maximum power (w/kg)	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6	
	β1	p-value	β2	p-value	β3	p-value	β4	p-value	β5	p-value	β6	p-value
Cereals	-0.0019	0.9660	-0.026	0.5471	-0.0584	0.1016	-0.05435	0.1294	0.0249	0.7127	-0.084	0.4551
Vegetables	-0.1019	0.1870	-0.092	0.2078	-0.1035	0.0804	-0.10928	0.0660	-0.0943	0.1168	0.0062	0.9607
Fruits	0.05308	0.0570	0.0343	0.2018	0.01537	0.4767	0.01466	0.4975	0.03076	0.2107	0.0603	0.1382
Legumes	0.16922	0.1370	0.1553	0.1497	0.0645	0.4611	0.04914	0.5791	0.07629	0.3998	-0.1269	0.3750
Meat and eggs	0.12745	0.1080	0.1284	0.0871	0.05238	0.3910	0.06373	0.3038	0.16515	0.0875	0.3168	0.0065
Dairy products	0.0852	0.3610	0.1392	0.1194	0.04628	0.5247	0.04645	0.5231	0.10837	0.2054	0.1720	0.0551
Oils	-0.0137	0.8550	0.0326	0.6492	-0.0143	0.8063	-0.02506	0.6717	0.0244	0.7239	-0.0842	0.4269
Sugars	0.0256	0.3750	0.0287	0.2934	0.01727	0.4345	0.01589	0.4727	0.07892	0.1224	0.0431	0.6133
R	0.21		0.38		0.66		0.66		0.66		0.68	

Simple linear regression (Model 1); coefficient adjusted for training hours (Model 2); coefficient adjusted for training hours and sex (Model 3); coefficient adjusted for training hours, sex, and BMI (Model 4); coefficient adjusted for training hours, sex, BMI, and consumption of kcal/kg of weight (Model 5); coefficient adjusted for carbohydrates (g/kg/d), proteins (g/kg/d) and lipids (g/kg/d) (Model 6).

Table VII. Value of beta (β) and p-value for VO_{2max} (w/kg) according to the food roups

VO_2 relative maximum (mL $O_2.kg^{-1}.min_{-1}$)	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6	
	β1	p-value	β2	p-value	β3	p-value	β4	p-value	β5	p-value	β6	p-value
Cereals	0.11094	0.4949	0.05604	0.7271	-0.02170	0.8840	0.03349	0.8165	-0.18630	0.4980	-0.080	0.4551
Vegetables	0.11122	0.6833	0.13341	0.6180	0.10548	0.6690	0.02709	0.9097	-0.01410	0.9530	0.0062	0.9607
Fruits	0.29268	0.0032	0.24984	0.0113	0.20460	0.0250	0.19487	0.0267	0.15020	0.1320	0.0603	0.1382
Legumes	-0.22890	0.5695	-0.26010	0.5100	-0.48030	0.1910	-0.68900	0.0557	-0.76420	0.0380	-0.1269	0.3750
Meat and eggs	0.11754	0.6745	0.11986	0.6623	-0.06460	0.8000	0.08959	0.7202	-0.19140	0.6230	-0.4428	0.0191
Dairy products	0.11592	0.7257	0.23747	0.4681	0.01200	0.9690	0.01422	0.9614	-0.15730	0.6490	-0.4361	0.0023
Oils	-0.12450	0.6399	-0.02025	0.9387	-0.13410	0.5830	-0.28040	0.2416	-0.41740	0.1370	-0.0842	0.4269
Sugars	0.13615	0.1834	0.14313	0.1541	0.11540	0.2140	0.09658	0.2807	-0.07810	0.7050	0.0431	0.6133
R	0.17		0.26		0.45		0.51		0.51		0.52	

Simple linear regression (Model 1); coefficient adjusted for training hours (Model 2); coefficient adjusted for training hours and sex (Model 3); coefficient adjusted for training hours, sex, and BMI (Model 4); coefficient adjusted for training hours, sex, BMI, and consumption of kcal/kg of weight (Model 5); coefficient adjusted for carbohydrates (g/kg/d), proteins (g/kg/d) and lipids (g/kg/d) (Model 6).

After adjustment for macronutrients (carbohydrates, proteins, lipids), the association between legumes and VO_{2max} lost its significance, indicating the possibility that it is the macronutrients and not the legumes themselves that are responsible for the associations observed in our study.

On the other hand, the legumes group was significantly more consumed in the tertile of better anaerobic performance (T3) when compared to the tertile of low anaerobic performance (T1). This difference can be explained by the fact that legumes are considered a good source of protein (35) and this nutrient in turn is associated with anaerobic performance (36-38).

According to the Brazilian food pyramid, the T1 group (low performance) and the T3 group (high performance) presented the same classification of consumption for most of the food groups but with values of different consumed portions, suggesting that small changes in the diet can make a difference between athletes with a low performance and athletes with a high performance. In our study, supplements did not alter the adequacy of dietary intake, partially corroborating a study with Brazilian athletes (30).

For fruits, T1 was the only tertile where consumption was as recommended in the food pyramid; the other tertiles (T2 and T3) were above recommendations. Vegetables and dairy products

were in all tertiles below recommendations. Regarding the groups of meats and eggs, legumes, and sugars all tertiles were above the issued recommendations.

Men consumed cereals in appropriate portions and fruit above the food pyramid's recommendations. Among female athletes, cereal intake was low and fruit intake was within the recommended range. Oils and fats were consumed in adequate amounts by both sexes

In general, the cereal and oil groups were within the recommendations (05 to 09 servings and 01 to 02 servings, respectively), while the fruit, meat, legume, and sugar groups were above the recommendations of the food pyramid as adapted to the Brazilian population (03 to 05 servings, 01 to 02 servings, 01 serving, and 01 to 02 servings, respectively). The vegetable and dairy groups (recommendation of 04 to 05 servings, and of 03 servings, respectively) were below the recommended values.

Of the 15 assessed modalities, 5 showed cereal consumption below the recommended amounts (athletics, cycling, futsal, Brazilian jiu-jitsu, and taekwondo), 8 were in accordance with the issued recommendations (soccer, American football, judo, karate, kung fu, swimming, and triathlon) and 2 were above the recommended values (bodybuilding and MMA). Regarding the consumption of fruits, 4 modalities presented consumption below the recommendations (athletics, bodybuilding, MMA, and taekwondo), 3 were within the recommended amounts (futsal, karate, and volleyball) and 8 were above the recommended values (cycling, soccer, American football, Brazilian jiu-jitsu, judo, kung fu, swimming, and triathlon). All modalities reported an intake of vegetables below the available recommendations. The meat group had only one modality within the recommendation (cycling) whereas the other modalities were above the recommended values. Seven modalities consumed legumes below the recommended amount (cycling, bodybuilding, American football, futsal, judo, MMA, and triathlon) and 8 consumed them above recommendations (athletics, soccer, Brazilian jiu-jitsu, karate, kung fu, taekwondo, swimming, and volleyball).

The present study does have limitations that should be acknowledged. This study used a cross-sectional design, which does not allow the establishment of cause-and-effect relationships. Our sample was comprised of predominantly male athletes, thus limiting the generalization of these results to women. Other limitation of this study was that we were unable to obtain a homogeneous distribution of athletes within each modality, so as to more accurately investigate the influence of this variable on eating habits. Despite these limitations, a strong point of our study is its sample size (168 athletes) and the adjustments for potential confounders in the association between intake of food groups and performance parameters. It should be noted that performances were separated into "aerobic" and "anaerobic" classes for didactic purposes, since both occur intermittently during exertion, albeit with predominance of one over the other.

The fact that this study is the only one to relate the various food groups to the physical performance of athletes denotes that there is still much to research. Future investigations considering sport modalities and modality-specific tests to measure aerobic and anaerobic fitness may help in the construction of this body of knowledge.

Through the information gathered in this study, nutritionists will have greater support when advising on the choice and quantity to be consumed for each food group, knowing the potential of each one of them. For example, the prescription of meat and eggs consumption may exert a positive or negative effect on physical performance depending on the sport practised by a given athlete. It is important to note that even with the controversial results regarding the performance of athletes with different dietary macronutrient profiles, it is important to have a balanced and cautious diet. Given the low bioavailability of certain nutrients found in plant sources, extra attention should be payed to the food and even the supplementation that is recommended for athletes whose diet is based on plant sources.

CONCLUSION

The consumption of meat and eggs showed a positive association with anaerobic performance, whereas the same group and dairy products had a negative association with aerobic performance. This type of result suggests that the same alimentary profile that assists a certain skill may harm another, so special attention on the part of the professionals involved is required when drafting a dietary plan. The consumption of the various food groups was shown to be one of the possible factors involved in an athlete's physical performance. In addition, our study researched a scarcely explored subject, thus highlighting the need for further research in this field.

REFERENCES

1. Sociedade Brasileira de Medicina do Esporte. Modificações dietéticas, reposição hídrica, suplementos alimentares e drogas: comprovação de ação ergogênica e potenciais riscos para a saúde. Revista Brasileira de Medicina do Esporte 2009.
2. Papadopoulou SK, Gouvianaki A, Grammatikopoulou MG, Maraki Z, Pagkalos IG, Malliaropoulos N, et al. Body Composition and Dietary Intake of Elite Cross-country Skiers Members of the Greek National Team. Asian J Sports Med 2012;3(4):257-66. DOI: 10.5812/asjsm.34548.
3. Rodriguez NR, DiMarco NM, Langley S. Position of the American Dietetic Association, Dietitians of Canada, and the American College of Sports Medicine: Nutrition and athletic performance. J Am Diet Assoc 2009;109(3):509-27. DOI: 10.1016/j.jada.2009.01.005.
4. Roy BD. Milk: the new sports drink? A Review. J Int Soc Sports Nutr 2008;5:15. DOI: 10.1186/1550-2783-5-15.
5. Filha EO, Araújo JS, Barbosa JS, Gaujac DP, Santos CFS, Silva DG. Consumo dos grupos alimentares em crianças usuárias da rede pública de saúde do município de Aracaju, Sergipe. Revista Paulista de Pediatria 2012;30:529-36. DOI: 10.1590/S0103-05822012000400011.
6. Farajian P, Kavouras SA, Yannakoulia M, Sidossis LS. Dietary intake and nutritional practices of elite Greek aquatic athletes. Int J Sport Nutr Exerc Metab 2004;14(5):574-85. DOI: 10.1123/ijsnem.14.5.574.
7. Lukaski HC. Vitamin and mineral status: effects on physical performance. Nutrition 2004;20(7-8):632-44. DOI: 10.1016/j.nut.2004.04.001.
8. Hargreaves M, Hawley JA, Jeukendrup A. Pre-exercise carbohydrate and fat ingestion: effects on metabolism and performance. J Sports Sci 2004;22(1):31-8. DOI: 10.1080/0264041031000140536.
9. Ivy JL, Res PT, Sprague RC, Widzer MO. Effect of a carbohydrate-protein supplement on endurance performance during exercise of varying intensity. Int J Sport Nutr Exerc Metab 2003;13(3):382-95. DOI: 10.1123/ijsnem.13.3.382.

10. Lima-Silva AE, Pires FO, Bertuzzi R, Silva-Cavalcante MD, Oliveira RS, Kiss MA, et al. Effects of a low- or a high-carbohydrate diet on performance, energy system contribution, and metabolic responses during supramaximal exercise. Appl Physiol Nutr Metab 2013;38(9):928-34. DOI: 10.1139/apnm-2012-0467.
11. Radavelli-Bagatini S, Zhu K, Lewis JR, Dhaliwal SS, Prince RL. Association of dairy intake with body composition and physical function in older community-dwelling women. J Acad Nutr Diet 2013;113(12):1669-74. DOI: 10.1016/j.jand.2013.05.019.
12. Neville CE, McKinley MC, Murray LJ, Boreham CA, Woodside JV. Fruit and vegetable consumption and muscle strength and power during adolescence: a cross-sectional analysis of the Northern Ireland Young Hearts Project 1999-2001. J Musculoskelet Neuronal Interact 2014;14(3):367-76.
13. Gracia-Marco L, Bel-Serrat S, Cuenca-García M, González-Gross M, Pedrero-Chamizo R, Manios Y, et al. Amino acids intake and physical fitness among adolescents. Amino acids 2017;49(6):1041-52. DOI: 10.1007/s00726-017-2393-6.
14. Qureshi MM, Singer MR, Moore LL. A cross-sectional study of food group intake and C-reactive protein among children. Nutrition & metabolism 2009;6:40. DOI: 10.1186/1743-7075-6-40.
15. Araujo CG, Scharhag J. Athlete: a working definition for medical and health sciences research. Scand J Med Sci Sports 2017;26(1):4-7.
16. Monego ET, Peixoto MRG, Santiago RAC, Gil M, Cordeiro MM, Campos MI, et al. Alimentos Brasileiros e Suas Porções: Um Guia para Avaliação do Consumo Alimentar Rio de Janeiro: Rúbio; 2013.
17. Pinheiro ABV, Lacerda EMA, Benzecry EH, Gomes MCS, da Costa VM. Tabela para Avaliação de Consumo Alimentar em Medidas Caseiras: Atheneu; 2009.
18. Phillipi ST, Latterza AR, Cruz ATR, Ribeiro LC. Pirâmide Alimentar Adaptada: Guia para escolha dos alimentos. Revista de Nutrição 1999;12(1):65-80. DOI: 10.1590/S1415-52731999000100006.
19. Zagatto AM, Beck WR, Gobatto CA. Validity of the running anaerobic sprint test for assessing anaerobic power and predicting short-distance performances. J Strength Cond Res 2009;23(6):1820-7. DOI: 10.1519/JSC.0b013e3181b3df32.
20. Mayorga-Vega D, Aguilar-Soto P, Viciana J. Criterion-Related Validity of the 20-M Shuttle Run Test for Estimating Cardiorespiratory Fitness: A Meta-Analysis. J Sports Sci Med 2015;14(3):536-47.
21. Leger LA, Mercier D, Gadoury C, Lambert J. The multistage 20 metre shuttle run test for aerobic fitness. J Sports Sci 1988;6(2):93-101. DOI: 10.1080/02640418808729800.
22. Koeth RA, Wang Z, Levison BS, Buffa JA, Org E, Sheehy BT, et al. Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. Nature medicine 2013;19(5):576-85. DOI: 10.1038/nm.3145.
23. Pekala J, Patkowska-Sokola B, Bodkowski R, Jamroz D, Nowakowski P, Lochynski S, et al. L-carnitine--metabolic functions and meaning in humans life. Curr Drug Metab 2011;12(7):667-78. DOI: 10.2174/138920011796504536.
24. Sharma S, Sheehy T, Kolonel LN. Contribution of meat to vitamin B(1)(2), iron and zinc intakes in five ethnic groups in the USA: implications for developing food-based dietary guidelines. J Hum Nutr Diet 2013;26(2):156-68. DOI: 10.1111/jhn.12035.
25. Allen LH. To what extent can food-based approaches improve micronutrient status? Asia Pac J Clin Nutr 2008;17(Suppl 1):103-5.
26. Cooper R, Naclerio F, Allgrove J, Jimenez A. Creatine supplementation with specific view to exercise/sports performance: an update. Journal of the International Society of Sports Nutrition 2012;9(1):33. DOI: 10.1186/1550-2783-9-33.
27. Baguet A, Bourgois J, Vanhee L, Achten E, Derave W. Important role of muscle carnosine in rowing performance. J Appl Physiol 1985;109(4):1096-101. DOI: 10.1152/japplphysiol.00141.2010.
28. Parkhouse WS, McKenzie DC. Possible contribution of skeletal muscle buffers to enhanced anaerobic performance: a brief review. Med Sci Sports Exerc 1984;16(4):328-38.
29. Varanoske AN, Hoffman JR, Church DD, Wang R, Baker KM, Dodd SJ, et al. Influence of Skeletal Muscle Carnosine Content on Fatigue during Repeated Resistance Exercise in Recreationally Active Women. Nutrients 2017;9(9):988. DOI: 10.3390/nu9090988.
30. Rodrigues VB, Ravagnani CDFC, Nabuco HCG, Ravagnani FCDP, Fernandes VLS, Espinosa MM. Adequacy of energy and macronutrient intake of food supplements for athletes. Revista de Nutrição 2017;30:593-603. DOI: 10.1590/1678-98652017000500005.
31. Silva MR, Silva MAAP. Aspectos nutricionais de fitatos e taninos. Revista de Nutrição 1999;12:21-32. DOI: 10.1590/S1415-52731999000100002.
32. Gupta RK, Gangoliya SS, Singh NK. Reduction of phytic acid and enhancement of bioavailable micronutrients in food grains. J Food Sci Technol 2015;52(2):676-84. DOI: 10.1007/s13197-013-0978-y.
33. Williams MH. Dietary Supplements and Sports Performance: Minerals. Journal of the International Society of Sports Nutrition 2005;2(1):43. DOI: 10.1186/1550-2783-2-1-43.
34. Micheletti A, Rossi R, Rufini S. Zinc status in athletes: relation to diet and exercise. Sports Med 2001;31(8):577-82. DOI: 10.2165/00007256-200131080-00002.
35. Polak R, Phillips EM, Campbell A. Legumes: Health Benefits and Culinary Approaches to Increase Intake. Clinical diabetes: a publication of the American Diabetes Association 2015;33(4):198-205. DOI: 10.2337/diaclin.33.4.198.
36. Artioli GG, Bertuzzi RC, Roschel H, Mendes SH, Lancha AH Jr, Franchini E. Determining the contribution of the energy systems during exercise. Journal of visualized experiments 2012;(61):3413. DOI: 10.3791/3413.
37. Laskowski R, Antosiewicz J. Increased adaptability of young judo sportsmen after protein supplementation. J Sports Med Phys Fitness 2003;43(3):342-6.
38. Wilborn CD, Taylor LW, Outlaw J, Williams L, Campbell B, Foster CA, et al. The Effects of Pre- and Post-Exercise Whey vs. Casein Protein Consumption on Body Composition and Performance Measures in Collegiate Female Athletes. J Sports Sci Med 2013;12(1):74-9.

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Nutrición Hospitalaria

Trabajo Original

Otros

Effects of a low-carbohydrate diet on performance and body composition in trained cyclists

Efectos de una dieta baja en hidratos de carbono en el rendimiento y la composición corporal de ciclistas entrenados

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Abstract

Previous evidence suggests that low-carbohydrate diets may improve body composition and performance relative to body weight in endurance athletes. This has been the first study that has attempted to evaluate the utility of low-carbohydrate diets in a sample of eleven trained and experienced road cyclists who consumed 10% of their caloric intake in the form of carbohydrates during four weeks while maintaining a neutral energy balance (50 kcal/kg/day). Body composition was evaluated through an electrical impedance assessment before and after the intervention while maximal power output (5 and 20 min) was measured on a bike trainer by following a standardized protocol and in the same room conditions for all the participants. The study was performed during the preseason, when the subjects could abstain from performing high-intensity workouts. The participants, eleven men aged 31 ± 5 years, performed four weekly 150 min training sessions at submaximal intensities and received nutritional support from a certified sport nutritionist. The intervention resulted in reduced total weight (-2.51 kg) and body fat percentage (2.42%), and improved relative power (+0.2 w/kg for 20 min and +0.25 w/kg for 5 min) values while absolute power remained unchanged. The results suggest that low-carbohydrate diets could be used in order to induce changes in body composition and improve relative power during the preseason. However, future research with larger sample sizes and a control group is needed in order to validate the results.

Key words:

Road cycling. Performance. Body composition. Low-carbohydrate diet.

Resumen

La evidencia científica previa sugiere que las dietas bajas en hidratos de carbono pueden mejorar la composición corporal y el rendimiento relativo al peso en deportistas de resistencia. Este ha sido el primer estudio que ha intentado evaluar la utilidad de este tipo de dieta en una muestra de once ciclistas de carretera entrenados y experimentados que consumieron un 10% de sus calorías diarias en forma de hidratos de carbono durante cuatro semanas mientras mantenían un balance energético neutro (50 kcal/kg/día). La composición corporal se evaluó con bioimpedancia eléctrica antes y después de la intervención mientras que la potencia máxima (5 y 20 min) se evaluó siguiendo un protocolo estandarizado sobre un rodillo de ciclismo en las mismas condiciones ambientales para todos los participantes. El estudio se realizó en la pretemporada, cuando todos los sujetos podían abstenerse de realizar entrenamientos de alta intensidad. Los participantes, once hombres con edades de 31 ± 5 años, realizaron cuatro sesiones de entrenamiento de 150 minutos de duración semanales y recibieron apoyo de un nutricionista deportivo titulado. La intervención resultó en una disminución del peso (-2,51 kg) y el porcentaje de grasa corporal (-2,42%), así como en un aumento de la potencia relativa (+0,2 w/kg en potencia 20 min y +0,25 w/kg en potencia 5 min) mientras que los valores de potencia absoluta no se modificaron. Los resultados sugieren que las dietas bajas en hidratos de carbono podrían utilizarse durante la pretemporada para inducir cambios en la composición corporal y mejorar la potencia relativa. Sin embargo, hacen falta estudios con una muestra más grande y un grupo de control para poder validar estos resultados.

Palabras clave:

Ciclismo de carretera. Rendimiento. Composición corporal. Dieta baja en hidratos de carbono.

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INTRODUCTION

Sport nutrition periodization has been one of the most popular research topics in the field of sports performance during the last years (1). Among the strategies commonly described in nutrition periodization, a strategy called "training low" may be highlighted (2). This strategy comprises several different approaches with a common point: training with low glycogen stores due to insufficient carbohydrate feeding (3). Besides other interventions, this effect can be achieved by following a low-carbohydrate diet on a day-by-day basis.

Low-carbohydrate diets are frequently used to induce changes in body composition in obese individuals with great results and no long-term side effects (4). It has been speculated that some of the main benefits of these dietary interventions are the filling properties of the commonly consumed food items and appetite suppression (5)the results of clinical trials investigating the effect of ketogenic diets on appetite are inconsistent. To evaluate quantitatively the effect of ketogenic diets on subjective appetite ratings, we conducted a systematic literature search and meta-analysis of studies that assessed appetite with visual analogue scales before (in energy balance. These properties would allow an ad-libitum character of the intervention, with no calorie counting needs and similar adherence rates to those observed in low fat calorie reducing interventions (6). The ability of these diets to induce changes in body composition in non-athletic populations could also play a role in sport disciplines in which power to weight ratio is one of the determinants of performance, such as road cycling.

One of the main characteristics of road cycling is the importance of the power to weight ratio during the key moments of the competitions such as mountain stages (7). Modifying body composition at the expense of losses of fat mass and maintenance or increases in lean mass has been shown to improve cycling performance (8), and slight increases in body mass at the expense of muscle mass have no detrimental effects on performance (9). Low-carbohydrate diets have been studied in sports that are highly dependent on relative power such as powerlifting and Olympic weightlifting (10) with weight-reducing results and no detrimental effects on strength, therefore improving the power-to-weight ratio. Only one previous study has investigated the effects of a low-carbohydrate intervention in cycling but it was conducted on off-road cyclists (11). In that study, the dietary manipulation resulted in increased relative values of maximal and threshold oxygen consumption due to changes in body composition associated to reductions in body fat. The authors speculated that a low-carbohydrate or ketogenic diet could be useful during the preseason in this sport discipline. It has also been previously speculated that low carbohydrate-adapted cyclists may compensate the reduced dietary carbohydrate availability by altering whole body substrate utilization (12), mainly by improving fat oxidation rates (13).

To the authors' knowledge no previous research has been conducted with highly trained road cyclists and low-carbohydrate diets. Therefore, this study attempted to verify and quantify the effects of these interventions on road cycling performance. The authors hypothesized that a low-carbohydrate diet could potentially reduce body fat while maintaining lean mass and peak power (5 and 20 min) levels in highly trained cyclists, therefore improving the power-to-weight ratio in this sport discipline as well as overall performance. According to all of this, the main objectives of the study were: a) to assess the efficacy of a low-carbohydrate diet in inducing body composition changes in a sample of trained cyclists, and b) to measure the changes in relative power values produced by the above-mentioned changes in body composition.

MATERIAL AND METHODS

PARTICIPANTS

Eleven highly-trained male road cyclists were recruited for the study. The main characteristics of the study sample were: age 31 ± 5 years; experience 9.4 ± 1.9 years; training 15 ± 3 hours per week; height 177.1 ± 4.8 cm, and weight 73.7 ± 3.2 kg. The inclusion criteria for the participants were: a) at least seven years of previous experience in cyclosportive events, and b) at least twelve hours of training volume per week. After being informed of the benefits and potential risks of the investigation, each participant completed a health-screening questionnaire (14) and provided his written informed consent prior to participation in the study. The study followed the ethical guidelines of the Declaration of Helsinki and received approval from the Research Ethics Committee of the autonomous region of Aragon, Spain (PI18/398).

TRAINING PROTOCOL

The experiment was conducted during the preparatory period of the annual training cycle, when low intensity dominates the daily training loads. Training loads of the same frequency, volume and intensity were adopted by all cyclists during the four weeks of the intervention period. The training protocol included high volume and moderate intensity in order to simulate common training practices in road cycling during the preseason. Participants performed four weekly (Monday, Wednesday, Friday and Saturday) training sessions at an intensity of 70 to 80% of their functional threshold power (FTP), and a duration of two and a half hours. The FTP results from subtracting 5% to the maximal power achieved during a 20-minute time trial. Participants used a left-side crank-based power meter for their training sessions (Stages Cycling, Colorado, USA). Participants extracted their training files from the bike computer and sent the data so the researchers could monitor the adherence to the training program. Energy expenditure was monitored with data extracted from the power meter in kilojoules (KJ).

DIETARY INTERVENTION

Participants were instructed to consume a low-carbohydrate diet (10% of calorie intake from carbohydrates, 25% from pro-

tein and 65% from fats) provided by a certified sports nutritionist. The distribution of macronutrients matched the definition of a low-carbohydrate diet accepted in the scientific literature (15). The total caloric intake was provided in relative values (50 kcal/kg/day), a quantity that was chosen in order to match the daily energy expenditure and avoid negative energy balances. An informative sheet with recommended foods and foods to be avoided was given to all participants. Intake was assessed with a previously validated once-weekly 72 h recall (16). Participants were considered as non-adherent when daily consumption of carbohydrates exceeded 15% of total daily calories.

ASSESSMENT OF BODY COMPOSITION AND PERFORMANCE

Body mass and body fat percentage were evaluated barefoot in the morning hours (7-8 am) after an overnight fast with the electrical impedance method (BC-602, Tanita Co., Tokyo, Japan) before and after the 4-week intervention period. Height was measured according to a previously established protocol (17) with a SECA 214 stadiometer, which is graduated up to 1 mm.

Two hours after breakfast, a power assessment test was performed following the protocol established by Hunter and Coggan (18) on the Tacx Neo Smart bike trainer (Tacx International, Rijksstraatweg, The Netherlands), which allows power, cadence and heart rate measurement. The protocol performed on the participants can be seen in table I. All participants performed the test in the same conditions (temperature, 20 ºC; humidity, 40%).

STATISTICAL ANALYSIS

The statistical analysis was performed with the R v3.5.3 (R Core Team, Vienna, Austria). Normality assumptions were verified using the Shapiro-Wilk test with Bonferroni correction. Statistics are presented as mean ± standard deviation (range) and estimates of parameters are stated as mean [95% confidence interval]. Mean comparisons were made using the t-test for paired samples, and statistical significance for confidence intervals was set at $\alpha = 0.05$. Effect size estimates were provided by calculating Hedge's *g* for paired samples, and interpreted according to Cohen (19): small, $g \leq 0.20$; medium, $g \leq 0.50$; large, $g \leq 0.80$.

Table I. Power assessment performed on the subjects, based on the work of Hunter & Coggan (2019)

Time (min)	% of functional threshold power
15	56-75
5	Max
10	56-75
20	100
15	56-75

RESULTS

The descriptive statistics may be seen in table II. Absolute power (AP) was comparable between measurements for both tests, 5 and 20 min (95% CI = -10.29 to 12.47 w, $t(10) = 0.21$, $p = 0.835$; and 95% CI = -1.56 to 6.27 w, $t(10) = 1.35$, $p = 0.208$, respectively). On the contrary, when adjusting power relative to body weight (RP) an increase of 95% CI = 0.04 to 0.46 w/kg was observed for the 5 min test ($t(10) = 2.7$, $p = 0.028$), corresponding to a small to medium effect size (95% CI = -0.14 to 1.7); and an increase of 95% CI = 0.12 to 0.28 w/kg in the 20 min test ($t(10) = 5.61$, $p < 0.001$), which corresponds to a medium to large effect according to Cohen (95% CI = 0.6 to 2.65). Participants lost a 95% CI = -1.71 to -3.9 kg after the intervention ($t(10) = -5.71$, $p < 0.001$), which corresponds to a medium to large effect size (95% CI = -0.63 to -2.69). Body fat was 95% CI = -1.29 to -3.54% lower after the intervention ($t(10) = -4.79$, $p < 0.001$), which corresponds to a small to large effect according to Cohen (95% CI = -0.4 to -2.38). Individual responses can be seen in figure 1. None of the 72 h recalls showed lack of compliance with the dietary intervention.

DISCUSSION

To the authors' knowledge, this has been the first study that has attempted to assess the effects of a low-carbohydrate diet on body composition and performance in trained road cyclists.

Table II. Participant characteristics and performance variables before and after the race

	Pre	Post
Age (years)	31 ± 5 (24-41)	
Experience (years)	9.5 ± 1.9 (7-13)	
Training (h/week)	15.1 ± 3 (12-20)	
Height (cm)	177.1 ± 4.8 (169-184)	
Weight (kg)	73.7 ± 3.2 (67.7-77.9)	70.9 ± 2.2 (66.8-74.5)
Body fat (%)	12.3 ± 1.4 (9.8-14.6)	9.9 ± 2 (7.8-13.9)
AP 5 min (w)	435 ± 68 (321-511)	436 ± 70 (325-503)
RP 5 min (w/kg)	5.89 ± 0.85 (4.51-7.15)	6.14 ± 0.93 (4.58-6.96)
AP 20 min (w)	314 ± 31 (272-377)	316 ± 31 (275-371)
RP 20 min (w/kg)	4.25 ± 0.33 (3.83-4.92)	4.45 ± 0.36 (3.88-5.12)

Results are presented as mean ± standard deviation (range). AP: absolute power; RP: relative power.

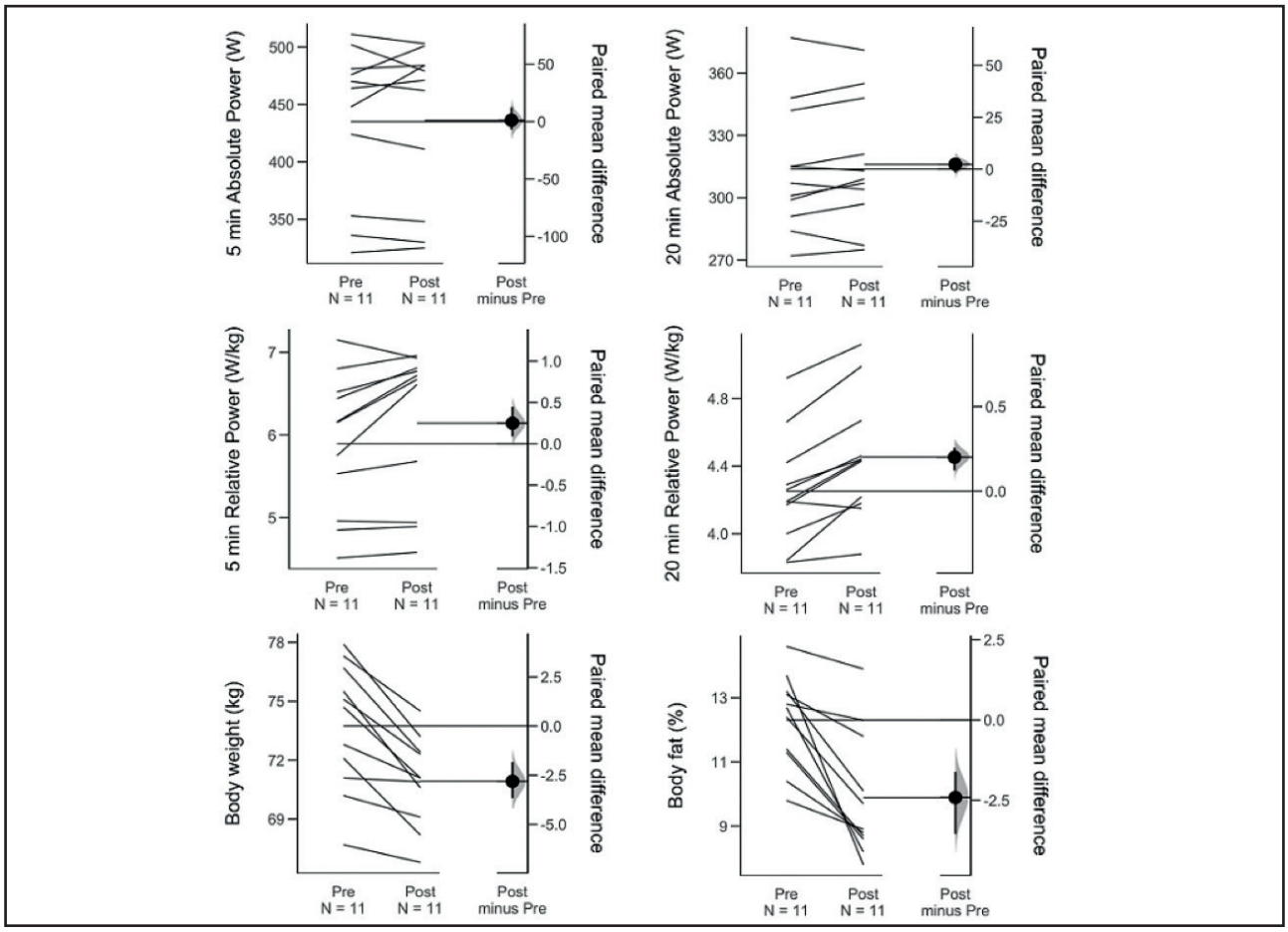

Figure 1.
Individual responses to the intervention.

The main findings of the study were: a) a low-carbohydrate diet did not have any influence on the absolute 5 and 20 min power output; b) body mass and body fat percentages were significantly reduced after four weeks on a low-carbohydrate diet in a sample of trained road cyclists; and c) as a consequence of the previous finding, the power-to-weight ratio expressed as w/kg was significantly increased after the dietary intervention.

These results are in accordance with the evidence provided by a previous systematic review (20), which found that low-carbohydrate diets typically had positive effects on body composition of endurance athletes and, therefore, improved relative power values. The only previous study performed on cyclists (11) also reported improvements in body composition and relative performance values, although the study sample was slightly different (off-road cyclists) and the dietary intervention limited even more the allowed quantity of carbohydrates (ketogenic diet).

It should be highlighted that the participants maintained a neutral energy balance during the study period, therefore a negative energy balance as the cause of the changes in body composition can be excluded. The study sample was composed of already trained cyclists who did not alter their physical activity substantially during the study period. Furthermore, the duration and intensity at which the workouts were performed were oriented to an environment in which, theoretically, a low-carbohydrate diet is more effective (13). It has also been reported that the "training low" strategy (workouts performed with low glycogen stores) could have beneficial effects on body composition (1), effects that are normally sought by endurance athletes during the preseason. According to all of this, the present study attempted to verify the utility of this dietary intervention in the most logical environment for its implementation.

In contrast, several concerns may arise when using a low-carbohydrate diet for performance enhancement. First, when training at high intensities with depleted carbohydrate stores there is a risk for low energy availability and drop in performance (22). Furthermore, although body composition changes associated to low-carbohydrate diets seem useful for attaining an appropriate power- to-weight ratio, carbohydrates are needed in order to optimize recovery (23), achieve higher rates of protein synthesis, and maintain desirable levels of muscle mass (24). With all these concerns in mind, preliminary evidence may suggest that a low-carbohydrate diet may not be an advisable nutritional

intervention for endurance athletes training at high intensities. The authors chose the preseason as the preferable time for implementing this strategy, when low relative intensities and high-volume work are used. These training characteristics could combine well with this type of intervention.

The authors acknowledge that the study had several limitations. First, the study sample was relatively small. Although eleven subjects may be a common sample size in similar studies, the number of participants and the lack of a control group make it difficult to isolate the role that the dietary intervention alone played in the results. Furthermore, the study period was relatively short for a dietary intervention as adaptations to low-carbohydrate and ketogenic diets normally occur after several weeks (25). The specificity of the study sample, that needed to incorporate high-intensity workouts into the schedule as soon as possible in order to be competitive, was one of the limiting factors when considering the duration of the intervention. The tool chosen for the assessment of body fat percentage is known for estimating this variable from total body water, and therefore is not a direct method. In summary, although the study provides preliminary results that suggest that a low-carbohydrate diet may be useful for road cyclists during the preseason, the conclusions should be interpreted with caution and further studies with larger sample sizes and a control group are needed in order to validate the results reported by the present study. Among other variables that could be of interest in future studies, intensities at which fat oxidation is maximal and changes in maximal oxygen consumption should be included.

CONCLUSIONS

A four-week intervention with a low-carbohydrate diet (10% of calories from carbohydrates) reduced body weight and body fat percentage, and improved relative power values (5 and 20 min) in a sample of eleven trained road cyclists. On the contrary, no effects were seen on absolute power values. Further research with larger sample sizes and a control group is needed in order to validate these results.

REFERENCES

1. Jeukendrup AE. Periodized Nutrition for Athletes. Sports Med 2017;47(Suppl 1):51-63. DOI: 10.1007/s40279-017-0694-2
2. Burke LM, Hawley JA, Wong SHS, Jeukendrup AE. Carbohydrates for training and competition. J Sports Sci 2011;29(sup1):S17-27. DOI: 10.1080/02640414.2011.585473
3. Bartlett JD, Hawley JA, Morton JP. Carbohydrate availability and exercise training adaptation: Too much of a good thing? Eur J Sport Sci 2015;15(1):3-12. DOI: 10.1080/17461391.2014.920926
4. Churuangsuk C, Kherouf M, Combet E, Lean M. Low-carbohydrate diets for overweight and obesity: a systematic review of the systematic reviews. Obes Rev 2018;19(12):1700-18. DOI: 10.1111/obr.12744
5. Gibson AA, Seimon RV, Lee CMY, Ayre J, Franklin J, Markovic TP, et al. Do ketogenic diets really suppress appetite? A systematic review and meta-analysis. Obes Rev 2015;16(1):64-76. DOI: 10.1111/obr.12230
6. Hu T, Yao L, Reynolds K, Niu T, Li S, Whelton PK, et al. Adherence to low-carbohydrate and low-fat diets in relation to weight loss and cardiovascular risk factors. Obes Sci Pract 2016;2(1):24-31. DOI: 10.1002/osp4.23
7. Sanders D, Heijboer M. Physical demands and power profile of different stage types within a cycling grand tour. Eur J Sport Sci 2018;1-9. DOI: 10.1080/17461391.2018.1554706
8. Maciejczyk M, Wiecek M, Szymura J, Szygula Z, Brown LE. Influence of Increased Body Mass and Body Composition on Cycling Anaerobic Power. J Strength Cond Res 2015;29(1):58-65. DOI: 10.1519/JSC.0000000000000727
9. Mujika I, Rønnestad BR, Martin DT. Effects of Increased Muscle Strength and Muscle Mass on Endurance-Cycling Performance. Int J Sports Physiol Perform 2016;11(3):283-9. DOI: 10.1123/ijspp.2015-0405
10. Greene DA, Varley BJ, Hartwig TB, Chapman P, Rigney M. A Low-Carbohydrate Ketogenic Diet Reduces Body Weight Without Compromising Performance in Powerlifting and Olympic Weightlifting Athletes. J Strength Cond Res 2018;32(12):1. DOI: 10.1519/JSC.0000000000002904
11. Zajac A, Poprzecki S, Maszczyk A, Czuba M, Michalczyk M, Zydek G. The Effects of a Ketogenic Diet on Exercise Metabolism and Physical Performance in Off-Road Cyclists. Nutrients 2014;6(7):2493. DOI: 10.3390/nu6072493
12. Webster CC, Noakes TD, Chacko SK, Swart J, Kohn TA, Smith JAH. Gluconeogenesis during endurance exercise in cyclists habituated to a long-term low carbohydrate high-fat diet. Authors J Physiol C 2016;594:4389-405. DOI: 10.1113/JP271934
13. Chang C-K, Borer K, Lin P-J. Low-Carbohydrate-High-Fat Diet: Can it Help Exercise Performance? J Hum Kinet 2017;56(1):81-92. DOI: 10.1515/hukin-2017-0025
14. Warburton DER, Jamnik V, Bredin SSD, Shephard RJ, Gledhill N. The 2019 Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and electronic Physical Activity Readiness Medical Examination (ePARmed-X+). Heal Fit J Canada 2018;11(4):80-3.
15. Feinman RD, Pogozelski WK, Astrup A, Bernstein RK, Fine EJ, Westman EC, et al. Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. Nutrition 2015;31(1):1-13. DOI: 10.1016/j.nut.2014.06.011
16. Schröder H, Covas MI, Marrugat J, Vila J, Pena A, Alcántara M, et al. Use of a three-day estimated food record, a 72-hour recall and a food-frequency questionnaire for dietary assessment in a Mediterranean Spanish population. Clin Nutr 2001;20(5):429-37. DOI: 10.1054/clnu.2001.0460
17. New Zealand Ministry of Health. Protocols for collecting, height, weight and waist measurements in NZHM surveys. 2008.
18. Allen H, Coggan A. Training and racing with a power meter. VeloPress; 2019.
19. Cohen J. Statistical Power Analysis for the Behavioral Sciences Second Edition. Routeledge; 1988.
20. Laval I, Sitko S. Dietas bajas en hidratos de carbono y rendimiento deportivo: Revisión Sistemática. J Negat No Posit Results 2019;4(6):634-43.
21. McSwiney FT, Wardrop B, Hyde PN, Lafountain RA, Volek JS, Doyle L. Keto-adaptation enhances exercise performance and body composition responses to training in endurance athletes. Metabolism 2018;81:25-34. DOI: 10.1016/j.metabol.2017.10.010
22. Jeukendrup AE, Killer SC. The Myths Surrounding Pre-Exercise Carbohydrate Feeding. Ann Nutr Metab 2010;57(s2):18-25. DOI: 10.1159/000322698
23. Burke LM, Jeukendrup AE, Jones AM, Mooses M. Contemporary Nutrition Strategies to Optimize Performance in Distance Runners and Race Walkers. Int J Sport Nutr Exerc Metab 2019;29(2):117-29. DOI: 10.1123/ijsnem.2019-0004
24. Jeukendrup AE. Nutrition for endurance sports: Marathon, triathlon, and road cycling. J Sports Sci. 2011 Jan 15;29(sup1):S91–9. DOI: 10.1080/02640414.2011.610348
25. Ma S, Suzuki K. Keto-Adaptation and Endurance Exercise Capacity, Fatigue Recovery, and Exercise-Induced Muscle and Organ Damage Prevention: A Narrative Review. Sport (Basel, Switzerland) 2019;7(2).

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ARÁN

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Revisión

Efecto de la suplementación de L-arginina y L-citrulina sobre el rendimiento físico: una revisión sistemática

The effect of supplementation with L-arginine and L-citrulline on physical performance: a systematic review

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Resumen

Introducción: los aminoácidos L-arginina (L-arg) y L-citrulina (L-citr) se han utilizado dentro de la nutrición deportiva y se cree que ejercen un efecto sobre el rendimiento físico. Sin embargo, la información existente es variada y poco concluyente.

Objetivo: revisar y analizar la evidencia científica existente dentro de los últimos diez años que relacionó los efectos de la suplementación con L-arg y L-citr sobre el rendimiento físico.

Material y método: el estudio corresponde a una revisión sistemática de estudios previamente publicados, siguiendo el modelo PRISMA. Se evaluaron artículos publicados entre los años 2008 y 2018 que relacionaron la suplementación de L-arg y L-citr sobre el rendimiento físico. La búsqueda electrónica se realizó a través de Web of Science, Scopus, Sport Discus, PubMed, Medline. Se incluyeron todos los artículos que utilizaron un protocolo de suplementación de estos aminoácidos por separado o en conjunto.

Resultados: se encontraron 38 artículos, los que se estratificaron según el protocolo utilizado: a) suplementación con L-arg (n = 19); b) suplementación con L-arg y L-citr (n = 1); y c) suplementación con L-citr (n = 18), tanto de corta duración como prolongada.

Conclusión: existe evidencia de que la L-citr puede funcionar mejor como ayuda ergogénica que la L-arg sobre el rendimiento físico, ya que la L-citr mostró un efecto positivo sobre la percepción subjetiva del esfuerzo y el dolor muscular, además de una disminución en las concentraciones de lactato y una disminución del tiempo en pruebas máximas. Sin embargo, aún falta evidencia para establecer la dosis de L-citr beneficiosa para el rendimiento físico.

Palabras clave:

Aminoácidos.
Ayudas ergogénicas.
Rendimiento físico.

Abstract

Introduction: the amino acids L-arginine (L-arg) and L-citrulline (L-citr) have been used in sports nutrition, and it is believed that they have an effect on physical performance. However, current information is varied and inconclusive.

Objective: to review and analyze the scientific evidence in the last ten years, which reflects a connection between the effect of L-arg and L-citr supplementation and physical performance.

Material and method: this study is a systematic review of articles previously published, following the PRISMA model. Those articles published between 2008 and 2018 that connected the effect of L-arg and L-citr supplementation with physical performance were analyzed. The electronic search was performed on Web of Science, Scopus, Sport Discus, PubMed, and Medline. All articles using a supplementation protocol with these amino acids, separately or in groups, were selected.

Results: a total of 38 articles were found, which were stratified according to the established protocol: a) supplementation with L-arg (n = 19); b) supplementation with L-arg and L-citr (n = 1); and c) supplementation with L-citr (n = 18), whether of short or prolonged duration.

Conclusion: there is evidence that L-citr works better as ergogenic than L-arg does on physical performance, since L-citr showed a positive effect on the rate of perceived exertion and muscular pain, in addition to a decrease in lactate concentrations and time in maximum tests. However, there is not enough evidence to establish a beneficial L-citr dosage for physical performance.

Key words:

Amino acids.
Ergogenic effects.
Sports performance.

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INTRODUCCIÓN

En búsqueda de mejorar el rendimiento deportivo, la nutrición deportiva ha puesto de manifiesto que los aminoácidos fisiológicos L-arginina (L-arg) y L-citrulina (L-citr) pueden ejercer un efecto ergogénico como precursores del óxido nítrico (NO) (1). Durante el ejercicio, y con la finalidad de suministrar más oxígeno y nutrientes a los músculos, el NO permite aumentar el flujo sanguíneo hacia los tejidos activos, mejorando así el rendimiento deportivo (2). También se ha evidenciado que la suplementación con L-arg podría disminuir las concentraciones de lactato ([La]) y amoniaco, ambos metabolitos implicados en el desarrollo de la fatiga muscular (3,4). Por su parte, junto con la L-arg y la ornitina (ORN), la L-citr es un componente del ciclo de la urea y está implicado en la desintoxicación de amoníaco en el hígado (2), siendo la producción de NO uno de los beneficios más documentados (1).

Considerando el rol del NO como vasodilatador (2), en los últimos años se han probado varios suplementos nutricionales que contienen precursores de este compuesto, evaluando así las posibles ayudas ergogénicas, tanto del NO como de sus precursores, sobre el rendimiento deportivo (5). De esta forma, sumadas al constante entrenamiento, estas ayudas ergogénicas proporcionarían, de forma legal, una ventaja competitiva sobre otros deportistas (6). Como se mencionó en párrafos anteriores, uno de los beneficios más importantes de L-arg es su papel en la producción de NO (1,7,8). Este precursor de NO ayudaría a promover la vasodilatación en el músculo durante el ejercicio (9), mejorando el flujo de sangre hacia los tejidos activos (8). Además, L-arg promueve la secreción de la hormona de crecimiento, aumentando la síntesis de proteínas y favoreciendo, de esta forma, la hipertrofia muscular (2), beneficiando así a los atletas que buscan aumentos en la fuerza y en la potencia (10). Sin embargo, la eficacia de la suplementación con L-arg es controvertida (11), ya que podría aumentar la tolerancia al ejercicio en sujetos sedentarios o moderadamente entrenados pero no en los sujetos altamente entrenados (11). Además, la L-arg oral es catabolizada por la arginasa intestinal en urea y ORN, reduciendo la biodisponibilidad de L-arg en plasma (12). Favorablemente, la L-citr tiene un efecto inhibitorio sobre la arginasa intestinal y, en el riñón, se convierte en argininosuccinato y L-arg (síntesis *de novo*) (12). En el intestino delgado de la mayoría de los mamíferos (incluidos seres humanos, cerdos y ratas) se puede sintetizar L-citr a partir de glutamina, glutamato y prolina (13), aunque muchos de los beneficios complementarios de la suplementación con L-citr para mejorar la masa muscular y el rendimiento, junto a la capacidad de ejercicio, aún se desconocen. Así, L-citr sigue siendo un aminoácido vital para la salud muscular y general del cuerpo, principalmente a través de su uso como precursor de L-arg (1).

De manera más específica, muy pocos estudios han examinado la suplementación con varias dosis de L-citr sobre el rendimiento deportivo (14), mientras que la suplementación de corta duración con alimentos ricos en L-citr (sandía o cápsulas) no ha demostrado efectos directos sobre el rendimiento físico (15,16). No obstante, estudios recientes respaldan el uso de la suplementación prolongada de L-citr, evidenciando un efecto ergogénico positivo en los ejercicios de resistencia (12), presuntamente indicando que la suplementación con este aminoácido puede tener influencias beneficiosas en la vía de la enzima óxido nítrico-sintasa (NOS) (con o sin la inclusión de malato), lo que podría mejorar el rendimiento durante los episodios repetidos de ejercicios de alta intensidad y/o los ejercicios continuos de naturaleza *start-stop* (17,18). Al parecer, la suplementación con L-citr podría otorgar una estrategia más efectiva para elevar la concentración extracelular de L-arg e incrementar la disponibilidad de NO, al menos cuando se consume en combinación con malato, aumentado de forma indirecta el rendimiento en los ejercicios aeróbicos de alta intensidad (11); sin embargo, se requieren estudios adicionales para investigar el potencial ergogénico de la L-citr sobre el rendimiento deportivo. Por estas razones sería importante esclarecer el efecto real que tienen tanto la L-arg como la L-citr sobre el rendimiento físico.

Durante las últimas décadas se han intentado descubrir y explicar las propiedades ergogénicas de los aminoácidos L-arg y L-citr, en todas sus formas, sobre el rendimiento deportivo, dando lugar a ensayos clínicos que tratan de confirmar estas propiedades (19-21). Sin embargo, a pesar de estas intensas y extensas investigaciones, los resultados son a menudo poco claros (22). Esto puede estar relacionado, en parte, con diferencias metodológicas entre los estudios, como la cantidad y duración de la suplementación, el tipo de ejercicio realizado y el nivel de entrenamiento de los sujetos (11). Por lo tanto, el objetivo de esta revisión sistemática fue revisar y analizar la evidencia científica existente dentro de los últimos diez años que relacionó los efectos de la suplementación con L-arg y L-citr sobre el rendimiento físico.

MATERIAL Y MÉTODO

PROCEDIMIENTO

El desarrollo de esta revisión sistemática se realizó a través de una minuciosa búsqueda orientada por referencias en distintas bases de datos y buscadores electrónicos: Web of Science (WOS), Scopus, SportDiscus, PubMed y Medline. Los límites de la búsqueda fueron: artículos publicados en los últimos diez años (enero de 2008 a julio 2018).

BÚSQUEDA BIBLIOGRÁFICA

La búsqueda bibliográfica se realizó de conformidad con las directrices de revisiones sistemáticas y metaanálisis (PRISMA) (23). En cada una de las bases de datos se realizaron búsquedas en el título, el resumen y los campos de búsqueda de palabras clave. Se utilizaron las siguientes palabras clave combinadas con los operadores booleanos AND/OR: "L-Citrulline" OR "L-Arginine" OR "Nitric-Oxide" OR "Nitric Oxide" OR "Nitrite" OR "Nitrate" AND "Ergogenic aid" OR "Supplementation" OR "Supplement" AND "Sport Performance" OR "Exercise Performance". Dos autores realizaron la búsqueda y revisaron los estudios; ambos decidieron si la inclusión de los estudios era apropiada. En caso de des-

acuerdo, se consultó al tercer autor. La estrategia de búsqueda y la selección de estudios se presentan en la figura 1.

CRITERIOS DE INCLUSIÓN Y EXCLUSIÓN

La importancia de cada estudio se evaluó de acuerdo con los siguientes criterios de inclusión: a) suplementación con L-arg y/o L-citr en todos sus formatos, ya sea una suplementación de corta duración o una suplementación prolongada; b) estudios con diseños experimentales; c) hombres y mujeres sanos; d) estudios que incluyeran una intervención basada en distintos entrenamientos de fuerza; e) estudios que declararan la línea de base y el grupo de control; f) estudios que reportaran cambios positivos o negativos en amoniaco, lactato, pH, frecuencia cardiaca, fatiga muscular y percepción de esfuerzo; g) estudios publicados en inglés, español, francés, portugués y alemán. Los estudios que no cumplieron los criterios de inclusión se excluyeron. Las discrepancias encontradas se resolvieron por consenso de los investigadores.

SUPLEMENTACIÓN DE DURACIÓN CORTA Y PROLONGADA

En cuanto a la clasificación de los protocolos de suplementación evaluados en esta revisión, se estableció como suplementación de corta duración aquella donde se usó una dosis única de suplemento en forma de L-arg, L-citr o citrulina malato (CM) entre los 0 minutos y las 24 horas previas o posteriores a la actividad física o el ejercicio. La suplementación prolongada se estableció como aquellos protocolos que usaron dosis repetidas de L-arg, L-citr o CM por más de 1 día y hasta por 6 semanas.

EVALUACIÓN DE LA CALIDAD METODOLÓGICA

Para evaluar la calidad de los estudios se utilizó la escala *Physiotherapy Evidence Database* (PEDro) (24,25). La clasificación se realizó en base a tres criterios: selección (máximo tres estrellas), comparabilidad (máximo tres estrellas) y resultados (máximo cuatro estrellas). Los artículos con puntuación de ocho a diez se consideraron de calidad metodológica alta, los puntuados de cuatro a siete de calidad moderada y los de puntuación menor de cuatro de calidad baja. La puntuación obtenida por los artículos según la escala PEDro indica que 27 estudios obtuvieron una puntuación alta y 11 una puntuación moderada (Tabla I).

RESULTADOS

En la búsqueda electrónica se identificaron 1211 artículos, de los cuales 673 eran duplicados. Los 538 artículos restantes se filtraron por títulos y resúmenes, quedando 69 artículos para la lectura y el análisis de forma íntegra. Tras revisar estos 69 artículos, 32 se eliminaron por no cumplir los criterios de inclusión. En la búsqueda de artículos orientada por las referencias bibliográficas se incluyó 1 estudio. Por lo anterior, la cantidad total de estudios para la revisión sistemática fue de 38 artículos. Estos artículos se estratificaron según el protocolo utilizado: a) suplementación con L-arg (n = 19; 11 con suplementación de corta duración y 8 con suplementación prolongada); b) suplementación con L-arg y L-citr (n = 1); y c) suplementación con L-citr (n = 18; 12 con suplementación de corta duración y 6 con suplementación prolongada) en forma de jugo de sandía, sintetizada o como CM (Tabla II).

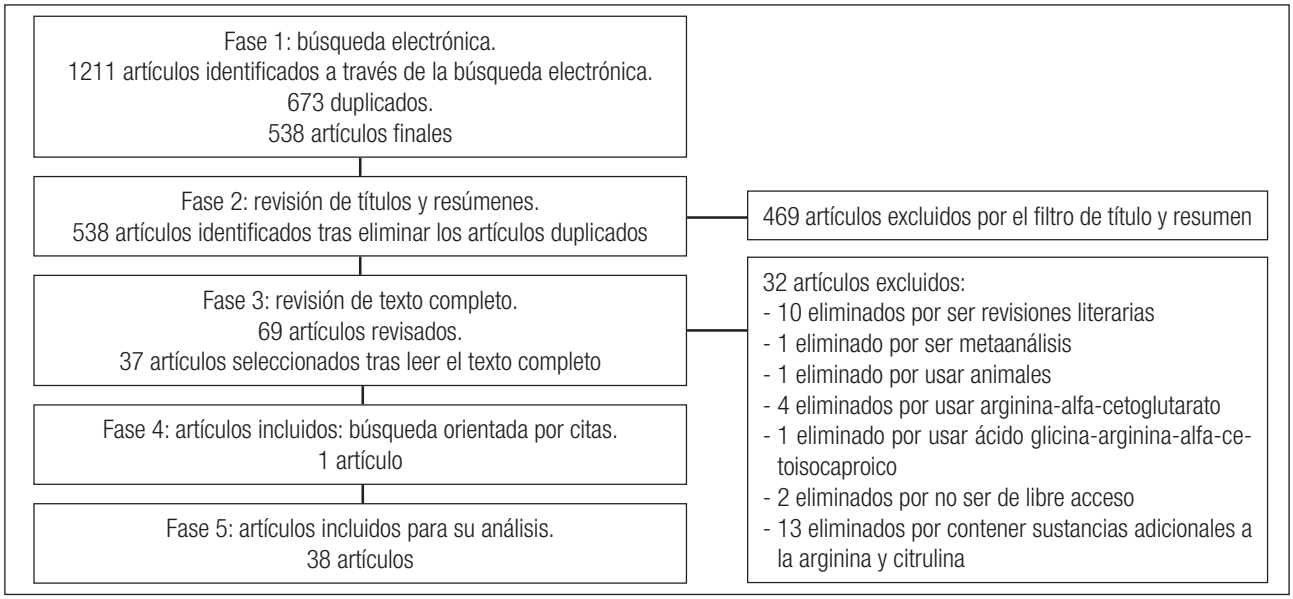

Figura 1.
Identificación de estudios en la revisión sistemática.

Tabla I. Lista de artículos incluidos con puntuación según la escala de PEDro

		Selección (1-2-3-4)	Comparabilidad (5-6-7)	Resultados (8-9-10-11)	Total
1	Tsai et al. (27)	#-*-0-*	*-0-0	*-*-*-*	7
2	Olek et al. (4)	#-*-*-*	*-*-0	*-*-*-*	9
3	Álvares et al. (32)	#-*-*-*	*-*-*	*-*-*-*	10
4	Álvares et al. (33)	#-*-*-*	*-*-*	*-*-*-*	10
5	Vanhatalo et al. (35)	#-*-*-*	*-*-*	*-*-*-*	10
6	Forbes et al. (34)	#-*-*-*	*-*-*	*-*-*-*	10
7	Forbes et al. (30)	#-*-*-*	*-*-0	*-*-*-*	9
8	Meirelles et al. (39)	#-*-*-*	*-*-*	*-*-*-*	10
9	Forbes et al. (37)	#-*-*-*	*-*-0	*-*-*-*	9
10	Yavuz et al. (21)	#-*-0-*	*-0-0	*-*-*-*	7
11	Aguiar et al. (38)	#-*-*-*	*-*-*	*-*-*-*	10
12	Bescós et al. (26)	#-*-0-*	0-0-0	*-*-*-*	6
13	Liu et al. (3)	#-*-0-*	*-0-0	*-*-*-*	7
14	Fahs et al. (28)	#-*-*-*	*-*-*	*-*-*-*	10
15	Imanipour et al. (31)	#-*-0-*	*-0-0	*-*-*-*	7
16	Sunderland et al. (29)	#-*-*-*	*-*-0	*-*-*-*	9
17	Álvares et al. (36)	#-*-*-*	*-*-*	*-*-*-*	10
18	Shirali et al. (41)	#-*-0-*	*-0-0	*-*-*-*	7
19	Mor et al. (40)	#-*-0-*	*-0-0	*-*-*-*	7
20	Bailey et al. (44)	#-*-*-*	*-*-*	*-*-*-*	10
21	Tarazona-Díaz et al. (16)	#-*-0-*	*-0-0	*-*-*-*	7
22	Martínez-Sánchez et al. (15)	#-*-*-*	*-*-*	*-*-*-*	10
23	Bailey et al. (42)	#-*-*-*	*-*-*	*-*-*-*	10
24	Shanely et al. (43)	#-*-0-*	*-0-0	*-*-*-*	7
25	Cutrufello et al. (14)	#-*-*-*	*-*-0	*-*-*-*	9
26	Suzuki et al. (18)	#-*-*-*	*-*-*	*-*-*-*	10
27	Gonzales et al. (45)	#-*-*-*	*-*-*	*-*-*-*	10
28	Ashley et al. (46)	#-*-*-*	*-*-*	*-*-*-*	10
29	Pérez-Guisado et al. (20)	#-*-*-*	*-*-*	*-*-*-*	10
30	Glenn et al. (17)	#-*-*-*	*-*-*	*-*-*-*	10
31	Glenn. (49)	#-*-*-*	*-*-*	*-*-*-*	10
32	Cunniffe et al. (48)	#-*-*-*	*-*-*	*-*-*-*	10
33	Wax et al. (6)	#-*-*-*	*-*-*	*-*-*-*	10
34	Wax et al. (47)	#-*-*-*	*-*-*	*-*-*-*	10
35	Da Silva et al. (50)	#-*-*-*	*-*-*	*-*-*-*	10
36	Farney et al. (51)	#-*-0-*	*-0-0	*-*-*-*	7
37	Gonzalez et al. (52)	#-*-*-*	*-*-*	*-*-*-*	10
38	Kiyici et al. (19)	#-*-0-*	*-0-0	*-*-*-*	7

Elementos en la escala PEDro: 1: los criterios de elegibilidad fueron especificados; 2: los sujetos fueron asignados al azar a grupos; 3: la asignación fue oculta; 4: los grupos fueron similares al inicio en relación a los indicadores de pronóstico más importantes; 5: todos los sujetos fueron enmascarados; 6: todos los terapeutas que administraron la terapia fueron enmascarados; 7: todos los evaluadores que midieron al menos un resultado clave fueron enmascarados; 8: las medidas de al menos uno de los resultados clave fueron obtenidas de más del 85% de los sujetos inicialmente asignados a los grupos; 9: se presentaron resultados de todos los sujetos que recibieron tratamiento o fueron asignados al grupo de control o, cuando esto no pudo ser, los datos de al menos un resultado clave fueron analizados por "intención de tratar"; 10: los resultados de comparaciones estadísticas entre grupos fueron informados para al menos un resultado clave; 11: el estudio proporciona medidas puntuales y de variabilidad para al menos un resultado clave; #: cuenta con los criterios de elección especificados pero no se contabiliza como puntuación.

Tabla II. Características de las publicaciones que relacionan la suplementación de L-arg y L-citr con el rendimiento físico

Referencia	Año	Objetivos	Sujetos	Variables	Protocolo	Resultados	Rendimiento
Efecto de la suplementación aguda con L-arg sobre el rendimiento físico							
Tsai et al. (27)	2009	Examinar los efectos del suplemento de L-arg sobre parámetros hormonales, metabólicos y de movilización de lípidos	H: 12	I: L-arg D: [glucosa], [insulina], [AGL], [glicerol], [La], [amoníaco], [CK] y [NO_x] plasmático	Post-ejercicio: GC: placebo GE: 0,1 g·kg·d^{-1} de L-arg	↑ [glucosa] y ↑ [insulina] en GE vs. GC ($p < 0,05$) ↓ [AGL] en GE vs. GC ($p < 0,05$) [NO_x], [CK], [La], [amoníaco] y [glicerol]: ns	↑
Olek et al. (4)	2010	Determinar el efecto de la L-arg, 60 minutosantes del ejercicio, sobre el rendimiento y el metabolismo durante la prueba anaeróbica de Wingate	H: 6	I: L-arg D: potencia (Watt), consumo de O_2, [La], [glucosa], [amoníaco] y [NO_x]	Pre-ejercicio: GC: placebo GE: 2 g·d^{-1} de L-arg	Potencia (Watt), consumo de O_2, [La], [glucosa], [amoníaco] y [NO_x]: ns	=
Álvares et al. (32)	2012	Identificar los efectos agudos de L-arg sobre el volumen sanguíneo, la oxigenación muscular y los marcadores de producción de NO-NO_x en sujetos masculinos sanos	H: 15	I: L-arg D: oxigenación muscular y volumen sanguíneo muscular	Pre-ejercicio: GC: placebo GE: 6 g·d^{-1} de L-arg	↑ Volumen sanguíneo muscular en el periodo de recuperación en GE vs. GC ($p < 0,05$) [NO_x], rendimiento de fuerza y oxigenación muscular: ns	=
Álvares et al. (33)	2012	Identificar los efectos agudos de la L-arg sobre los indicadores de rendimiento muscular y recuperación	H: 17	I: L-arg D: potencia promedio, trabajo total, relación de recuperación de trabajo, NO y [NO_x]	Pre-ejercicio: GC: placebo GE: 16 g·d^{-1} de L-arg	Potencia promedio, trabajo total, relación de recuperación de trabajo, NO y [NO_x]: ns	=
Vanhatalo et al. (35)	2013	Determinar si la L-arg mejora el biomarcador de la producción de NO endógeno, reduce el coste de O_2 durante el ejercicio y mejora la tolerancia al ejercicio	H: 23	I: L-arg D: [NO],[NOx], PA, VO_2 y tolerancia al ejercicio	Pre-ejercicio: GC: placebo GE_1: 6 g·d^{-1} de L-Arg GE_2: 6 g·d^{-1} de L -Arg + 25 g de CHO	[NO_3], [NO_2], PA, VO_2 y tolerancia al ejercicio: ns	=
Forbes et al. (34)	2013	Investigar el efecto de la ingestión aguda de L-arginina sobre la respuesta hormonal y metabólica durante el ejercicio submáximo en ciclistas entrenados	H: 15	I: L-arg D: [GH], [AGL], [La], [glucosa], VO_2, VCO_2, RER, oxidación de CHO y [NO_x]	Pre-ejercicio: GC: placebo GE: 0,075 g·Kg·d^{-1} de L-arg	↑ Oxidación de grasas al inicio del ejercicio en GE vs. GC ($p < 0,05$) ↑ [glicerol] a los 45 min de ejercicio en GE vs. GC ($p < 0,05$) ↑ [arg] en GE vs. GC ($p < 0,05$) [GH], [AGL], [La], [glucosa], VO_2, VCO_2, RER, oxidación de CHO y [NO_x]: ns	=
Forbes et al. (30)	2011	Investigar el efecto de una dosis baja y alta de L-arg en relación con la masa corporal de sujetos físicamente activos	H: 14	I: L-arg D: L-arg, [NO_x], GH, IGF-1 e insulina	Pre-ejercicio: GC: placebo GE_1: 0,075 g·kg·d^{-1} de L- arg GE_2: 0,15 g·kg·d^{-1} de L- arg	↑ [L-arg] en GE_1 y GE_2 vs. GC ($p < 0,05$) [NO_x], GH, IGF-1 e insulina: ns	=
Meirelles et al. (39)	2018	Determinar el efecto agudo de la suplementación con L-arg sobre el rendimiento de la fuerza y la producción de NO	H: 12	I: L-arg D: [NO] y número de repeticiones	Pre-ejercicio GC: placebo GE: 6 g·d^{-1} de L-arg	[NO] y número de repeticiones: ns	=
Forbes et al. (37)	2014	Estudiar los efectos combinados del ejercicio de resistencia muscular y la suplementación con L-arg sobre GH, secretores de GH e IGF-1	H: 14	I: L-arg D: GH, grelina, hormona inhibidora de GH e IGF-1	Pre-ejercicio GC: placebo GE: 0,075 g·kg·d^{-1} de L-arg	↑ [L-arg] en GE vs. GC ($p < 0,05$) ↓ Hormona inhibidora de GH en GE vs. GC ($p < 0,05$) [GH], [hormona liberadora de GH], [grelina] o IGF-1: ns	=
Yavuz et al. (21)	2014	Evaluar el posible efecto de la ingesta aguda de L-arg sobre el rendimiento y el metabolismo durante el ejercicio exhaustivo incremental en luchadores de élite	H: 9	I: L-arg D: $VO_{2máx}$, FC, [La] durante ejercicio y recuperación	Pre-ejercicio GC: placebo GE: suplemento de 1,5 g·10 kg·d^{-1} de L -arg	Mayor tiempo de ejecución en prueba hasta el agotamiento en GE vs. GC ($p < 0,05$) [La], $VO_{2máx}$ y FC: ns	↑
Aguiar et al. (38)	2015	Examinar los efectos de L-arg sobre la vasodilatación periférica y el rendimiento muscular	F: 20	I: L-arg D: flujo sanguíneo femoral y variables de fuerza (isocinética, isométrica y funcional)	Pre-ejercicio GC: placebo GE: 8 g·d^{-1} de L-arg	Flujo sanguíneo femoral y variables de fuerza (isocinética, isométrica y funcional): ns	=

(Continúa en la página siguiente)

Tabla II (Cont.). Características de las publicaciones que relacionan la suplementación de L-arg y L-citr con el rendimiento físico

Referencia	Año	Objetivos	Sujetos	Variables	Protocolo	Resultados	Rendimiento
Efecto de la suplementación crónica con L-arg sobre el rendimiento físico							
Bescós et al. (26)	2009	Determinar si el aumento de la ingesta de L-arg aumenta la entrega de NO y reduce los valores de $VO_{2máx}$ y/o [La] durante el ejercicio	H: 9	I: L-arg D: [NO_3], [La], $VO_{2máx}$ y FC	Pre-ejercicio GC: 5,5 g·d^{-1} de L-arg GE_1: 9,0 g·d^{-1} de L-arg GE_2: 20,5 g·d^{-1} de L-arg	↓ [La] a los 5 min de ejercicio en GE_2 vs. GC y G_1 ($p < 0,05$) [NO_3], $VO_{2máx}$ y FC: ns	=
Liu et al. (3)	2009	Evaluar el efecto de la suplementación con L-arg sobre el rendimiento en el ejercicio intermitente	H: 10	I: L-arg D: [NO_3], [NO_2], [NO], [L-citr], [amoníaco] y [La]	3 días: GC: placebo GE: 6 g·d^{-1} de L-arg	↑ [NO_3] 6 min post-ejercicio en GE vs. GC ($p < 0,05$) ↑ [NO_2] 6 min post-ejercicio en GE vs. GC ($p < 0,05$) [NO], [La] y [amoníaco]: ns	=
Fahs et al. (28)	2009	Examinar el efecto de la suplementación con L-arg aguda y el ejercicio de resistencia muscular sobre la función arterial	H: 18	I: L-arg D: AiX, la rigidez arterial y FBF	GC: Placebo GE: 7 g·d^{-1} de L-arg c/serie ejercicio	↓ Rigidez braquial en GE vs. GC ($p = 0,0001$) ↑ Rigidez aórtica central en GE vs. GC ($p = 0,004$) ↑ AiX en GE vs. GC ($p = 0,023$) ↑ FBF en GE vs. GC ($p = 0,000$) Flujo sanguíneo: ns	=
Imanipour et al. (31)	2011	Investigar el efecto de la L-arg a largo plazo sobre el NO en el ejercicio anaeróbico intermitente	H: 30	I: L-arg D: NO	6 semanas GC: placebo GE: 12 g·d^{-1} de L-arg	NO: ns	=
Sunderland et al. (29)	2011	Determinar si 28 días de suplementación con L-arg mejoran el $VO_{2máx}$ y retrasan el VT en ciclistas aprendices	H: 18	I: L-arg D: $VO_{2máx}$ y VT	4 semanas: GC: placebo GE: 12 g·d^{-1} de L-arg	$VO_{2máx}$ y VT: ns	=
Álvares et al. (36)	2014	Investigar los efectos de 4 semanas de suplementación con L-arg sobre parámetros metabólicos y hormonales en reposo y ejercicio	H: 11 M: 4	I: L-arg D: tiempo total de prueba [NO], [NOx], GMPc, [La], [amoníaco], [insulina], [GH], IGFH-1 y [cortisol]	4 semanas: GC: placebo GE: 6 g·d^{-1} de L -arg	Tiempo total de prueba, [NO], [NO_x], GMPc, [La], [amoníaco], [insulina], [GH], IGFH-1 y [cortisol]: ns	=
Shirali et al. (41)	2016	Comparar los efectos de 4 semanas de entrenamiento de resistencia muscular y el consumo L-arg sobre la GH e IGF-1	H: 40	I: L-arg D: [GH] e IGF-1.	4 semanas: GC: placebo GE_1: entrenamiento resistido de 4 semanas, 3 veces/semana, 3 series de 10 ejercicios, 6-10 rep., 80-95% 1RM GE_2: 0,1 g·kg·d^{-1} de L-arg GE_3: entrenamiento + 0,1 g·kg·d^{-1} de L-arg	↑ GH, IGF, IGFBP-III en GE_1 y GE_3 vs. GE_2 y GC ($p < 0,05$)	↑ en GE_1 y GE_3
Mor et al. (40)	2018	Determinar el efecto de la L-arg sobre el rendimiento y la recuperación anaeróbica	H: 28	I: L-arg D: IMC, capacidad anaeróbica, [La], FC y marcadores bioquímicos	2 semanas: GC: placebo GE: 6 g·d^{-1} de L-arg (3 g pre y post-prueba)	↓ IMC, [LDH], [AST] y [ALT] en GE vs. GC ($p < 0,05$) FC: ns	↑

(Continúa en la página siguiente)

Tabla II (Cont.). Características de las publicaciones que relacionan la suplementación de L-arg y L-citr con el rendimiento físico

Referencia	Año	Objetivos	Sujetos	Variables	Protocolo	Resultados	Rendimiento
Efecto de la suplementación con L-arg y L-citr sobre el rendimiento físico							
Bailey et al. (44)	2015	Comparar los efectos de L-citr y L-arg sobre los biomarcadores de NO, la captación pulmonar de O_2 y el rendimiento del ejercicio	F: 10	I: L-arg y L-citr D: [NO], PA, cinética de VO_2 pulmonar, oxigenación muscular y rendimiento del ejercicio	7 días: GC: placebo GE_1: 6 g·d^{-1} de L-arg GE_2: 6 g·d^{-1} de L-citr	↓ Tiempo de respuesta medio del VO_2: en GE_1 vs. GE_2 y GC ($p < 0,05$) ↓ PA en GE_2 vs. GE_1 y GC ($p < 0,05$) Mejoró la tolerancia al ejercicio de intensidad elevada y el tiempo total de ejercicio en GE_2 vs. GE_1 y GC ($p < 0,05$)	↑
Efecto de la suplementación aguda con L-citr de jugo de sandía sobre el rendimiento físico							
Tarazona-Díaz et al. (16)	2013	Determinar la biodisponibilidad de la L-citr a través de su suplementación en el rendimiento del atletismo	H: 7	I: L-citr D: [La], FC, dolor muscular y esfuerzo percibido	Pre-ejercicio: GC: placebo GE_1: 500 mL de jugo de sandía natural (1,17 g·d^{-1} de L-citr) GE2: 500 mL de jugo de sandía enriquecido con 6 g·d^{-1} de L-citr (1,17 g de sandía + 4,83 g añadidos)	↓ FC a los 1-3 min de ejercicio en GE_1 y GE_2 vs. GC ($p < 0,05$) ↓ Percepción del dolor 24 h post-ejercicio en GE_1 y GE_2 vs. GC ($p < 0,05$)	↑
Martínez-Sánchez et al. (15)	2017	Evaluar el efecto del jugo de sandía enriquecido con L-citr sobre el rendimiento físico y los marcadores bioquímicos después de una carrera de media maratón	H: 21	I: jugo de sandía + L-citr D: altura del salto, FC, esfuerzo percibido, dolor muscular y marcadores bioquímicos	Pre-ejercicio: GC: placebo GE: 3,45 g·d^{-1} de L-citr/500 mL de jugo	↓ SJ y CMJ en GC vs. GE ($p < 0,05$) ↓ Percepción del dolor muscular 24 a 72 h post carrera GE vs. GC ($p < 0,05$) [La], [glucosa] y [L-arg]: ns	↑ dolor muscular = [La], [glucosa] y [L-arg]
Efecto de la suplementación crónica con L-citr de jugo de sandía sobre el rendimiento físico							
Bailey et al. (42)	2016	Evaluar los efectos del jugo de sandía sobre las concentraciones de L-citr, L-arg y NO_2 en plasma, la oxigenación del músculo, la captación de oxígeno pulmonar y el rendimiento del ejercicio	H: 8	I: L-arg y L-citr D: PA, [L-citr] en plasma, [L-arg] en plasma, [NO_2], oxigenación del músculo y tiempo hasta el agotamiento durante el ejercicio de intensidad elevada	16 días: GC_1: sin suplemento GC_2: placebo GE: 300 mL de zumo de sandía (3,4 g·d^{-1} de L-citr)	↑ [L-citr], [L-arg] y [NO_2]: GC_2 y GE vs. GC_1 ($p < 0,01$) Mayor índice de oxigenación del músculo en el ejercicio de intensidad moderada en GE vs. GC_1 y GC_2 ($p < 0,05$) Tiempo hasta agotamiento: ns	↑ GE
Shanely et al. (43)	2016	Comparar el efecto del jugo de sandía y las bebidas de HC sobre la inflamación sistémica, la disfunción inmunitaria y la capacidad antioxidante del plasma	H: 20	I: jugo de sandía y/o bebida de HC D: [NO], capacidad antioxidante, citoquinas y FC	2 semanas: GE_1: suplemento con 0,2 g·kg·d^{-1} de HC GE_2: 980 mL de jugo de sandía (1,47 g·d^{-1} de L-citr)	↑ [L-citr] y [L-arg] en GE_2 vs. GE_1 ($p < 0,0125$) ↑ Capacidad antioxidante después del ejercicio ($p < 0,05$) en GE_2 vs. GE_1 Citoquinas: ns	↑ GE_2 vs. GE_1
Efecto de la suplementación aguda con L-citr sintetizada en el rendimiento físico							
Cutrufello et al. (14)	2014	Examinar el efecto de la suplementación de L-citr sobre el número total de repeticiones en press banca, el $VO_{2máx}$, el umbral anaeróbico y el flujo sanguíneo	H: 11 M: 11	I: L-citr D: número total de repeticiones, tiempo hasta el agotamiento, $VO_{2máx}$, umbral anaeróbico y flujo sanguíneo	Pre-ejercicio: GC: placebo GE_1: 6 g·d^{-1} de L-citr GE_2: 710 mL de jugo de sandia (equivalente a 1 g·d^{-1} de L-citr)	Número total de repeticiones, tiempo hasta el agotamiento, $VO_{2máx}$, umbral anaeróbico y flujo sanguíneo: ns	=

(Continúa en la página siguiente)

Tabla II (Cont.). Características de las publicaciones que relacionan la suplementación de L-arg y L-citr con el rendimiento físico

Referencia	Año	Objetivos	Sujetos	Variables	Protocolo	Resultados	Rendimiento
Efecto de la suplementación crónica con L-citr sintetizada sobre el rendimiento físico							
Suzukiy et al. (18)	2016	Investigar el efecto de la suplementación de L-citr sobre el rendimiento en pruebas de ciclismo	H: 25	I: L-citr D: potencia de salida, $VO_{2máx}$, [NOx], $[NO_2]$, [aminoácidos] y tiempo de prueba	2 semanas: GC: placebo GE: 2,4 g·d^{-1} de L-citr	↑ [L-arg] y [L-citr] en GE vs. GC ($p < 0,05$), menor percepción de fatiga muscular y mejora de concentración en GE vs. GC ($p < 0,05$) ↓ Tiempo de ejecución de la prueba en GE vs. GC ($p < 0,05$) Potencia de salida en GE vs. GC ($p < 0,025$) $[NO_x]$ y respuesta del $VO_{2máx}$: ns	↑
Gonzales et al. (45)	2017	Probar el efecto de la L-citr en dosis crónica sobre el flujo sanguíneo muscular y la dilatación periférica durante el ejercicio	H: 12 M: 13	I: L-citr D: FC, PA y flujo sanguíneo	2 semanas: GC: placebo GE: 6 g·d^{-1} de L-citr	↓ PA diastólica en hombres ($p = 0,02$) y ns en mujeres ↑ Flujo sanguíneo y conducción vascular durante el ejercicio a mayores cargas de trabajo ($p = 0,01$) en hombres y ns en mujeres	↑ pero no en M
Ashley et al. (46)	2018	Probar los efectos de la L-citr sobre la cinética del VO_2 durante la marcha	H: 11 M: 15	I: L-citr D: VO_2 pulmonar, coste neto de O_2, tiempo medio de respuesta y déficit de O_2	1 semana: GC: placebo GE: 6 g·d^{-1} de L-citr	Adultos jóvenes presentaron tiempo medio de respuesta menor en GE vs. GC ($p < 0,05$) VO_2 pulmonar, costo neto de O_2 y déficit de O_2: ns	↑ en M
Efecto de la suplementación aguda con CM sobre el rendimiento físico							
Pérez-Guisado et al. (20)	2010	Determinar el efecto de la suplementación de CM sobre el rendimiento del ejercicio anaeróbico de alta intensidad y el dolor muscular	H: 41	I: CM D: número de repeticiones en press banca y nivel de dolor muscular	Pre-ejercicio: GC: placebo GE: 8 g·d^{-1} de CM	↑ Número de repeticiones en GE vs. GC ($p < 0,0001$) ↓ Percepción del dolor 24 h y 48 h post-ejercicio en GE vs. GC ($p < 0,0001$)	↑
Glenn et al. (17)	2015	Evaluar el efecto de la suplementación con CM sobre el rendimiento en el levantamiento de pesas	M: 15	I: CM D: número de repeticiones completadas, FC y percepción del esfuerzo	Pre-ejercicio: GC: placebo GE_1: 8 g·d^{-1} de CM	↑ Número de repeticiones en press banca en GE vs. GC ($p = 0,045$) ↑ Número de repeticiones en press piernas en GE vs. GC ($p = 0,03$) ↓ Percepción del esfuerzo en GE vs. GC ($p = 0,02$) FC: ns	↑
Glenn et al. (49)	2016	Examinar el efecto de la suplementación con CM sobre la fuerza de agarre, la potencia vertical y el rendimiento del ciclismo anaeróbico en jugadoras de tenis máster	M: 17	I: CM D: fuerza de prensión y potencia	Pre-ejercicio: GC: placebo GE: 8 g·d^{-1} de CM	↑ Fuerza de prensión máxima en GE vs. GC ($p = 0,042$) Mayor potencia máxima y potencia explosiva en GE vs. GC ($p < 0,001$)	↑
Cunniffe et al. (48)	2016	Examinar el efecto de la suplementación de CM sobre el equilibrio ácido-base y el rendimiento en el ejercicio de alta intensidad	H: 10	I: CM D: [L-citr], FC, esfuerzo percibido, [La], pH y tiempo de agotamiento	Pre-ejercicio: GC: Placebo GE: 12 g de CM en 400 mL	↑ [L-citr], [ORN], [glutamina] durante el ejercicio en GE vs. GC ($p < 0,05$) Potencia media, índice de fatiga, esfuerzo percibido, pH, La y bicarbonato: ns	=

(Continúa en la página siguiente)

Tabla II (Cont.). Características de las publicaciones que relacionan la suplementación de L-arg y L-citr con el rendimiento físico

Referencia	Año	Objetivos	Sujetos	Variables	Protocolo	Resultados	Rendimiento
Efecto de la suplementación aguda con CM sobre el rendimiento físico (cont.)							
Wax et al. (6)	2015	Evaluar la eficacia de la suplementación con CM sobre el rendimiento, el lactato, la FC y la PA durante el ejercicio de resistencia dinámica de la parte inferior del cuerpo	H: 12	I: CM D: número de repeticiones, [La], FC, PA sistólica y diastólica	Pre-ejercicio: GC: Placebo GE: 8 g·d^{-1} de CM	↑ Número de repeticiones en GE vs. GC ($p < 0,05$) [La], FC, PA sistólica y diastólica: ns	↑
Wax et al. (47)	2016	Investigar el efecto de la suplementación con CM durante episodios repetidos de ejercicios resistidos del miembro superior	H: 14	I: CM D: número de repeticiones máximas, FC y [La]	Pre-ejercicio: GC: placebo GE: 8 g·d^{-1} de CM	↑ Número de repeticiones de dominadas en GE vs. GC ($p = 0,003$) ↑ Dominadas inversas en GE vs. GC ($p = 0,017$) ↑ Flexiones en GE vs. GC ($p < 0,001$) [La]: ns	↑
Da Silva et al. (50)	2017	Determinar el efecto de la suplementación con CM sobre la recuperación muscular después de una sesión de ejercicios de resistencia de alta intensidad	H: 9	I: CM D: número de repeticiones máximas, señal electromiográfica, dolor muscular y esfuerzo percibido, [CK], [La], [insulina], testosterona y cortisol	Pre-ejercicio: GC: placebo GE: 6 g·d^{-1} de CM	Número de repeticiones máximas, señal electromiográfica, dolor muscular y esfuerzo percibido, [CK], [La], [insulina] y testosterona y cortisol: ns	=
Farney et al. (51)	2018	Examinar los efectos de la suplementación con CM sobre la fatiga muscular	H: 6 M: 6	I: CM D: Tasa de fatiga, potencia máxima y [La]	Pre-ejercicio: GC: placebo GE: 8 g·d^{-1} de CM	↓ Torque máximo ($p = 0,003$), potencia máxima ($p = 0,003$) y tasa de fatiga en GE vs. GC ($p = 0,001$). ↑ Acumulación de lactato desde pre/post-ejercicio en GE vs. GC ($p = 0,0001$)	↓
González et al. (52)	2017	Investigar los efectos de la suplementación con CM sobre cantidad de repeticiones, potencia de salida, respuesta de hinchazón muscular y medidas subjetivas de concentración, energía y fatiga durante ejercicios de fuerza	H: 12	I: CM D: medidas subjetivas de energía, concentración, fatiga y esfuerzo percibido, y grosor muscular del tríceps braquial	Pre-ejercicio: GC: placebo GE: 8 g·d^{-1} de CM	↓ Concentración, fatiga, esfuerzo percibido en GE vs. GC ($p < 0,05$) ↑ Grosor muscular del tríceps braquial en GE vs. GC ($p<0,05$) Sensación subjetiva de energía: ns	↑
Efecto de la suplementación crónica con CM sobre el rendimiento físico							
Kiyici et al. (19)	2017	Examinar el efecto de la suplementación de CM con entrenamiento intensivo en el nivel de lactato en sangre	H: 22	I: CM D: [La]	4 semanas: GC: placebo GE: 3 g•d^{-1} de CM (1 g 3 veces al día)	↓ [La] en GE *vs.* GC ($p < 0,05$)	↑

I: independiente; D: dependiente; H: hombre; M: mujer; ↑: aumenta; ↓: disminuye; =: se mantiene; GC: grupo de control; GE: grupo experimental; ns: no significativo; NO: óxido nítrico; NO_x: óxidos de nitrógeno; NO_2: nitrito; NO_3: nitrato; $VO_{2máx}$: consumo máximo de oxígeno; CK: creatina-quinasa; La: lactato; [La]: concentración de lactato; FC: frecuencia cardiaca; IMC: índice de masa corporal; LDH: lactato-deshidrogenasa; GMPc: guanosina monofosfato cíclico; g: gramos; kg: kilogramos; mg: miligramos; CM: citrulina malato; L-arg: L-arginina; L-citr: L-citrulina; HC: hidratos de carbono; AG: ácidos grasos; O_2: oxígeno; PA: presión arterial; AST: aspartato-aminotransferasa; ALT: alanina-aminotransferasa); AiX: índice de aumento radial; FBF: flujo de sangre del antebrazo; CB: circunferencia del brazo; VT: umbral ventilatorio.

DISCUSIÓN

EFECTO DE LA SUPLEMENTACIÓN DE CORTA DURACIÓN CON L-arg SOBRE EL RENDIMIENTO FÍSICO

En relación a los estudios consultados e independientemente de la dosis suministrada (desde 0,075 hasta 8,0 $g \cdot d^{-1}$), la tendencia del efecto de la suplementación de corta duración con L-arg parece no tener influencias en variables como el óxido de nitrógeno (NO_x) (32,33), la oxigenación muscular (33), el consumo de oxígeno, la secreción de hormona del crecimiento o la [La] (34); tampoco produce cambios sobre el dióxido de nitrógeno (NO_2), el nitrato (NO_3) o la tolerancia al ejercicio (35). Pese a ello, algunas investigaciones han reportado un aumento del volumen sanguíneo (33), un descenso en la presión arterial de reposo (35) y un aumento de la L-citr plasmática luego de una ingesta de L-arg de corta duración (30,34). Estos últimos hallazgos, pese a que son neutros para el rendimiento deportivo, estarían asociados a vasodilatación del tejido activo (9), aumentando el flujo de sangre hacia los músculos en ejercicio. Sin embargo, y hasta donde el conocimiento alcanza, la suplementación de corta duración con L-arg no ayuda a mejorar el rendimiento deportivo.

EFECTO DE LA SUPLEMENTACIÓN PROLONGADA CON L-arg SOBRE EL RENDIMIENTO FÍSICO

La revisión sistemática permitió visualizar que la experimentación prolongada con L-arg se ha probado desde los 3 días (3,26) hasta 6 las semanas (31), con dosis máximas de 12 $g \cdot d^{-1}$ (29,31). Pese a ello, al término de la revisión se pudo observar que una suplementación prolongada de 3 días, independientemente de la dosis utilizada, es demasiado breve para generar cambios en las variables fisiológicas y el rendimiento físico (3,26). De forma paralela, protocolos más extensos (28 días) tampoco han reportado mejoras significativas en las variables ventilatorias después de la suplementación con L-arg (29), evidenciando que la suplementación prolongada no tiene efectos sobre la producción de NO ni el ejercicio anaeróbico intermitente (31), y tampoco sobre las respuestas hemodinámicas y vasculares en los ejercicios resistidos o de fuerza (28), la [La], el consumo máximo de oxígeno ($VO_{2máx}$), la insulina, el cortisol, la hormona del crecimiento o el factor de crecimiento insulínico tipo 1 (IGF-1) (36). Sin embargo, al término de la búsqueda también se encontró una investigación que reportó un efecto significativo de la suplementación prolongada con L-arg sobre el rendimiento en ejercicio, evidenciando una recuperación más rápida de las lesiones musculares causadas por la disminución de los niveles de la enzima lactato-deshidrogenasa (LDH) después del entrenamiento, y un impacto positivo en el rendimiento anaeróbico, principalmente por acelerar los procesos de recuperación muscular (40).

Antes de la revisión sistemática se tenía el antecedente de que la L-arg promovía la secreción de la hormona de crecimiento, aumentando la síntesis de proteínas y favoreciendo la hipertrofia muscular en los deportistas (2), beneficiando principalmente a los atletas de deportes de fuerza y de potencia (10). Al parecer, las vías fisiológicas de estas secreciones y síntesis proteicas existen y se desarrollan (2,10), pero el tiempo necesario para generar estas adaptaciones debe ser superior al usado en las investigaciones reportadas (3,26,28,36). También se debe considerar que la L-arg oral es catabolizada por la arginasa intestinal en urea y ORN, reduciendo la biodisponibilidad de L-arg en el plasma (12). Por lo tanto, la tendencia general muestra que la suplementación prolongada con L-arg no parece mejorar las respuestas hemodinámicas, vasculares, ni morfo-estructurales en los deportistas.

EFECTO DE LA SUPLEMENTACIÓN CON L-arg Y L-citr SOBRE EL RENDIMIENTO FÍSICO

Luego de los filtros realizados en la revisión sistemática se obtuvo solo un estudio que comparaba el efecto de la suplementación con L-arg y L-citr sobre el rendimiento en el ejercicio (42). En esa investigación, Bailey et al. (42) compararon los efectos de la suplementación por 7 días (6 $g \cdot d^{-1}$) tanto con L-arg como con L-citr sobre los biomarcadores de NO, la ventilación pulmonar de oxígeno (O_2), la cinética del consumo de oxígeno (VO_2) y el rendimiento en el ejercicio; al término de la investigación se concluyó que la administración a corto plazo de L-citr, pero no de L-arg, puede mejorar la presión arterial (PA), la cinética del VO_2 y el rendimiento en el ejercicio en los adultos sanos.

EFECTO DE LA SUPLEMENTACIÓN CON L-citr SOBRE EL RENDIMIENTO EN FÍSICO

Al término de la revisión sistemática se pudo visualizar que tanto la suplementación de corta duración como la prolongada con L-citr, asociada al rendimiento físico, se ha llevado a cabo mediante alimentos naturales, L-citr sintetizada y CM. Considerando que la L-citr ($C_6H_{13}N_3O_3$) es un aminoácido no esencial que se biosintetiza en el cuerpo a partir de dos aminoácidos relacionados (L-glutamina y L-arg), es importante considerar que los suplementos con L-citr incluidos en la revisión fueron ingeridos de forma aislada o como sal de otros aniones. Un ejemplo de esto último es el malato (ácido tricarboxílico intermedio del ciclo de Krebs), que da origen a la formación de CM. Por lo anterior, y para un mejor entendimiento, se desarrollará una discusión de forma separada.

EFECTO DE LA SUPLEMENTACIÓN DE CORTA DURACIÓN CON L-citr EN JUGO DE SANDÍA SOBRE EL RENDIMIENTO FÍSICO

Los estudios hallados que relacionaron la suplementación de corta duración con L-citr en jugo de sandía permitieron observar que este aminoácido disminuye la percepción del dolor muscular

post-ejercicio. Es así como, en una investigación desarrollada por Tarazona et al. (16), se estudió la suplementación con 1,17 g de L-citr, contenida en un compuesto de jugo de sandía enriquecido con L-citr, sobre la percepción del dolor, la [La] y la frecuencia cardíaca (FC) en jóvenes deportistas. El estudio *in vitro* mostró una mayor biodisponibilidad de L-citr cuando esta estaba contenida en una matriz natural, como el jugo de sandía no pasteurizado; a su vez, el jugo natural de sandía, enriquecido o no con L-citr, ayudó a reducir el dolor muscular de forma significativa después de 24 horas tras el ejercicio (16). Estos resultados se complementaron con el estudio de Martínez-Díaz et al. (15), donde se evaluó el efecto del jugo de sandía enriquecido con L-citr (3,45 g de L-citr/500 mL de jugo) sobre el rendimiento físico y los marcadores bioquímicos después de una carrera de media maratón; al término del estudio, los investigadores encontraron que la dosis suministrada había disminuido la percepción del dolor muscular de 24 a 72 horas después de la carrera, y había mantenido concentraciones más bajas de lactato en plasma después de un ejercicio agotador (15). Quizás, un posible mecanismo de acción para estos resultados sea la conversión de L-citr en argininosuccinato y L-arg a través de la síntesis *de novo* (12), y este aumento en la biodisponibilidad de L-arg permitiría aumentar el flujo sanguíneo, disminuyendo la percepción del dolor muscular (9).

EFECTO DE LA SUPLEMENTACIÓN PROLONGADA CON L-citr EN JUGO DE SANDÍA SOBRE EL RENDIMIENTO FÍSICO

De acuerdo con las investigaciones encontradas en la revisión, la tendencia general del efecto crónico del jugo de sandía fue un aumento de variables fisiológicas como las concentraciones plasmáticas de NO_2 y la oxigenación muscular. A su vez, la búsqueda permitió visualizar que la experimentación prolongada con L-citr en jugo de sandía oscila entre 14 y 16 días (43,44) con dosis de 980 mL·d^{-1} (43) a 6,0 g·d^{-1} (44).

Esta suplementación ha demostrado, entre otras cosas, un aumento en las concentraciones plasmáticas de NO_2, mecanismo que podría estar asociado a una mayor producción de NO a través de NOS. Así mismo, durante el ejercicio de intensidad moderada, el O_2 pulmonar no ha mostrado ser diferente, pero sí la oxigenación muscular después de la suplementación con jugo de sandía (esto podría implicar que la suplementación con jugo de sandía mejora el equilibrio entre el suministro de O_2 muscular y la demanda muscular de O_2 durante el ejercicio de intensidad moderada). Además, se ha evidenciado que los participantes experimentan molestias gastrointestinales y aumentos de la PA en reposo y la FC después de la suplementación con jugo de sandía (44). De forma paralela, Shanely et al. (43) reportaron una escala de percepción del esfuerzo (RPE) mayor en los sujetos suplementados, así como aumentos de L-citr, L-arg y NO_2 total en plasma, pero sin efectos agudos perceptibles sobre la inflamación post-ejercicio y la función inmunitaria innata (43).

Por lo tanto, aunque los resultados son concluyentes sobre las mejoras en la producción de NO y la oxigenación muscular durante el ejercicio de intensidad moderada, el rendimiento intenso no se vio afectado, mientras que la PA en reposo, la FC y la RPE aumentaron después de la suplementación con jugo de sandía (41).

EFECTO DE LA SUPLEMENTACIÓN DE CORTA DURACIÓN CON L-citr SINTETIZADA SOBRE EL RENDIMIENTO FÍSICO

En cuanto a la suplementación de corta duración con L-citr sintetizada, Cutrufello et al. (14) examinaron el efecto de este aminoácido en varias dosis de corta duración, siendo la más alta de 6 g·d^{-1}, sobre el número máximo total de repeticiones (*press* de pecho), el tiempo hasta el agotamiento (utilizando un protocolo de rutina incremental), el $VO_{2máx}$, el umbral anaeróbico y la vasodilatación mediada por flujo en hombres y mujeres sanos en edad universitaria. Al término del estudio, los investigadores concluyeron que estas dosis habían sido ineficaces para mejorar el rendimiento deportivo, específicamente en el número total de repeticiones, el tiempo hasta el agotamiento, el $VO_{2máx}$, el umbral anaeróbico y el flujo sanguíneo.

EFECTO DE LA SUPLEMENTACIÓN PROLONGADA CON L-citr SINTETIZADA SOBRE EL RENDIMIENTO FÍSICO

De acuerdo con las investigaciones filtradas, la experimentación prolongada con L-citr sintetizada oscila entre 6 y 8 días (46,18) con dosis de 2,4 g·d^{-1} (18) a 6,0 g·d^{-1} (46). Como tendencia general, se pudieron observar un aumento significativo de la biodisponibilidad de NO (18,46), un aumento del flujo sanguíneo (45), una disminución del tiempo en las pruebas contrarreloj y del dolor muscular después del esfuerzo (18), y un aumento en la tasa de VO_2 (46). De forma específica, Gonzáles et al. (45) evidenciaron que la suplementación con L-citr había aumentado el flujo de sangre femoral en un 11 % y la conductancia vascular en un 14 % durante ejercicios de miembros inferiores en hombres mayores, mientras que no se observaron cambios en las mujeres mayores (45). A su vez, Ahsley et al. (46) reportaron que la suplementación con L-citr no había alterado el costo de oxígeno de la caminata a intensidad moderada en adultos jóvenes o mayores, aunque sí mejoró la cinética de absorción de oxígeno en los hombres (46). Estos hallazgos sugieren que los efectos de la L-citr pueden estar relacionados con una mejor disponibilidad de NO en el plasma, lo que a su vez puede mejorar el rendimiento deportivo (18).

EFECTO DE LA SUPLEMENTACIÓN DE CORTA DURACIÓN CON CM SOBRE EL RENDIMIENTO FÍSICO

En relación a los estudios consultados, e independientemente de la dosis suministrada (desde 8,0 hasta 12,0 g·d^{-1}), la evidencia

muestra un efecto positivo de la suplementación de corta duración con CM sobre el rendimiento deportivo (17,20,47,48,52). La disminución de la RPE y del dolor muscular después del esfuerzo emerge como principal beneficio de este compuesto (17,20). En este sentido, Pérez-Guisado et al. (20) reportaron una menor percepción del dolor muscular a las 24 y 48 horas después del esfuerzo al comparar el tratamiento de CM con placebo, y también una menor percepción del dolor muscular a las 24 y 48 horas post-esfuerzo. De forma paralela, Glenn et al. (17) también reportaron un descenso de la RPE posterior a la suplementación de corta duración con 8 g·d^{-1} de CM. Al parecer, la capacidad de la CM para amortiguar la acidosis, la [La] y el amonio sería la responsable de la reducción de la RPE y el dolor muscular a las 24 y 48 horas del esfuerzo (20). Sin embargo, Cunnife et al. (48) examinaron los efectos de la suplementación de corta duración con CM sobre el equilibrio ácido-base y el rendimiento del ejercicio de alta intensidad, y el principal hallazgo fue que la suplementación de corta duración de 12 g·d^{-1} no había atenuado la fatiga inducida por ciclos repetidos de alta intensidad, ni prolongado el tiempo hasta el agotamiento; además, observaron cambios en la potencia máxima individual o la potencia media, concluyendo que no existe un efecto significativo de las dosis de corta duración sobre el rendimiento de alta intensidad (48). Wax et al. (6) evaluaron la eficacia de la suplementación de 8 g·d^{-1} de CM sobre el rendimiento durante el ejercicio y, en este estudio, los resultados indicaron que el rendimiento había mejorado de promedio un 9 %, mientras que la suplementación no había afectado la [La] en sangre, la PA, ni la FC, es decir, que el rendimiento mejorado no había tenido relación con estas variables. Sin embargo, los autores concluyen que la suplementación con CM puede ser beneficiosa para mejorar el rendimiento durante el ejercicio de fuerza múltiple de la parte inferior del cuerpo en los hombres entrenados en fuerza (6).

En relación con las variables físicas, la suplementación de corta duración con CM ha reportado un incremento del número de repeticiones al comparar el tratamiento de CM con placebo ($p < 0,0001$) (20) y un aumento de los ejercicios resistidos de las extremidades superiores e inferiores (17), la fuerza de agarre, la potencia vertical y el rendimiento en el ciclismo anaeróbico en jugadoras de *Tennis Masters* (49), así como el trabajo realizado en las extremidades superiores, aumentando el volumen de entrenamiento en varones de edad universitaria (47).

Sin embargo, Da Silva et al. (50) analizaron el efecto de la suplementación con CM sobre la recuperación muscular posterior a una sesión única de ejercicios de fuerza de alta intensidad en hombres adultos jóvenes no entrenados, y los resultados indicaron que la suplementación de CM (dosis única de 6 g antes del entrenamiento) no había mejorado el proceso de recuperación muscular después de una sesión, sin mostrar diferencias significativas en los marcadores de fatiga muscular (dolor muscular, [La], creatinquinasa [CK], cortisol) (50). Igualmente, Farney et al. (51) examinaron los efectos de CM (8 g·d^{-1} 60 minutos antes de realizar una sesión de ejercicio de alta intensidad) sobre la fatiga muscular en personas sanas, entrenadas recreativamente; al término de la investigación los autores reportaron que la dosis empleada no fue efectiva para reducir la fatiga o aumentar la cantidad de repeticiones en estos individuos. Así mismo, González et al. (52) investigaron el efecto de suplementos de CM (8 g·d^{-1} de CM 40 min antes del protocolo de ejercicio de resistencia) sobre repeticiones totales, potencia de salida, hinchazón muscular, medidas subjetivas de concentración, energía y fatiga en hombres recreacionalmente entrenados en fuerza; los resultados no evidenciaron aumentos del rendimiento deportivo, ni respuesta de hinchazón muscular al entrenamiento, ni cambios en la RPE (52).

De acuerdo con estas investigaciones, la tendencia general de la suplementación de corta duración con CM sobre el rendimiento deportivo se dirige hacia la disminución de la fatiga muscular y la percepción del dolor muscular tras el ejercicio (17,20), y hacia un incremento del número de repeticiones durante los entrenamientos de fuerza (6,17,20,49). De igual forma, se necesita más evidencia para generalizar estos hallazgos.

EFECTO DE LA SUPLEMENTACIÓN PROLONGADA CON CM SOBRE EL RENDIMIENTO FÍSICO

En cuanto a la suplementación prolongada con CM, al término de la revisión solo se encontró un estudio realizado por Kiyici et al. (19). Estos investigadores examinaron los efectos de un entrenamiento intensivo sobre la [La] en sangre en jugadores activos de balonmano. Al término de la investigación se observó una disminución de la [La] en sangre de los atletas que recibieron el suplemento. Esta investigación sugiere que la suplementación prolongada con CM puede contribuir positivamente al rendimiento físico, retardando la aparición de la fatiga muscular. Sin embargo, se necesitan más estudios para generalizar estos resultados.

CONCLUSIÓN

De acuerdo con la revisión sistemática realizada, existe evidencia de que la L-citr podría funcionar como ayuda ergogénica mejor que la L-arg sobre el rendimiento físico, puesto que en gran parte de los estudios filtrados, que evaluaron los efectos del consumo de L-arg tanto la administración prolongada como la de corta duración, no evidenciaron efectos significativos en variables tales como NOx, FC, PA, [La], amoníaco, fatiga muscular y número de repeticiones. Por tanto, la mayoría de estas investigaciones no apoyan el uso de L-arg como suplemento para lograr mejoras en el rendimiento deportivo.

En cuanto a la L-citr, precursor de la L-arg, se observaron 3 formas de suplementación: (i) L-citr en jugo de sandía, (ii) L-citr sintetizada y (iii) CM. Esta última presentó el mayor número de evidencias científicas tanto de forma prolongada como en corta duración (solo se contó con un estudio de administración prolongada de CM en dosis de 8 g·d^{-1}, información insuficiente para determinar si la suplementación prolongada permite generar incrementos del rendimiento físico). No obstante, las 3 formas de suplementación mostraron efectos positivos sobre las variables

fisiológicas y de rendimiento físico, específicamente sobre la percepción subjetiva del esfuerzo y el dolor muscular posterior al esfuerzo. Sumado a esto, luego de la suplementación con L-citr y CM, también se evidenciaron mejoras en el número de repeticiones, disminución en la [La] sanguínea y disminución del tiempo en pruebas máximas. Sin embargo, se necesitan más datos que evidencien el efecto real de las dosis de corta duración o prolongadas de L-citr y/o CM sobre el rendimiento físico.

BIBLIOGRAFÍA

1. Botchlett R, Lawler JM, Wu G. L-Arginine and L-Citrulline in Sports Nutrition and Health. En: Bagchi D, Nair S, Sen C, editores. Nutrition and Enhanced Sports Performance: Muscle Building, Endurance, and Strength; 2013. p. 439-46. DOI: 10.1016/B978-0-12-396454-0.00045-X
2. Takeda K, Takemasa T. An Overview of Ornithine, Arginine and Citrulline in Exercise and Sports Nutrition. En: Bagchi D, Nair S, Sen C, editores. Nutrition and Enhanced Sports Performance: Muscle Building, Endurance, and Strength; 2013. p. 423-31. DOI: 10.1016/B978-0-12-396454-0.00043-6
3. Liu TH, Wu CL, Chiang CW, Lo YW, Tseng HF, Chang CK. No effect of short-term arginine supplementation on nitric oxide production, metabolism and performance in intermittent exercise in athletes. J Nutr Biochem 2009;20(6):462-8. DOI: 10.1016/j.jnutbio.2008.05.005
4. Olek RA, Ziemann E, Grzywacz T, Kujach S, Luszczyk M, Antosiewicz J, et al. A single oral intake of arginine does not affect performance during repeated Wingate anaerobic test. J Sports Med Phys Fitness 2010;50(1):52-6.
5. Jones AM, Haramizu S, Ranchordas M, Burke L, Stear S, Castell LM. A-Z of nutritional supplements: dietary supplements, sports nutrition foods and ergogenic aids for health and performance--Part 27. Br J Sports Med 2011;45(15):1246-8. DOI: 10.1136/bjsports-2011-090669
6. Wax B, Kavazis AN, Weldon K, Sperlak J. Effects of supplemental citrulline malate ingestion during repeated bouts of lower-body exercise in advanced weightlifters. J Strength Cond Res 2015;29(3):786-92. DOI: 10.1519/JSC.0000000000000670
7. Bailey SJ, Winyard PG, Vanhatalo A, Blackwell JR, DiMenna FJ, Wilkerson DP, et al. Acute L-arginine supplementation reduces the O2 cost of moderate-intensity exercise and enhances high-intensity exercise tolerance. J Appl Physiol 2010;109(5):1394-403. DOI: 10.1152/japplphysiol.00503.2010
8. Camic CL, Housh TJ, Zuniga JM, Hendrix RC, Mielke M, Johnson GO, et al. Effects of arginine-based supplements on the physical working capacity at the fatigue threshold. J Strength Cond Res 2010;24(5):1306-12. DOI: 10.1519/JSC.0b013e3181d68816
9. Álvares TS, Meirelles CM, Bhambhani YN, Paschoalin VMF, Gomes PSC. L-Arginine as a potential ergogenic aid in healthy subjects. Sports Med 2011;41(3):233-48. DOI: 10.2165/11538590-000000000-00000
10. Wilson JM, Wilson SMC, Loenneke JP, Wray M, Norton LE, Campbell BI, et al. Effects of amino acids and their metabolites on aerobic and anaerobic sports. J Strength Cond Res 2012;34(4):33-48. DOI: 10.1519/SSC.0b013e31825663bd
11. Jones A. Precursores de óxido nítrico en la dieta y rendimiento en el ejercicio. Sports Science Exchange 2016;28(156):1-6. Disponible en: https://www.gssiweb.org/docs/librariesprovider9/sse-pdfs/156_andrew_m_jones.pdf?sfvrsn=2
12. Figueroa A, Wong A, Jaime SJ, Gonzales JU. Influence of l-citrulline and watermelon supplementation on vascular function and exercise performance. Curr Opin Clin Nutr Metab Care 2017;20(1):92-8. DOI: 10.1097/MCO.0000000000000340
13. Marini JC. Arginine and ornithine are the main precursors for citrulline synthesis in mice. J Nutr 2012;142(3):572-80. DOI: 10.3945/jn.111.153825
14. Cutrufello PT, Gadomski SJ, Zavorsky GS. The effect of l-citrulline and watermelon juice supplementation on anaerobic and aerobic exercise performance. J Sports Sci 2015;33(14):1459-66. DOI: 10.1080/02640414.2014.990495
15. Martínez-Sánchez A, Alacid F, Rubio-Arias JA, Fernández-Lobato B, Ramos-Campo DJ, Aguayo E. Consumption of watermelon juice enriched in L-citrulline and pomegranate ellagitannins enhanced metabolism during physical exercise. J Agric Food Chem 2017;65(22):4395-404. DOI: 10.1021/acs.jafc.7b00586
16. Tarazona-Díaz MP, Alacid F, Carrasco M, Martínez I, Aguayo E. Watermelon juice: potential functional drink for sore muscle relief in athletes. J Agric Food Chem 2013;61(31):7522-8. DOI: 10.1021/jf400964r
17. Glenn JM, Gray M, Jensen A, Stone MS, Vincenzo JL. Acute citrulline-malate supplementation improves maximal strength and anaerobic power in female, masters athletes tennis players. Eur J Sport Sci 2016;16(8):1095-103. DOI: 10.1080/17461391.2016.1158321
18. Suzuki T, Morita M, Kobayashi Y, Kamimura A. Oral L-citrulline supplementation enhances cycling time trial performance in healthy trained men: Double-blind randomized placebo-controlled 2-way crossover study. J Int Soc Sports Nutr 2016 19;13:6. DOI: 10.1186/s12970-016-0117-z
19. Kiyici F, Eroglu H, Kishali NF, Burmaoglu G. The Effect of Citrulline/Malate on Blood Lactate Levels in Intensive Exercise. Biochem Genet 2017;55(5-6):387-94. DOI: 10.1007/s10528-017-9807-8
20. Pérez-Guisado J, Jakeman PM. Citrulline Malate enhances athletic anaerobic performance and relieves muscle soreness. J Strength Cond Res 2010;24(5):1215-22. DOI: 10.1519/JSC.0b013e3181cb28e0
21. Yavuz HU, Turnagol H, Demirel AH. Pre-exercise arginine supplementation increases time to exhaustion in elite male wrestlers. Biol Sport 2014;31(3):187-91. DOI: 10.5604/20831862.1111436
22. Goron A, Moinard C. Amino acids and sport: a true love story? Amino Acids 2018;50(8):969-80. DOI: 10.1007/s00726-018-2591-x
23. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P), 2015 statement. Syst Rev 2015;4:1-9. DOI: 10.1186/2046-4053-4-1
24. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro Scale for Rating Quality of Randomized Controlled Trials. Phys Ther 2003;83:713-21.
25. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. Aust J Physiother 2009;55:129-33. DOI: 10.1016/S0004-9514(09)70043-1
26. Bescós R, González-Haro C, Pujol P, Drobnic F, Alonso E, Santolaria mL, et al. Effects of dietary L-arginine intake on cardiorespiratory and metabolic adaptation in athletes. Int J Sport Nutr Exer Metab 2009;19(4):355-65. DOI: 10.1123/ijsnem.19.4.355
27. Tsai PH, Tang TK, Juang CL, Chen KW, Chi CA, Hsu MC. Effects of arginine supplementation on post-exercise metabolic responses. Chin J Physiol 2009;52(3):136-42. DOI: 10.4077/CJP.2009.AMH037
28. Fahs CA, Heffernan KS, Fernhall B. Hemodynamic and vascular response to resistance exercise with L-arginine. Med Sci Sports Exerc 2009;41(4):773-9. DOI: 10.1249/MSS.0b013e3181909d9d
29. Sunderland KL, Greer F, Morales J. VO2max and ventilatory threshold of trained cyclists are not affected by 28-day L-arginine supplementation. J Strength Cond Res 2011;25(3):833-7. DOI: 10.1519/JSC.0b013e3181c6a14d
30. Forbes SC, Bell GJ. The acute effects of a low and high dose of oral L-arginine supplementation in young active males at rest. Appl Physiol Nutr Metab 2011;36(3):405-11. DOI: 10.1139/h11-035
31. Imanipour V, Naderi A, Mahdi F, Shahedi V. The effects of supplementary L-Arginine dietary on serum Nitric Oxide concentration in the male bodybuilders. 2011 International Conference on Bioscience, Biochemistry and Bioinformatics 2011;5:276-8.
32. Álvares TS, Conte CA, Paschoalin VM, Silva JT, Meirelles Cde M, Bhambhani YN, et al. Acute l-arginine supplementation increases muscle blood volume but not strength performance. Appl Physiol Nutr Metab 2012;37(1):115-26. DOI: 10.1139/h11-144
33. Álvares TS, Conte-Junior CA, Silva JT, Paschoalin VMF. No effect of L-arginine supplementation on nitric oxide production and muscle recovery. Arch Med Deporte 2012;29(149):660-8.
34. Forbes SC, Harber V, Bell GJ. The acute effects of L-arginine on hormonal and metabolic responses during submaximal exercise in trained cyclists. Int J Sport Nutr Exerc Metab 2013;23(4):369-77. DOI: 10.1123/ijsnem.23.4.369
35. Vanhatalo A, Bailey SJ, DiMenna FJ, Blackwell JR, Wallis GA, Jones AM. No effect of acute l-arginine supplementation on O2 cost or exercise tolerance. Eur J Appl Physiol 2013;113(7):1805-19. DOI: 10.1007/s00421-013-2593-z
36. Alvares TS, Conte-Junior CA, Silva JT, Paschoalin VM. L-arginine does not improve biochemical and hormonal response in trained runners after 4 weeks of supplementation. Nutr Res 2014;34(1):31-9. DOI: 10.1016/j.nutres.2013.10.006
37. Forbes SC, Harber V, Bell GJ. Oral L-arginine before resistance exercise blunts growth hormone in strength trained males. Int J Sport Nutr Exerc Metab 2014;24(2):236-44. DOI: 10.1123/ijsnem.2013-0106
38. Aguiar AF, Balvedi MC, Buzzachera CF, Altimari LR, Lozovoy MA, Bigliassi M, et al. L-Arginine supplementation does not enhance blood flow and muscle performance in healthy and physically active older women. Eur J Nutr 2016;55(6):2053-62. DOI: 10.1007/s00394-015-1019-6

39. Meirelles CM, Matsuura C. Acute supplementation of L-arginine affects neither strength performance nor nitric oxide production. J Sports Med Phys Fitness 2018;58(3):216-20.
40. Mor A, Atan T, Agaoglu SA, Ayyildiz M. Effect of arginine supplementation on footballers' anaerobic performance and recovery. Progress in Nutrition 2018;20(1):104-12.
41. Shirali S, Idani I, Yadollahpour A, Hosseini SA, Barari A. Investigating the effects of resistance training on the functions of GH/IGF1 axis and L-arginine supplementation. Int J Pharm Res Allied Sci 2016;5(2):234-41.
42. Bailey SJ, Blackwell JR, Lord T, Vanhatalo A, Winyard PG, Jones AM. L-Citrulline supplementation improves O2 uptake kinetics and high-intensity exercise performance in humans. J Appl Physiol 2015;119(4):385-95. DOI: 10.1152/japplphysiol.00192.2014
43. Shanely RA, Nieman DC, Perkins-Veazie P, Henson DA, Meaney MP, Knab AM, et al. Comparison of watermelon and carbohydrate beverage on exercise-induced alterations in systemic inflammation, immune dysfunction, and plasma antioxidant capacity. Nutrients 016;8(8):518. DOI: 10.3390/nu8080518
44. Bailey SJ, Blackwell JR, Williams E, Vanhatalo A, Wylie LJ, Winyard PG, et al. Two weeks of watermelon juice supplementation improves nitric oxide bioavailability but not endurance exercise performance in humans. Nitric Oxide Biol Chem 2016;59:10-20. DOI: 10.1016/j.niox.2016.06.008
45. Gonzales JU, Raymond A, Ashley J, Kim Y. Does l-citrulline supplementation improve exercise blood flow in older adults? Exp Physiol 2017;102(12):1661-71. DOI: 10.1113/EP086587
46. Ashley J, Kim Y, Gonzales JU. Impact of L-citrulline supplementation on oxygen uptake kinetics during walking. Appl Physiol Nutr Met 2018;43(6):631-7. DOI: 10.1139/apnm-2017-0696
47. Wax B, Kavazis AN, Luckett W. Effects of supplemental Citrulline-Malate ingestion on blood lactate, cardiovascular dynamics, and resistance exercise performance in trained males. J Diet Suppl 2016;13(3):269-82. DOI: 10.3109/19390211.2015.1008615
48. Cunniffe B, Papageorgiou M, O'Brien B, Davies NA, Grimble GK, Cardinale M. Acute citrulline-malate supplementation and high-intensity cycling performance. J Strength Cond Res 2016;30(9):2638-47. DOI: 10.1519/JSC.0000000000001338
49. Glenn JM, Gray M, Wethington LN, Stone MS, Stewart RW,Jr, Moyen NE. Acute citrulline malate supplementation improves upper- and lower-body submaximal weightlifting exercise performance in resistance-trained females. Eur J Nutr 2017;56(2):775-84. DOI: 10.1007/s00394-015-1124-6
50. da Silva DK, Jacinto JL, de Andrade WB, Roveratti MC, Estoche JM, Balvedi MCW, et al. Citrulline Malate does not improve muscle recovery after resistance exercise in untrained young adult men. Nutrients 2017;9(10):1132. DOI: 10.3390/nu9101132
51. Farney TM, Bliss MV, Hearon CM, Salazar DA. The Effect of Citrulline Malate supplementation on muscle fatigue among healthy participants. J Strength Cond Res 2017.
52. González AM, Spitz RW, Ghigiarelli JJ, Sell KM, Mangine GT. Acute effect of citrulline malate supplementation on upper-body resistance exercise performance in recreationally resistance-trained men. J Strength Cond Res 2018;32(11):3088-94. DOI: 10.1519/JSC.0000000000002373

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Revisión

Diet, physical activity and telomere length in adults

Dieta, actividad física y longitud telomérica en adultos

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Abstract

Telomere length (TL) is a predictive biomarker of premature aging. Telomere shortening has been linked to age-related diseases and noncommunicable diseases (NCD), and may reflect the effects of behavioral, psychosocial and environmental factors on health status. Telomere attrition can be affected by lifestyle factors such as diet and physical activity. The search of studies included in this review was conducted on PubMed Central database. A majority of studies are cross-sectional, as there is a clear lack of prospective studies to evaluate the individual effect of dietary components, dietary patterns, and physical activity on TL in the long term. The current literature suggests that high adherence to Mediterranean diet (MD), with consumption of antioxidants, fiber and vegetables, as well as seeds and walnuts, is associated with longer TL. The dietary components of a healthy diet, such as carotenoids, vitamins A, C, D, E, polyphenols, fiber, and omega-3 fatty acids could help maintain TL. In contrast, a high consumption of sugary beverages, processed meat, and proinflammatory diets is associated with telomere shortening. In a majority of studies TL is positively associated with moderate physical activity. The predominant mechanisms through which a healthy diet and moderate physical exercise could mitigate telomere attrition include decreasing oxidative stress and inflammation. We shall not discuss the associations of possible risk or protective factors in terms of causality since the majority of studies are cross-sectional and randomized controlled trials are limited; accordingly, some results are inconclusive. For future research, we suggest evaluating the individual effects of dietary components, dietary patterns and physical activity, considering repeated measurements and exercise intensity, on TL. It is also advisable to include biomarkers of oxidative stress and inflammation proteins, and to measure telomerase activity.

Key words:

Telomere length. Diet. Physical activity.

Resumen

La longitud de los telómeros (TL) es un biomarcador predictivo del envejecimiento prematuro. El acortamiento de los telómeros se ha relacionado con las enfermedades asociadas a la edad y las enfermedades no transmisibles (ENT), y puede reflejar los efectos de los factores conductuales, psicosociales y ambientales en el estado de salud. El desgaste de los telómeros puede verse afectado por factores del estilo de vida, como la dieta y la actividad física. La búsqueda de los estudios incluidos en esta revisión se realizó en la base de datos PubMed Central. La mayoría de los estudios son transversales, por lo que está clara la falta de estudios prospectivos que evalúen el efecto individual de los componentes dietéticos, los patrones dietéticos y la actividad física sobre el TL a largo plazo. La literatura actual sugiere que una alta adherencia a la dieta mediterránea (DM) y el consumo de antioxidantes, fibra y vegetales, así como semillas y nueces, se asocia a una mayor TL. Los componentes dietéticos de una dieta saludable, como los carotenoides, las vitaminas A, C, D, E, los polifenoles, la fibra y los ácidos grasos omega-3, podrían ayudar a mantener la TL. En contraste, el alto consumo de bebidas azucaradas, carne procesada y dietas proinflamatorias se asocia al acortamiento de los telómeros. En la mayoría de los estudios, el TL se asocia positivamente con la actividad física moderada. Los mecanismos predominantes que, a través de una dieta saludable y un ejercicio físico moderado, podrían mitigar el desgaste de los telómeros son la disminución del estrés oxidativo y la inflamación. No se discute la asociación de posibles factores de riesgo o de protección en términos de causalidad, ya que la mayoría de los estudios son transversales y los ensayos controlados aleatorios son limitados; por consiguiente, algunos resultados no son concluyentes. Para investigaciones futuras se sugiere evaluar los efectos individuales de los componentes dietéticos, los patrones de actividad física y dietética, considerando mediciones repetidas y la intensidad del ejercicio, sobre el TL. También es aconsejable incluir biomarcadores de estrés oxidativo y proteínas inflamatorias, y medir la actividad de la telomerasa.

Palabras clave:

Longitud de los telómeros. Dieta. Actividad física.

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INTRODUCTION

Telomeres are cellular structures composed of repetitions of DNA sequences (TTAGGG), located at the end of chromosomes; their function is to protect chromosomes from degradation during each cell cycle (1). Telomerase is the enzyme responsible for the maintenance of TL, and its function is to add TTAGGG repeats to the 3' end of the sequence by retrotranscription (2). The largest telomerase activity is observed mainly in gametes, stem cells, and tumor cells (3). In somatic cells during cellular replication, TL shortens gradually, and this shortening gives rise to mutagenesis and chromosomal instability; as a consequence, there is tumorigenesis when excessive shortening occurs after reaching a certain threshold (4). TL may reflect the effects of behavioral, psychosocial and environmental factors on health status, and may predict morbidity and mortality (5). Short TL has been linked to age-related diseases and NCDs. In epidemiological studies telomere shortening has been associated with risk for various cancers, such as bladder (6), gastric (7), colorectal (8), and breast cancer (9,10).

Telomere shortening has been related to high levels of inflammation (11), oxidative stress (12-14), and metabolic factors such as abdominal fat, elevated blood glucose levels, and hypertension (15,16). A shorter TL has also been linked to conditions associated with lifestyle that are potentially modifiable factors, such as a decrease in fruit consumption (7) and physical inactivity (17,18). A longer TL has been linked with having a healthy diet, moderate alcohol consumption, maintaining a healthy body weight, abstaining from smoking, and participating in moderate or vigorous physical activity (19). Thus, findings from different studies show that lifestyle changes, including healthy dietary patterns and an increase in physical activity, may decrease telomere shortening. However, some studies have not found such associations, which leads to contradictory results regarding the effect of physical activity or diet on TL. The aim of this review is to examine the results of human studies that evaluated the role of lifestyle factors, such as dietary patterns, nutrients and physical exercise, on the promotion of TL changes. We also discuss the possible mechanisms of action that influence this process, with the perspective that TL could be a novel biomarker, measurable in blood samples, to indicate the risk of suffering age-related diseases or NCDs; it could be useful for promoting healthy lifestyles in the population. TL is highly variable among tissues and blood cell subpopulations due to their different proliferative history (20). Therefore, the studies that were included in this review measured TL from whole blood, buccal cells, and peripheral blood mononuclear cells.

The studies included in this review were identified by a literature search conducted in the PubMed Central database. The following keywords were used as search criteria: "telomere length and nutrients" OR "diet" OR "antioxidants" OR "micronutrients" OR "food" OR "vitamins" OR "exercise" OR "physical activity". We conducted the last search in December 2018. The search included cross-sectional designs, case-control and cohort studies, and clinical trials. We considered studies involving male or female adults, healthy or with any condition such as cancer, diabetes, hypertension, or overweight and obesity. Among the scientific articles dealing with diet or physical activity included in this review, thirty describe the effect of diet on TL (Table I), fifteen evaluate the effect of physical activity (Table II), and five focus on the effects of both diet and physical activity on TL (Table III). The majority of studies are cross-sectional (twenty-nine), eight studies are cohort studies, ten are randomized controlled trials, one is a clinical trial, and two are case-control studies.

DIET AND DIETARY PATTERNS LINKED TO TELOMERE LENGTH

Several studies reported that adherence to dietary patterns or different dietary components, such as consumption of fiber, antioxidants, fatty acids and vitamins, as well as consumption of food groups such as fruits, vegetables, nuts, seeds, legumes, fish, sweetened beverages, and others, may be related to changes in telomere attrition (Table I). Dietary patterns describe the eating habits of a population; examples include MD, western diet, vegetarian diet, vegan diet, and others. Dietary patterns also reflect adherence to the formal dietary guidelines recommended for disease prevention (21). MD is a healthy diet that has been studied as protective against various chronic diseases (22), and is characterized by consumption of fruits and fresh vegetables, fish, cereals, vegetable fibers, nuts, and low saturated fat. Crous Bou et al. (23) conducted a study involving 4,676 healthy American women, and greater adherence to MD was significantly associated with longer TL. Boccardi et al. (15) reported that older adults without hypertension, myocardial infarction, vascular disease, dementia, stroke or heart failure, and with greater adherence to MD had higher telomerase enzyme activity and consequently longer TL as compared to those with low adherence to MD. In addition, participants also had low levels of some inflammation biomarkers such as C-reactive protein (CRP), interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α), as well as low levels of nitrotyrosine.

The pro- or anti-inflammatory potential of diets has been studied in relation to TL using the dietary inflammation index, which is a tool for assessing a diet's inflammatory capacity; it is thus a population-based index representing a refined scoring algorithm based on an extensive review of the literature. Dietary variables are classified and scored according to their pro-inflammatory effect, anti-inflammatory effect or no effect on inflammatory biomarkers such as, IL-1b, IL-4, IL-6, IL-10, TNF- α, and C-reactive protein (24,25). García Calzon et al. (24) evaluated whether a diet associated with inflammation could modify telomere attrition rate by applying an intervention where MD was used for 5 years in 520 participants at high risk for cardiovascular disease. At baseline, the authors found that participants who had an anti-inflammatory diet had longer telomeres compared to those with pro-inflammatory diets. In addition, after 5 years of follow-up, participants with a pro-inflammatory diet had a 2-fold higher risk of accelerated telomere attrition when compared to participants with an anti-inflammatory diet.

Table I. Effect of diet on telomere length

References	Study design	Population	Method	Factor	Results
Richards et al., 2007 (49)	Prospective cohort	2,160 women twins from the United Kindom aged 18–80 years. Study duration: 6.1 and 17.4 years (mean 11.2 ± 2 years)	PBL/TRF. Southern blot	Serum vitamin D	Serum vitamin D was positively associated with leukocyte TL after adjustment for age ($r = 0.09$, $p < 0.0001$). The difference in leukocyte TL between the highest and lowest tertiles of vitamin D was 107 base pairs ($p = 0.0009$)
Nettleton et al., 2008 (29)	Cross-sectional	40 white, black, and Hispanic adults - The Multi-Ethnic Study of Atherosclerosis	PBL/qPCR	Intake of whole grains, fruits and vegetables, low-fat dairy, nuts or seeds, nonfried fish, coffee, refined grains, fried foods, red meat, processed meat, and sugar-sweetened soda	Processed meat intake was associated with TL. For every additional 1 serving/day of processed meat, the T/S ratio was 0.07 smaller ($\beta \pm SE$: -0.07 ± 0.03, $p = 0.006$)
Farzaneh-Far et al., 2010 (51)	Prospective cohort	608 outpatients in California with stable coronary artery disease - Heart and Soul Study. Study duration: 6 years	PBL/qPCR	Omega-3 fatty acid blood levels	Log omega-3 fatty acid levels were associated with a decrease in telomere shortening (OR: 0.68; 95% CI: 0.47 to 0.98)
Tiainen et al., 2012 (36)	Cross-sectional	1,942 males and females aged 57-70 years from the Helsinki Birth Cohort Study	PBL /qPCR	Intake of fat, fruits and vegetables	Total fat and SFA intake were inversely associated with leukocyte TL in men ($\beta = -0.001$; $p = 0.04$). In women, vegetable intake was positively associated with leukocyte TL ($\beta = 0.009$; $p = 0.05$)
Marcon et al., 2012 (37)	Cross-sectional	56 Italian adults (25 males and 31 females)	DNA/TRF. Southern blot	Diet	Higher consumption of vegetables was related to higher mean TL ($p = 0.013$); a significant role of beta-carotene on telomere maintenance ($p = 0.004$)
Liu et al., 2013 (47)	Cross-sectional	2,741 American females from NHS aged 30 to 55 years	PBL/qPCR	Plasma vitamin D	Higher 25(OH)D levels were significantly associated with longer TL (p-trend = 0.05). Total calcium intake modified this association
Borras et al., 2012 (48)	Case-control	132 Spanish subjets (62 stable HD patients and 60 healthy sex-matched controls)	PBMC/TRF. Southern blot	Role active vitamin D	In the HD subgroup patients under active vitamin D treatment had greater TL in PBMC than untreated patients (9.5 (0.2) kbp *vs.* 8.4 (0.2) kbp; $p = 0.003$)
Boccardi et al., 2013 (15)	Cross-sectional	217 elderly Italian subjects (102 females and 115 males)	PBL /qPCR	Adherence to Mediterranean diet	The group with high adherence to MD showed longer leukocyte TL ($p = 0.003$) and higher telomerase activity ($p = 0.013$) compared to the group with lower adherence
Fretts et al., 2013 (28)	Cross-sectional	2,846 (1,708 females and 1,138 males) American indians from the Strong Heart Family Study who participated in the 2001-2003 examination	PBL/qPCR	Consumption of processed meat and unprocessed red meat	Processed meat negatively related to leukocyte TL ($\beta = -0.021$, $p = 0.009$). No association was observed with the intake of unprocessed red meat
Kiecolt-Glaser et al., 2013 (52)	Double-blind, randomized, controlled trial	106 men and women, ages 40-85, from the Greater Columbus Ohio area Study duration: 4 months	PBL/qPCR	Omega-3 PUFA supplementation	TL had an increase of 21 bp for the low-dose group and an increase of 50 bp in the high-dose group compared to a decrease of 43 bp for placebo; differences between groups were not significant

(Continuation in the next page)

Table I (Cont.). Effect of diet on telomere length

References	Study design	Population	Method	Factor	Results
O'Callaghan et al., 2014 (20)	Randomized, controlled trial; pilot study	Thirty-three adults ages > 65 yrs with mild cognitive impairment. Study duration: 6 months	Whole blood/qPCR	B supplement, rich in long-chain ω-3 PUFAs	The intervention did not show an increase in TL with treatment, and there was a trend toward telomere shortening during the intervention period. Increased erythrocyte DHA levels were associated with reduced telomere shortening ($r = -0.67$; $p = 0.02$)
Crous-bou et al., 2014 (23)	Prospective cohort	4,676 disease-free women from the NHS. Study duration: 24 years	PBL/qPCR	Adherence to MD	Greater adherence to MD was associated with longer telomeres after adjustment for confounders. Least squares mean telomere length z scores were 0.038 for the lowest MD score groups and 0.072 for the highest group (p-trend = 0.004)
Leung et al., 2014 (34)	Cross-sectional	5,309 American adults (2,473 males and 2,839 females) aged 20 to 65 years	Whole blood/qPCR	Consumption of sugar-sweetened beverages	Sugar-sweetened soda consumption was associated with shorter telomeres (β: -0.010, $p = 0.04$). Consumption of 100% fruit juice was marginally associated with longer telomeres (β: 0.016, $p = 0.05$)
Sen et al., 2014 (45)	Cross-sectional	786 (456 females and 330 males) participants in the Austrian Stroke Prevention Study	PBL/qPCR	Concentrations of vitamin C, lutein and zeaxanthin, beta-cryptoxanthin, canthaxanthin, lycopene, alpha-tocopherol, c-tocopherol, alpha-carotene, beta-carotene, and retinol in plasma	Lutein, zeaxanthin and vitamin C remained significantly and independently associated with leukocyte TL (Lu~Zx: $\beta = 0.079$, $p = 0.03$; vitamin C: $\beta = 0.160$, $p < 0.001$)
García-Calzón et al., 2015 (24)	Randomized, controlled trial	520 (females and males) participants at high cardiovascular disease risk: PREDIMED-NAVARRA. Study duration: 5 years	Buffy coat/ qPCR	Dietary Inflammatory Index	Participants with a proinflammatory diet index had shorter telomeres compared to participants with an anti-inflammatory diet (OR = 1.80, 95% CI: 1.03 to 3.17)
Lian et al., 2015 (38)	Case-control	271 hypertensive patients and 455 normotensive controls aged 40-70 years from Yinzhou, Zhejiang Province, China	PBL/qPCR	Vegetable intake	Longer relative TL was significantly associated with lower hypertension risk in those with greater vegetable consumption (OR = 0.28, 95% CI: 0.14 to 0.57; $p < 0.001$), but not in those with lower vegetable intake (p-interaction = 0.008)
Lee et al., 2015 (35)	Prospective cohort	1,958 middle-aged and older Korean adults. Study duration: 10 years	PBL/qPCR	Prudent dietary pattern: high intake of whole grains, seafood, legumes, vegetables and seaweed. Western dietary pattern: high intake of refined grain, red meat or processed meat and sweetened carbonated beverages	The prudent dietary pattern was positively associated with leukocyte TL. Higher consumption of legumes, nuts, seaweed, fruits and dairy products, and lower consumption of red meat or processed meat and sweetened carbonated beverages was associated with longer leukocyte TL
Zhou et al., 2016 (27)	Cross-sectional	556 Chinese subjects (159 with diabetes, 197 with prediabetes and 200 with normal glucose)	PBL/qPCR	Diet	Consumption of legumes ($\beta = 0.105$, $p = 0.018$), nuts ($\beta = 0.110$, $p = 0.011$), fish ($\beta = 0.118$, $p = 0.007$), and seaweed sugars ($\beta = -0.120$, $p = 0.004$) were positively associated with TL

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Table I (Cont.). Effect of diet on telomere length

References	Study design	Population	Method	Factor	Results
Shivapa et al., 2016 (25)	Cross-sectional	7,215 (3,790 females and 3,425 males) adults over 19 years, NHANES participants	PBL/qPCR	Dietary Inflammatory Index	Higher DII scores were associated with shorter leukocyte TL when used continuously (β = -0.003; 95% CI = -0.005 to 0.0002) and as quartiles (β = -0.013; 95% CI = -0.025 to 0.001; p-trend = 0.03)
Min and Min, 2016 (44)	Cross-sectional	1,879 females and 1,781 males from NHANES aged over 20 years	PBL /qPCR	Blood carotenoid levels	Doubling of blood alpha-carotene, beta-carotene (*trans* + *cis*), and beta-cryptoxanthin was associated with 1.76%, 2.22%, and 2.02% longer telomeres, respectively
Yabuta et al., 2016 (40)	Cross-sectional	70 healthy Japanese adults	Buccal cells/qPCR	Daily intake of retinol, vitamin C, alpha-tocopherol, alpha-carotene, beta-carotene and cryptoxanthin	Daily α-carotene or beta-carotene intakes had a positive effect on buccal relative TL in the ISX rs362090 G-allele carrier + BCMO1 rs6564851 GG-genotype group (p = 0.026). Daily intake of alpha-tocopherol was positively associated with buccal relative TL in the ISX rs362090 AA-homozygote + BCMO1 rs6564851 T-allele carrier group (p = 0.037)
Lee et al., 2017 (41)	Prospective cohort	1,958 Korean males and females aged 40 to 69 years. Study duration: 2 years	PBL/qPCR	Consumption of micronutrients, including antioxidant nutrients and vitamins	Leukocyte TL was positively associated with consumption of vitamin C (p < 0.05), folate (p = 0.05) and potassium (p = 0.05) in all participants
Beilfuss et al., 2017 (46)	Cross-sectional	1,542 younger adults (20-39 years), 1,336 middle-aged adults (40-59 years), and 1,382 older adults (≥ 60 years) from the NHANES 2001–02.	PBL /qPCR	Serum 25-hydroxyvitamin D (25(OH)D) concentrations	In the participants aged 40–59 yrs an increment in serum 25(OH)D of 10 nmol/L was associated with a 0.03 ± 0.01 kilo-base pairs longer leukocyte TL (p = 0.001), and 25(OH) D concentrations of 50 nmol/L were associated with a 0.13 to 6 0.04 kilo-base pairs longer leukocyte TL than those for 25(OH)D concentrations < 50 nmol/L (p = 0.01)
Bethancourt et al., 2017 (33)	Prospective cohort	1,459 Filipino young adults. Study duration: 21.5 years	Whole blood/qPCR	Diet and adiposity	No associations between blood TL and any of the measures of adiposity or between blood TL and the seven dietary factors examined: processed meats, fried/grilled meats and fish, non-fried fish, coconut oil, fruits and vegetables, bread and bread products, and sugar-sweetened beverages
Julin et al., 2017 (50)	Cross-sectional	1,832 American men	PBL/ qPCR	Plasma vitamin D	Vitamin D concentrations were not associated with relative leukocyte TL. For 25-dihydroxyvitamin D (p-trend = 0.69) and for 1,25-dihydroxyvitamin D (p-trend = 0.41)

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Table I (Cont.). Effect of diet on telomere length

References	Study design	Population	Method	Factor	Results
Gong et al., 2017 (39)	Prospective cohort	553 Chinese adults (50.8% men) aged 25 to 65 years. Study duration: 3 years	Whole blood/TRF. Southern blot	Dietary patterns	Vegetable-rich pattern characterized by higher intake of fruits, whole grains, various vegetable groups, dairy products, nuts, eggs and tea, was positively related to TL in women ($\beta = 160.81$, p for trend < 0.05)
Nomura et al., 2017 (42)	Cross-sectional	4,018 participants from NHANES, aged ≥ 20 years	Whole blood/ qPCR	Serum concentrations of vitamins and carotenoids	Serum vitamin A was positively associated (percentage of LTL difference per 1 mg/L = 4.01; 95% CI: 0.26, 7.90) and gamma-tocopherol was inversely associated (percentage of LTL difference per 1 mg/dL = -2.49; 95% CI: -4.21, -0.73) with LTL Serum carotenoids were generally positively associated with LTL
Meyer et al., 2018 (26)	Cross-sectional	2,524 Belgian males and females aged 35 to 55 years	Whole blood/Southern blot	Diet	No associations were found between TL and overall dietary variables. A higher daily intake of deep-fried potato products was associated with shorter telomeres ($p = 0.002$, 151 base pairs per 100 g/day) in both sexes
Mazidi et al., 2018 (43)	Cross-sectional	5,992 participants from NHANES, 47.5% (n = 2,844) were men. Mean age was 46.9 years overall	PBL/qPCR	Serum concentrations of retinol, alfa-carotene, trans-beta-carotene, cis beta-carotene, beta-cryptoxanthin, combined lutein/zeaxanthin, and trans-lycopene	Serum alfa-carotene, trans-beta-carotene, cis beta-carotene, beta-cryptoxanthin, and combined lutein/zeaxanthin were positively and significantly associated with TL (all $p < 0.001$)
Freitas-Simoes et al., 2018 (53)	Randomized, controlled trial	149 Spanish, cognitively healthy elders aged 63 to 79. Study duration: 2 years	PMBC/FISH	Walnut intake	Mean LTL values in controls were 7.36 kb (7.084, 7.636) at baseline and 7.06 kb (6.835, 7.288) after 2 years; corresponding values in the walnut group were 7.06 (6.807, 7.320) and 7.07 (6.864, 7.284)

DII: dietary inflammation index; TL: telomere length; NHS: Nurses' Health Study; F: Fisher's test; β: regression coefficient; OR: odds ratio; PREDIMED: Prevention with Mediterranean Diet; qPCR: quantitative polymerase chain reaction; TRF: telomere restriction fragment; T/S: the ratio of telomere PCR value to single-copy gene value derived from quantitative PCR; FISH: fluorescence in situ hybridization; PBL: peripheral blood leukocytes; PMBC: peripherial blood mononuclear cells; NHANES: National Health and Nutrition Examination Survey; BMI: body mass index; SFA: saturated fatty acids; PUFA: polyunsaturated fatty acids; EPA: eicosapentaenoic acid; DHA: docosa-hexaenoic acid.

Table II. Effect of physical activity on telomere length

References	Study design	Population	Method	Factor	Results
Cherkas et al., 2008 (14)	Cross-sectional	2,401 white twins (2,152 females and 249 males) from the United Kingdom.	PBL/TRF, Southern blot	Physical activity	Leukocyte TL in the most active subjects was 200 nucleotides longer than in the least active subjects (7.1 and 6.9 kb respectively; p = 0.006)
Ludlow et al., 2008 (57)	Cross-sectional	69 males and postmenopausal females aged 50-70 years	PBMC/qPCR	The relationship of exercise energy expenditure with both telomere length and telomerase activity	Moderate physical activity levels may provide a protective effect on PBMC telomere length compared with both low and high exercise energy expenditure levels. Telomerase activity was not different between exercise energy expenditure quartiles
Garland et al., 2014 (69)	Cross-sectional	392 postmenopausal women with stage I-III breast cancer	PBMC/TRF, Southern blot	Physical activity	Women with no physical activity had significantly shorter TL (β = -0.22; 95% CI: 0.41 to -0.03; p = 0.03) compared to those with moderate to vigorous physical activity
Du et al., 2012 (54)	Cross-sectional	7813 females aged 43–70 years in the NHS	PBL/ qPCR	Physical activity and sedentary behavior	Moderately or highly active women had a 0.07 SD increase in leukocyte TL (p-trend = 0.02) compared with the least active. Greater moderate or vigorous-intensity activity was associated with increased leukocyte TL (SD = 0.11 for 2–4 h vs. < 1 hour/week and 0.04 for ≥ 7 h vs. < 1 hour/week; p-trend = 0.02)
Sjögren et al., 2014 (62)	Randomized controlled trial	49 individuals (14 men and 35 women). Study duration: 6 months	Whole blood/ qPCR	Changes in physical activity level and sedentary behavior	No associations between changes in steps per day and changes in TL were noted. In the intervention group there was a negative correlation between changes in time spent exercising and changes in TL (rho = -0.39, p = 0.07), and telomere lengthening was significantly associated with reduced sitting time (rho = -0.68, p = 0.02)
Ennour-Idrissi et al., 2016 (18)	Cross-sectional	162 Canadian participants with breast cancer	Buffy coat/ qPCR	Physical activity	TL was positively associated with total physical activity (rs = 0.17, p = 0.033; p trend = 0.069), occupational physical activity (rs = 0.15, p = 0.054; p-trend = 0.054) and transportation-related physical activity (rs = 0.19, p = 0.019; p = 0.005)
Edwards et al., 2016 (55)	Cross-sectional	1,868 (949 males and 919 females) adults from NHANES 1999-2002	PBL/qPCR	Moderate to vigorous physical activity, sedentary behavior and cardiorespiratory fitness	Only moderate to vigorous physical activity was positively associated with TL (OR = 1.37; 95% CI: 0.99 to 1.90; p = 0.05)
Loprinzi and Sng. 2016 (58)	Cross-sectional	6,474 (3,263 females and 3,211 males) adults from NHANES 1999-2002	PBL/ qPCR	Physical activity: aerobics (unweighted), basketball (n = 129), bicycle (n = 240), dancing (n = 149), running (n = 200), climbing stairs (n = 86), weight lifting (n = 169)	The only mode of physical activity that was significantly associated with leukocyte TL was meeting physical activity guidelines for running (β = 0.06; 95% CI: 0.01, 0.11; p = 0.03)
Latifovic et al., 2016 (56)	Cross-sectional	477 healthy volunteers aged 20 to 50 years from Ottawa, Ontario, Kingston, and Halifax, Nova Scotia	PBL/qPCR	Diet, cigarette smoking, and physical activity	Compared with the lowest quartile, the highest quartile of vigorous physical activity was associated with longer relative leukocyte TL. A significant linear trend of increasing relative leukocyte TL with increasing vigorous physical activity was observed (p = 0.02)

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Table II (Cont.). Effect of physical activity on telomere length

References	Study design	Population	Method	Factor	Results
Dankel et al., 2016 (64)	Cross-sectional	4,881 adults from NHANES aged 36 to 85 years categorized in Group 1: active, normal weight now and 10 years ago; Group 2: inactive, normal weight now and 10 years ago; Group 3: active, overweight/obese now but not 10 years ago; Group 4: active, overweight/obese now and 10 years ago; Group 5: inactive, overweight/obese now but not 10 years ago; Group 6: inactive, overweight/obese now and 10 years ago	Whole blood/ qPCR	Physical activity	All active individuals, except those overweight/obese for longer durations, were associated with longer telomeres in comparison to sedentary individuals. Group 2: (β = -0.03 (95% CI: -0.06, -0.01), p = 0.008); Group 3: (β = -0.01 (95% CI: -0.06, 0.04), p = 0.64); Group 4: (β = -0.05 (95% CI: -0.07, -0.03), p < 0.001); Group 5: (β = -0.05 (95% CI: -0.09, -0.01), p = 0.008), and Group 6: (β = -0.05 (95% CI: -0.07, -0.02), p = 0.008)
Tucker, 2017 (59)	Cross-sectional	A total of 5,823 participants, 2,766 men and 3,057 women from NHANES	PBL/qPCR	Physical activity, indexed using MET-minutes	Physical activity was inversely related to leukocyte TL after adjusting for all the covariates (F = 8.3, p = 0.0004). Telomere base pair differences between adults with high activity and those in the sedentary, low, and moderate groups were 140, 137, and 111, respectively
Loprinzi et al., 2017 (68)	Prospective cohort	6,611 participants aged 20-85 years from NHANES	Whole blood/ qPCR	Mortality and physical activity behavior	Compared to those in the first leukocyte TL tertile, the adjusted hazard ratio for all-cause mortality for those in the 2nd and 3rd leukocyte TL tertiles, respectively, was 0.82 (95% CI: 0.60, 1.12) and 0.76 (95% CI: 0.50, 1.14). After adjustments, leukocyte TL tertile 3 (*vs.* 1) was associated with all-cause mortality (HR = 0.37; 95% CI: 0.14, 0.93) for those with moderate-intensity exercise
Fretts et al., 2018 (60)	Cross-sectional	2,312 participants (American indians, 60.3% females)	PBL/qPCR	Physical activity	Compared to participants in the lowest quartile, participants in the upper three quartiles of steps per day had longer leukocyte TL: $\beta \pm$ SE = 0.0195 ± 0.0144, 0.0273 ± 0.0139, and 0.0375 ± 0.0143 T/S ratio units longer (p-trend = 0.010) after adjustment for potential confounders
Friedenreich et al., 2018 (63)	Randomized controlled trial	212 Canadian postmenopausal women from ALPHA trial. Study duration: 12 months	Buffy coat/ qPCR	Aerobic exercise	No evidence that LTL change differed between groups (12-month mean LTL change for the exercise group: -13% (95% CI: -32%, 11%) versus controls: –8% (95% CI: -27%, 15%)
Puterman et al., 2018 (61)	Randomized controlled trial	68 American females and males. Study duration: 24 weeks	PMBC/ qPCR	Aerobic exercise	High (81%) adherence to 120 min/week of aerobic exercise. TL changes across time were significantly apparent between groups (67.3 base pairs, 95% CI 3.1, 131.5)

TL: telomere length; NHS: Nurses' Health Study; β: regression coefficient; OR: odds ratio; CRP: C-reactive protein; qPCR: quantitative polymerase chain reaction; TRF: telomere restriction fragment; T/S: the ratio of telomere PCR value to single-copy gene value derived from quantitative PCR; PBL: peripheral blood leukocytes; PMBC: peripheral blood mononuclear cell; NHANES: National Health and Nutrition Examination Survey; ALPHA: Alberta Physical Activity and Breast Cancer Prevention; BMI: body mass index; MET: metabolic equivalent of task; HDL: high-density lipoprotein; CVD: cardiovascular disease.

Table III. Joint effect of diet and physical activity on telomere length

References	Study design	Population	Source/ Method	Factor	Results
Hovatta et al., 2012 (32)	Randomized controlled trial	522 Finnish individuals with impaired glucose tolerance, age 40-64 years. Study duration: 4 years	PBL/qPCR	Weight loss, reduced intake of total and saturated fat, and increased intake of dietary fiber, and physical activity	The lifestyle intervention during the 4.5-year follow-up period, with weight loss, increased physical activity, and healthy diet did not have an independent effect on TL
Mason et al., 2013 (65)	Randomized controlled trial	439 American overweight or obese women (50–75 years) from The Nutrition and Exercise in Women study were randomized to: a) dietary weight loss (n = 118); b) aerobic exercise (n = 117); c) diet + exercise (n = 117); d) control (n = 87). Study duration: 12 months	PBL/qPCR	Caloric restriction/exercise	Twelve months of dietary weight loss and exercise did not change TL in postmenopausal women
Ornish et al., 2013 (31)	Clinical trial	35 American males (10 with prostate cancer risk and 25 controls). Study duration: 5 years	PBMC/ qPCR	Adherence to lifestyle changes (diet, activity, stress management, and social support)	Relative TL increased from baseline by a median of 0.06 telomere to single-copy gene ratio units (IQR: -0.05 to 0.11) in the lifestyle intervention group, and decreased in the control group (-0.03 T/S units, IQR: -0-05 to 0.03, p = 0.03)
Kalsielski et al., 2016 (30)	Cross-sectional	28 subjects (7 males and 21 females, aged 18-65 years)	PBMC/ qPCR	Diet and physical activity	Individuals with increased consumption of red meat had a higher T/S ratio, and the strongest significant differences were observed between consumer groups: "never" and "1-2 daily" (p = 0.02)
Sanft et al., 2018 (67)	Randomized controlled trial	151 breast cancer survivors (90% non-Hispanic white). Study duration: 6 months	Buffy coat/ qPCR	Diet and physical activity	After 6 months, women with stage 0/I in the intervention group experienced 7% telomere lengthening compared to 8% shortening in the usual care group (p = 0.01). No intervention effect was observed in women with stage II/III breast cancer

PBMC: peripheral blood mononuclear cells; TL: telomere length; PBL: peripheral blood leukocytes; qPCR: quantitative polymerase chain reaction; T/S: the ratio of telomere PCR value to single-copy gene value derived from quantitative PCR; LDL: low-density lipoprotein; HDL: High-density lipoprotein; IQR: interquartile range.

Likewise, a cross-sectional study carried out by Shivappa et al. (25) in American adults evaluated the inflammatory potential of diet from a calculation of the dietary inflammation index obtained by the implementation of 24-hour recalls to participants. This study found that the highest dietary inflammation index scores were associated with telomere shortening. Another study reported no significant associations between TL and dietary inflammatory index or daily energy and fiber intake (26). The findings of these investigations suggested limited results of association studies between dietary patterns and TL. On the other hand, in a cross-sectional study in Chinese adults with diabetes, prediabetes, or normal glucose, Zhou et al. (27) evaluated the influence of diet on leukocyte TL, inflammation markers, and oxidative stress. The authors reported that consumption of legumes, nuts, fish and seaweed are factors associated with reduced telomere shortening, since they found a direct association between consumption of these foods and greater TL.

Contradictory findings have emerged on the consumption of meats and fats, and on their association with TL. In the study by Zhou et al. (27) consumption of meat, fat, and carbohydrates was

not associated with telomere shortening but with an increase in inflammation as determined by TNF-α and IL-6 levels. Meanwhile, Fretts et al. (28) found that the consumption of processed meats was associated with a telomere shortening rate of 0.02 units per additional serving consumed per day. This finding is similar to that reported by Nettleton et al. (29), who found that for each additional serving/day of processed meat, the ratio of quantitative polymerase chain reaction telomere to single-copy gene (T/S ratio) was smaller by 0.07. Fretts et al. (28) describe a possible mechanism related to this finding, which is that processed meats have high concentrations of advanced glycation products, which are formed during the processing of meat and have been associated with telomere shortening by its ability to induce high levels of inflammation and oxidative stress. In addition, the authors refer to the importance of paying attention to the portion and frequency of consumption, not only to type of food. In this sense, Kasielski et al. (30) reported that consumption of red meats 1 to 2 times per week is associated with an increase in TL; this finding differs from those published by Fretts et al. (28) and Nettleton et al. (29), who reported that daily intake of meat is associated with telomere attrition.

In an intervention study to promote lifestyle changes in adults, the authors found that healthy changes (diet rich in whole grain foods, vegetables, fruits, and low-fat proteins, and moderate aerobic exercise, stress management, and increased social support) at 5 years of follow-up were associated with an increase in relative TL in the intervention group versus controls (31). Meanwhile, Hovatta et al. (32) obtained different results, since they reported that a lifestyle intervention during a 4.5-year follow-up period of weight loss, increased physical activity, and healthy diet did not have an effect on TL. Similarly, Bethancourt et al. (33) found no associations between blood TL and body mass index or dietary factors such as processed meats, fried/grilled meats and fish, nonfried fish, coconut oil, fruits, vegetables, bread products, and sugar-sweetened beverages. The consumption of the latter was associated with telomere shortening in a cross-sectional study (34). On the other hand, Lee et al. (35) evaluated the association between two dietary patterns and TL in the remote past. The first one was called a prudent dietary pattern, characterized by a high intake of whole grains, seafood, legumes, vegetables and seaweed. The second was the Western dietary pattern, characterized by a high intake of refined grain, red or processed meat and sweetened carbonated beverages. Consistent with previous findings, Lee et al. found that high adherence to a prudent dietary pattern was positively associated with TL. In addition, according to the analysis of particular food items, consumption of products such as legumes, nuts, seaweed, fruits and dairy products, and lower consumption of red meat or processed meat and sweetened carbonated beverages, were associated with longer TL (32,34).

Several studies report that dietary patterns with a high consumption of fruits and vegetables are related to an increase in TL (36-39). However, fruits and vegetables are taken as a whole group, and no particular type of fruit or vegetable is evaluated. Thus, it is difficult to attribute the aforementioned effect to a specific fruit or vegetable. A broader view is observed in the study conducted by Marcon et al. (37), who reported that a higher intake of vegetables was related to a higher mean TL, and the effect was specifically attributed to the intake of root vegetables, peppers and carrots. In an interesting study involving diet, TL and disease, Lian et al. (38) assessed the relationship between consumption of fruits and vegetables with TL in normotensive and hypertensive adults. In normotensive participants, increased intake of vegetables was associated with increased age-adjusted TL. In addition, the authors found that a longer TL was associated with a reduced risk of high blood pressure in participants with a higher consumption of vegetables. These data suggest that a high intake of vegetables in the diet promotes improvement in biomarkers such as TL, which can serve as a prognostic marker for cardiovascular disease.

MICRONUTRIENTS, ESSENTIAL FATTY ACIDS AND TELOMERE LENGTH

Epidemiological studies report a direct association between dietary micronutrients and TL (Table I), including the study by Marcon et al. (37), in which the analysis of the association between micronutrients and mean TL highlighted a significant role of antioxidant intake, especially beta-carotene, on telomere maintenance. Likewise, Yabuta et al. (40) reported that high intake of dietary beta-carotene and alpha-tocopherol protects buccal cells from telomeric shortening. In addition, carotenoids and other micronutrients, such as vitamin C, folate and potassium, have been positively associated with TL in Korean populations according to Lee et al. (41).

In another aspect of dietary information, there are studies that evaluated the relationship between serum or plasma concentrations of carotenoids or vitamins with TL (Table I). A study by Nomura et al. (42) reported that serum carotenoids are positively associated with leukocyte TL. Additionally, Mazidi et al. (43) reported that serum α-carotene, trans-β-carotene, cis-β-carotene, β-cryptoxanthin and combined lutein/zeaxanthin were positively and significantly associated with TL. Min and Min (44) only found a significant association of provitamin A carotenoids, such as alpha-carotene, beta-carotene (trans + cis), and beta-cryptoxanthin with TL; they found no association between nonvitamin A carotenoids (combined lutein/zeaxanthin and trans-lycopene) and TL. Another study provides evidence that higher plasma lutein, zeaxanthin, and vitamin C concentrations are associated with longer TL (45). Furthermore, plasma or serum 25-hydroxyvitamin (vitamin D) levels from diet (46,47) and supplements (48,49) were positively associated with leukocyte TL, while in another study plasma vitamin D concentrations from the diet were not associated with relative leukocyte TL (50).

Studies that consider omega-3 and omega-6 fatty acids cannot be ignored. Thus, in a study performed in adults with coronary heart disease, Farzaneh-Far et al. (51) reported that the consumption of marine omega-3 fatty acids after 5 years of follow-up increased blood omega-3 levels, an increment that was associated with a 32% decrease in the odds of telomere shortening. Indeed, two randomized controlled trials evaluated the impact of omega-3 fatty acid supplementation on telomere shortening.

The first trial (52) included 138 participants and demonstrated that supplementation with omega-3 fatty acids has an impact on reducing telomere shortening; the authors suggest the importance of considering the ω-6:ω-3 PUFA ratios for future nutritional interventions. The second trial that evaluated supplementation with omega-3 fatty acids (20) did not show an increase in telomere length, probably due to a smaller sample size (33 participants) as compared to the study by Kiecolt-Glaser et al. (52). In another controlled randomized trial the intake of nuts for two years in older individuals tended to delay telomere attrition compared with individuals with a usual diet without nuts; the authors suggest that nuts are rich in omega-3 fatty acids and other antioxidants that might have an impact on the aging process (53).

There are few studies on the association between micronutrients and telomere length, and a majority of such studies have evaluated intakes of vitamin A, C, D, carotenoids, and omega-3 fatty acids. However, other micronutrients may be found in the diet, such as folate, potassium and zinc that could be related to cellular aging. The information compiled in this review highlights the importance of promoting further intervention studies that include supplementation with specific micronutrients and other diet components to determine their causal relationship with changes in TL.

PHYSICAL EXERCISE AND ITS LINKAGE TO TELOMERE LENGTH

As previously described, physical activity has positive effects on TL. In this way, some authors reported that only moderate to vigorous physical activity, which includes walking briskly, jogging, running, bicycling, swimming, tennis, and aerobics, can reduce telomere shortening (54-56). Nevertheless, Ludlow et al. (57) reported that moderate physical activity has a positive relationship on TL, and this effect is lost at higher physical activity levels. Loprinzi and Sng (58), working with data from the National Health and Nutrition Examination Survey (NHANES), reported that running was the only type of physical activity that was positively related to leukocyte TL. A recent study from NHANES performed by Tucker (59) reported that participants with a sedentary lifestyle had 1.95 times the likelihood of having short telomeres compared to those with high physical activity; the results obtained for sedentary patients did not differ for low or moderate levels of activity. Fretts et al. (60), in a cross-sectional study, found that ambulatory physical activity measured by the number of steps taken per day, was related to TL, and therefore, participants who accumulated more steps had longer leukocyte TL than participants who accumulated fewer steps per day. A recent randomized controlled trial (RCT) that evaluated the effect of aerobic exercise (120 min per week) versus usual inactivity reported that exercise induced changes in TL, promoting telomere lengthening (61). A different result was obtained in an intervention study made by Sjögren et al., since no significant associations were found between changes in steps per day and changes in TL (62). Moreover, Friedenreich et al. (63) found no effect of aerobic exercise on telomere attrition.

A study that included 2,401 Caucasian twins, of which 2,152 were women, reported that TL was positively associated with increased physical activity, and the most active subjects had an increase of approximately 200 nucleotides in TL as compared to the least active subjects (14). The above study is similar to a cross-sectional study performed by Dankel et al. (64), in which the participants who had an active life had longer telomeres compared to sedentary individuals. However, this relationship was not found in overweight or obese participants who were active; therefore, the authors suggest that obesity can mitigate the positive effects of physical activity on TL. This is consistent with the study reported by Mason et al. (65) in postmenopausal women, in which the authors did not find changes in TL among women who were overweight or obese, nor did they found significant changes in TL from the effect of dietary weight loss and aerobic exercise for 12 months. Based on these results the authors suggest that exercise intensity or duration may not be enough to change TL. However, moderate physical activity can have a positive impact through a reduction in adiposity, and can also reduce inflammation levels and oxidative stress (66), factors that attenuate telomere attrition. The latter two studies contradict the findings mentioned above and reflect the importance of carrying out more intervention studies to assess the effect of physical activity on TL.

In studies conducted with cancer patients or cancer survivors, the effect of physical activity on TL maintenance seems to be similar. An RCT performed with overweight and obese breast cancer survivors examined the effect of a 6-month diet and exercise-induced weight loss intervention versus usual care on TL. The authors found changes in TL among women with breast cancer in stage 0-I; there was a 7% telomere lengthening in the intervention group compared to an 8% shortening in the usual care group ($p = 0.01$) (67). Another study conducted by Loprinzi and Loenneke (68) found an inverse association between leukocyte TL and all causes of mortality among men who engage in moderate-intensity exercise, which suggests that moderate exercise prevents telomere shortening and increases survival. Ennour Idrissi et al. (18) found that total and occupational physical activity were positively associated with longer TL in 162 premenopausal and postmenopausal women with breast cancer. Furthermore, in a study performed with breast cancer survivors by Garland et al. (69), participants with moderate to vigorous physical activity had a longer TL compared with sedentary women. Physical activity may protect individuals from aging-related diseases, acting as a regulator of the cellular aging process. In this avenue of research, it makes sense to use TL as a biomarker of breast cancer risk and, at the same time, as an indicator of lifestyle changes.

POSSIBLE MECHANISMS OF ACTION OF OXIDATIVE STRESS AND INFLAMMATION IMPLIED IN THE REDUCTION OF TELOMERE SHORTENING

TL is a major determinant of biological age and represents a measurable outcome of the additive repercussions of both inflam-

mation and oxidative stress (70); however, the mechanisms are not fully understood. Telomeres shorten at a rate of 40-200 bp per division (71). The rate of telomere shortening by cell division is not an innate constant and changes from one cell to another, possibly from one cycle of division to the next, depending on oxidative stress and defensive antioxidants (12). Telomeres are rich in guanines, which are prone to be oxidized to 8-oxo-2′-deoxyguanosine and 2,6-diamino-4-oxo-5-formamidopyrimidine. Reactive oxygen species, especially hydroxyl radicals, produce single-strand breaks, either directly or as an intermediate step in the repair of oxidative base modifications. Therefore, telomeric DNA appears to be deficient in the repair of single-strand breaks, which may increase the sensitivity of telomeres to the accumulation of 8-oxo-2′-deoxyguanosine DNA strand breaks (13,72). In addition, oxidative stress directly triggers the activation of the transcription factor NFκB, which is the key regulator of the inflammatory process that regulates transcription for various molecules such as interleukins and TNF-α, and is involved in the modulation of telomerase activity (73).

A majority of the reviewed studies conclude that the possible effects of diet or physical activity on reduced telomere attrition is due to a decrease in oxidative stress and inflammation. Among the main mechanisms attributable to physical activity and telomeric shortening are improved REDOX balance, favoring an expression response in antioxidant proteins and DNA repairing enzymes, as well as a reduction of reactive oxygen species, and therefore CRP, IL-6 and TNF-α levels (72). Additionally, exercise training potentially facilitates TL maintenance through many molecular mechanisms, since TL is regulated by epigenetic modifications such as histone changes (methylation and acetylation) and DNA methylation (73). Exercise also acts as a stimulus for telomerase transcription or activity. The hypothetical signaling pathways posited by the authors suggest increased TERT gene transcription as a response to exercise (74).

Chilton et al. (75) first reported that acute exercise can lead to the transcriptional regulation of several main telomeric genes in immune cells. Their results show an upregulation of the key telomeric gene TERT mRNA, which plays an important molecular role in telomere maintenance since it is related to telomerase activity, and a downregulation of TERF2IP mRNA. The authors also reported that exercise regulates miRNAs, including miR-186 and miR-96, with the potential to control the downstream expression of genes involved in telomere homeostasis. It is interesting to note that the mechanisms involved may depend on the specific exercise modality (75), such as resistance training adaptability (76) and aerobic fitness levels (77).

On the other hand, a healthy diet that contains antioxidant and anti-inflammatory components, coupled with physical activity, leads to improved inflammation levels and decreased oxidative stress, mechanisms that are involved in telomere shortening. A study reported that a high adherence to MD can stimulate telomerase activity in mononuclear cells, either directly by the effect of some specific nutrients included in the diet or indirectly by the global effect of the diet on the modulation of inflammation and oxidative stress (15,70). Specifically, IL-6 and TNF-α have been associated with telomere shortening due to their promotion of cell renewal, replicative senescence, induction of oxidative stress, and inhibition or promotion of telomerase activity (11). Likewise, the levels of IL-6 and TNF-α have been associated with daily energy intake, diet carbohydrate/fat proportions, cereals, and meat intake (27). The impact of diet on TL can be by dietary components in the food groups, such as isoflavones from legumes and seaweeds, by antioxidants, and by folic acid, all of which play an important role in DNA methylation and integrity. Another example is fish, which contains vitamin D and has anti-inflammatory and antiproliferative properties that limit the turnover of cells, thus potentially reducing their telomere length attrition (27). Figure 1 shows the possible effects of lifestyle factors (diet and physical activity) and their underlying biological mechanisms that may cause changes in telomere length.

CONCLUSIONS, LIMITATIONS AND FUTURE RESEARCH

The studies that evaluated the potential association of diet and TL found that adherence to MD and consumption of antioxidants, fiber, vegetables, seeds, and walnuts are associated with greater TL. In contrast, high consumption of sugary beverages, processed meat, and proinflammatory diets was associated with telomere shortening. Therefore, a healthy diet rich in antioxidants, such as carotenoids and vitamins C and E, and in anti-inflammatory components, such as vitamins A and D, polyphenols, fiber, and omega-3 fatty acids, has a greater effect on the decline in the

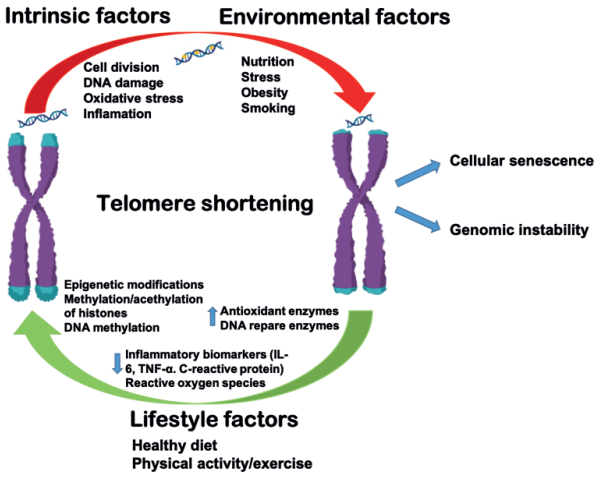

Figure 1.
Potential influence of healthy diet and physical activity on the maintenance of telomere length. This scheme represents how individually and collectively a healthy diet and the performance of physical activity can modify the mechanisms involved in maintaining telomere length, such as increased antioxidants and DNA repair enzymes, decreases reactive oxygen species, and reduced pro-inflammatory cytokines, as well as in promoting the methylation or acetylation of histones and DNA methylation.

rate of telomere shortening. These dietary components, especially omega-3 fatty acids, influence the potential mechanisms that reduce telomere shortening (51,78,79) due to their anti-inflammatory and antioxidant properties, as suggested by the study by Kiecolt-Glaser et al. (52), in which the intake of omega-3 fatty acids caused a decrease in IL-6, and IL-6 was associated with telomere lengthening.

On the other hand, findings from all studies demonstrated that performing moderate physical activity is associated with a longer TL; only one study reported that obesity attenuates this relationship, which could be related to the inflammation levels usually associated with obesity. Following this hypothesis, it is possible to say that an increase in physical activity together with a healthy diet may reduce inflammation and oxidative stress levels, and consequently telomere shortening rate. By reducing telomere shortening, these potentially modifiable factors can indirectly contribute to lowering the risk of chronic degenerative diseases such as cancer, or to improving the survival rate of people who have had cancer. However, recent papers regarding the relationship between TL and cancer risk revealed a complex scenario with contradictory findings depending on different cancer types (80,81). Likewise, Weischer et al. (82) measured leukocyte TL in a prospective study of 47,102 Danish population who were followed for up to 20 years for cancer diagnosis and death, and the authors found that short telomere length is associated with reduced survival after cancer but not with cancer risk. Therefore, the role of the relationship between TL and cancer risk remains to be demonstrated, and it could be a focus for future research.

It is important to emphasize that most of the studies presented in this review, and that evaluate the effect of diet or physical activity on TL, are cross-sectional in design. Therefore, the associations that were found referred to risk or protective factors and not to causality, since the criterion of temporality is not met. It is suggested that clinical intervention studies should be carried out to evaluate the effect of changes in adherence to a healthy diet and the performance of long-term physical activity on TL, considering the duration and intensity of the exercise ultimately practiced. It is also recommended that repeated measurements of TL over time be included in the design. For future studies food cooking habits of food are worth considering in order to evaluate the relationship between deeply fried or highly roasted foods and telomere shortening or lengthening. It is also recommended that studies be carried out that evaluate the joint effect of diet and physical activity on TL, since there are few studies on the subject – indeed, we only found four studies on this subject (30,31,32,65).

To build a complete picture of the possible mechanisms involved in the impact of these changes on the rate of telomeric shortening, of those that can be modulated with a healthy lifestyle, it is important to include biomarkers of oxidative stress, since telomeres are highly sensitive to the damage produced by this type of stress (14). Likewise, it is important to measure telomerase activity, since lifestyle factors may also affect this enzyme. While considering that diet is important, future research is also needed to provide evidence of the effect of individual dietary components, which in turn are part of the whole diet, on telomere shortening. Based on these findings, dietary guidelines could be created so that the population may acquire a healthier type of diet and, at the same time, reduce the risk of suffering from NCDs related to cellular aging or the shortening of telomeres.

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REFERENCES

1. Blackburn, EH. Structure and function of telomeres. Nature 1991;350:569-73.
2. Greider CW, Blackburn EH. Identification of a specific telomere terminal transferase activity in tetrahymena extracts. Cell 1985;43:405-13.
3. Mengual DL, Armando RG, Farina HG, Gómez DE. Telomerasa y telómero: su estructura y dinámica en salud y enfermedad. Medicina 2014:74(1):69-76.
4. Wu X, Amos CI, Zhu Y, Zhao H, Grossman BH, Shay JW, et al. Telomere dysfunction: a potential cancer predisposition factor. J Natl Cancer Inst 2003;95(16):1211-8.
5. Lin J, Epel E, Cheon J, Kroenke C, Sinclair E, Bigos M, et al. Analyses and comparisons of telomerase activity and telomere length in human T and B cells: Insights for epidemiology of telomere maintenance. J Immunol Methods 2010;352(1-2):71-80.
6. McGrath M, Wong J, Michaud D, Hunter DJ, De Vivo I. Telomere length, cigarette smoking, and bladder cancer risk in men and women. Cancer Epidemiol Biomarkers Prev 2007;16(4):815-9.
7. Hou L, Savage SA, Blaser MJ, Perez-Perez G, Hoxha M, Dioni L, et al. Telomere length in peripheral leukocyte DNA and gastric cancer risk. Cancer Epidemiol Biomarkers Prev 2009;18(11):3103-9.
8. Cui Y, Cai Q, Qu S, Chow WH, Wen W, Xiang YB, et al. Association of leukocyte telomere length with colorectal cancer risk: nested case-control findings from the Shanghai Women's Health Study. Cancer Epidemiol Biomarkers Prev 2012;(10):1807-13.
9. Zheng Y-L, Ambrosone C, Byrne C, Davis W, Nesline M, McCann SE. Telomere length from blood cells and breast cancer risk: investigations in two case-control studies. Breast Cancer Res Treat 2010;120(3):769–75.
10. Qu S, Wen W, Shu X-C, Chow WH, Xiang YB, Wu J, et al. Association of leukocyte telomere length with breast cancer risk: nested case-control findings from the Shanghai women's health study. Am J Epidemiol 2013;177(7):617–24.
11. O'Donovan A, Pantell MS, Puterman E, Dhabhar FS, Blackburn EH, Yaffe K, et al. Cumulative inflammatory load is associated with short leukocyte telomere length in the Health, Aging and Body Composition Study. PLoS One 2011;6(5):e19687.
12. Von Zglinicki T. Oxidative stress shortens telomeres. Trends in Biochemical Sciences 2002;27(7):339-44.
13. Houben JM, Moonen HJ, van Schooten FJ, Hageman GJ. Telomere length assessment: Biomarker of chronic oxidative stress? Free Radic Biol Med 2008;44:235–46.
14. Cherkas LF, Hunkin JL, Kato BS, Richards JB, Gardner JP, Surdulescu GL, et al. The association between physical activity in leisure time and leukocyte telomere length. Arch Intern Med 2008;168(2):154–8.
15. Boccardi V, Esposito A, Rizzo MR, Marfella R, Barbieri M, Paolisso G. Mediterranean diet, telomere maintenance and health status among elderly. PLoS ONE 2013;8(4):e62781.
16. Zgheib NK, Sleiman F, Nasreddine L, Nasrallah M, Nakhoul N, Isma'eel H, et al. Short Telomere Length is Associated with Aging, Central Obesity, Poor Sleep and Hypertension in Lebanese Individuals. A&D 2018;9(1):77-89.
17. Puterman E, Lin J, Blackburn E, O'Donovan A, Adler N, Epel E. The power of exercise: buffering the effect of chronic stress on telomere length. PLoS One 2010;5(5):e10837.
18. Ennour-Idrissi K, Têtu B, Maunsell E, Poirier B, Montoni A, Rochette PJ, et al. Association of telomere length with breast cancer prognostic factors. PLoS ONE 2016;11(8):e0161903.
19. Sun Q, Shi L, Prescott J, Chiuve SE, Hu FB, De Vivo I, et al. Healthy lifestyle and leukocyte telomere length in U.S. women. PLoS ONE 2012;7(5):e38374.

20. O'Callaghan N, Parletta N, Milte CM, Benassi-Evans B, Fenech M, Howe P. Telomere shortening in elderly individuals with mild cognitive impairment may be attenuated with ω-3 fatty acid supplementation: a randomized controlled pilot study. Nutrition 2014;30:489-91.
21. Bamia C. Dietary patterns in association to cancer incidence and survival: concept, current evidence, and suggestions for future research. Eur J Clin Nutr 2018.
22. Sofi F, Macchi C, Abbate R, Gensini GF, Casini A. Mediterranean diet and health status: an updated meta-analysis and a proposal for a literature-based adherence score. Public Health Nutr 2014;17(12):2769–82.
23. Crous-Bou M, Fung TT, Prescott J, Julin B, Du M, Sun Q, et al. Mediterranean diet and telomere length in Nurses' Health Study: population based cohort study. BMJ 2014;2(349):g6674.
24. García-Calzón S, Zalba G, Ruiz-Canela M, Shivappa N, Hébert JR, Martínez A, et al. Dietary inflammatory index and telomere length in subjects with a high cardiovascular disease risk from the PREDIMED-NAVARRA study: cross-sectional and longitudinal analyses over 5 y. Am J Clin Nutr 2015;102:897-904.
25. Shivappa N, Wirth MD, Hurley TG, Hébert JR. Association between the Dietary Inflammatory Index (DII) and telomere length and c-reactive protein from the National Health and Nutrition Examination Survey-1999-2002. Mol Nutr Food Res 2016;1600630-6.
26. De Meyer T, Bekaert S, De Buyzere mL, De Bacquer DD, Langlois MR, Shivappa N, et al. Leukocyte telomere length and diet in the apparently healthy, middle-aged Asklepios population. Sci Rep 2018 Apr 25;8(1):6540.
27. Zhou M, Zhu L, Cui X, Feng L, Zhao X, He S, et al. Influence of diet on leukocyte telomere length, markers of inflammation and oxidative stress in individuals with varied glucose tolerance: a Chinese population study. Nutrition Journal 2016;15:39-48.
28. Fretts AM, Howard BV, Siscovick DS, Best LG, Beresford SA, Mete M, et al. Processed meat, but not unprocessed red meat, is inversely associated with leukocyte telomere length in the Strong Heart Family Study. J Nutr 2016;146(10):2013-8.
29. Nettleton J, Diez-Rouz A, Jenny NS, Firtzpatrick AL, Jacobs DR. Dietary patterns, food groups, and telomere length in the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Clin Nutr 2008;88(5):1405–12.
30. Kasielski M, Makandjou-Ola E, Pietruczuk M, Nowak D. The relationship between peripheral blood mononuclear cells telomere length and diet - unexpected effect of red meat. Nutr J 2016;15:68-74.
31. Ornish D, Chan JM, Epel E, Kemp C, Weidner G, Marlin R, et al. Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study. Lancet Oncol 2013;14:1112-20.
32. Hovatta I, de Mello VD, Kananen L, Lindström J, Eriksson JG, Ilanne-Parikka P, et al. Leukocyte telomere length in the Finnish diabetes prevention study. PLoS One 2012;7(4):e34948.
33. Bethancourt HJ, Kratz M, Beresford SAA, Hayes MG, Kuzawa CW, Duazo PL, et al. No association between blood telomere length and longitudinally assessed diet or adiposity in a young adult Filipino population. Eur J Nutr 2017;56(1):295-308.
34. Leung CW, Laraia BA, Needham BL, Rehkopf DH, Adler NE, Lin J, et al. Soda and cell aging: associations between sugar-sweetened beverage consumption and leukocyte telomere length in Healthy Adults from the National Health and Nutrition Examination Surveys. Am J Public Health 2014;104(12):2425-31.
35. Lee JY, Jun NR, Yoo D, Shin C, Baik I. Association between dietary patterns in the remote past and telomere length. Eur J Clin Nutr 2015;69:1048-52.
36. Tiainen AM, Männistö S, Blomstedt PA, Moltchanova E, Perälä MM, Kaartinen NE, et al. Leukocyte telomere length and its relation to food and nutrient intake in an elderly population. Eur J Clin Nutr 2012;66(12):1290-4.
37. Marcon F, Siniscalchi E, Crebelli R, Saieva C, Sera F, Fortini P, et al. Diet-related telomere shortening and chromosome stability. Mutagenesis 2012;27(1):49-57.
38. Lian F, Wang J, Huang X, Wu Y, Cao Y, Tan X, et al. Effect of vegetable consumption on the association between peripheral leucocyte telomere length and hypertension: a case-control study. BMJ 2015;5:e009305.
39. Gong Y, Tian G, Xue H, Zhang X, Zhao Y, Cheng G. Higher adherence to the 'vegetable-rich' dietary pattern is related to longer telomere length in women. Clin Nutr 2018;37(4):1232-7.
40. Yabuta S, Masaki M, Shidoji Y. Associations of buccal cell telomere length with daily intake of β-carotene or α-tocopherol are dependent on carotenoid metabolism-related gene polymorphisms in healthy Japanese adults. J Nutr Health Aging 2016;20(3):267-74.
41. Lee JY, Shin C, Baik I. Longitudinal associations between micronutrient consumption and leukocyte telomere length. J Hum Nutr Diet 2017;30(2):236-43.
42. Nomura S, Robien K, Zota AR. Serum folate, vitamin B-12, vitamin A, γ-tocopherol, α-tocopherol, and carotenoids do not modify associations between cadmium exposure and leukocyte telomere length in the general US adult population. J Nutr 2017;147:538-48.
43. Mazidi M, Kengne AP, Cheskin LJ, Banach M. Serum lipophilic antioxidants levels are associated with leucocyte telomere length among US adults. Lipids Health Dis 2018;17(1):164.
44. Min KB, Min JY. Association between leukocyte telomere length and serum carotenoid in US adults. Eur J Nutr 2017;56:1045-52.
45. Sen A, Marsche G, Freudenberger P, Schallert M, Toeglhofer AM, Nagl C, et al. Association between higher plasma lutein, zeaxanthin, and vitamin C concentrations and longer telomere length: results of the Austrian Stroke Prevention Study. J Am Geriatr Soc 2014;62:222-9.
46. Beilfuss J, Camargo CA, Kamychevas E. Serum 25-hydroxyvitamin D has a modest positive association with leukocyte telomere length in middle-aged US adults. J Nutr 2017;147:514-20.
47. Liu J, Prescott J, Giovannucci E, Hankinson SE, Rosner B, Han J, et al. Plasma vitamin D biomarkers and leukocyte telomere length. Am J Epidemiol 2013;177(12):1411-7.
48. Borras M, Panizo S, Sarró F, Valdivielso JM, Fernandez E. Assessment of the potential role of active vitamin D treatment in telomere length: a case-control study in hemodialysis patients. Clin Ther 2012;34(4):849-56.
49. Richards JB, Valdes AM, Gardner JP, Paximadas D, Kimura M, Nessa A, et al. Higher serum vitamin D concentrations are associated with longer leukocyte telomere length in women. Am J Clin Nutr 2007; 86(5):1420-5.
50. Julin B, Shui IM, Prescott J, Giovannucci EL, De Vivo I. Plasma vitamin D biomarkers and leukocyte telomere length in men. Eur J Nutr 2017;56:501-8.
51. Farzaneh-Far R, Lin J, Epel ES, Harris WS, Blackburn EH, Whooley MA. Association of marine omega-3 fatty acid levels with telomeric aging in patients with coronary heart disease. JAMA 2010;20;303(3):250-66.
52. Kiecolt-Glaser JK, Epel ES, Belury MA, Andridge R, Lin J, Glaser R, et al. Omega-3 fatty acids, oxidative stress, and leukocyte telomere length: a randomized controlled trial. Brain Behav Immun 2013;28:16-24.
53. Freitas-Simoes TM, Cofán M, Blasco MA, Soberón N, Foronda M, Serra-Mir M, et al. Walnut consumption for two years and leukocyte telomere attrition in Mediterranean elders: results of a randomized controlled trial. Nutrients 2018;4:(10):E1907.
54. Du M, Prescott J, Kraft P, Han J, Giovannucci E, Hankinson SE, et al. Physical activity, sedentary behavior, and leukocyte telomere length in women. Am J Epidemiol 2012;175(5):414-22.
55. Edwards MK, Loprinzi PD. Sedentary behavior, physical activity and cardiorespiratory fitness on leukocyte telomere length. Health Promot Perspect 2017;7(1):22-7.
56. Latifovic L, Peacock SD, Massey TE, King WD. The influence of alcohol consumption, cigarette smoking, and physical activity on leukocyte telomere length. Cancer Epidemiol Biomarkers Prev 2016;25(2):374-80.
57. Ludlow AT, Zimmerman JB, Witkowski S, Hearn JW, Hatfield BD, Roth SM. Relationship between physical activity level, telomere length, and telomerase activity. Med Sci Sports Exerc 2008;40(10):1764-71.
58. Loprinzi PD, Sng E. Mode-specific physical activity and leukocyte telomere length among U.S. adults: Implications of running on cellular aging. Prev Med 2016;85:17-9.
59. Tucker LA, Physical activity and telomere length in U.S. men and women: An NHANES investigation. Prev Med 2017;100:145-51.
60. Fretts AM, Mete M, Howard BV, Best LG, Siscovick DS, Eilat-Adar S, et al. Physical activity and telomere length in American indians: the Strong Heart Study. Eur J Epidemiol 2018.
61. Puterman E, Weiss J, Lin J, Schilf S, Slusher A, Johansen KL, et al. Aerobic exercise lengthens telomeres and reduces stress in family caregivers: A randomized controlled trial - Curt Richter Award Paper 2018. Psychoneuroendocrinology 2018.
62. Sjögren P, Fisher R, Kallings L, Svenson U, Roos G, Hellénius mL. Stand up for health—avoiding sedentary behaviour might lengthen your telomeres: secondary outcomes from a physical activity RCT in older people. Br J Sports Med 2014;0:1-3.
63. Friedenreich CM, Wang Q, Ting NS, Brenner DR, Conroy SM, McIntyre JB, et al. Effect of a 12-month exercise intervention on leukocyte telomere length: results from the ALPHA Trial. Cancer Epidemiol 2018;56:67-74.
64. Dankel SJ, Loenneke JP, Loprinzi PD. The impact of overweight/obesity duration and physical activity on telomere length: an application of the WATCH paradigm. Obes Res Clin Pract 2016;16:30417-3.
65. Mason C, Risques RA, Xiao L, Duggan CR, Imayama I, Campbell KL, et al. Independent and combined effects of dietary weight loss and exercise on leukocyte telomere length in postmenopausal women. See comment in PubMed Commons belowObesity 2013;21(12):E549–E554.

66. Neilson HK, Friedenreich CM, Brockton NT, Millikan RC. Physical activity and postmenopausal breast cancer: proposed biologic mechanisms and areas for future research. Cancer Epidemiol Biomarkers Prev 2009;18(1):11-27.
67. Sanft T, Usiskin I, Harrigan M, Cartmel B, Lu L, Li FY, et al. Randomized controlled trial of weight loss versus usual care on telomere length in women with breast cancer: the lifestyle, exercise and nutrition (LEAN) study. Breast Cancer Res Treat 2018;172(1):105-12.
68. Loprinzi PD, Loenneke JP. Leukocyte telomere length and mortality among U.S. adults: Effect modification by physical activity behaviour. J Sports Sci 2017;36(2):213-9.
69. Garland SN, Johson B, Palmer C, Speck RM, Donelson M, Xie SX, et al. Physical activity and telomere length in early stage breast cancer survivors. Breast Cancer Res 2014;16:413-21.
70. Zhang J, Rane G, Dai X, Shanmugam MK, Arfuso F, Samy RP, et al. Ageing and the telomere connection: An intimate relationship with inflammation. Ageing Res Rev 2016;25:55-69.
71. Notaro R, Cimmino A, Tabarini D, Rotoli B, Luzzatto L. In vivo telomere dynamics of human hematopoietic stem cells. Proceedings of the National Academy of Sciences of the United States of America 1997;94:13782-5.
72. Mundstock E, Zatti H, Mattos F, Goecks S, Guma F, Migliorini M, et al. Effects of physical activity in telomere length: systematic review and meta-analysis. Ageing Res Rev 2015;22:72-80.
73. Denham J, O'Brien BJ, Charchar FJ. Telomere length maintenance and cardio-metabolic disease prevention through exercise training. Sports Med 2016;46(9):1213-37.
74. Lang PF, Fröhlich KU. The influence of physical exercise and sports on telomere length - A model for telomere length and telomerase activity regulation based on a comparative assessment of literature. Peer J Preprints 2016;4:e1965v1.
75. Chilton WL, Marques FZ, West J, Kannourakis G, Berzins SP, O' Brien BJ, et al. Acute Exercise Leads to Regulation of Telomere-Associated Genes and MicroRNA Expression in Immune Cells. PLoS ONE 2014;9(4):e92088.
76. Davidsen PK, Gallagher IJ, Hartman JW, Tarnopolsky MA, Dela F, Timmons JA, et al. High responders to resistance exercise training demonstrate differential regulation of skeletal muscle microRNA expression. J Appl Physiol 2011;110:309–17.
77. Bye A, Røsjø H, Aspenes ST, Condorelli G, Omland T, Wisløff U. Circulating MicroRNAs and aerobic Fitness–The HUNT-study. PLoS One 2013;8:e57496.
78. Paul L. Diet, nutrition and telomere length. J Nutr Biochem 2011;22:895-901.
79. Ornish D, Lin J, Daubenmier J, Weidner G, Epel E, Kemp C, et al. Increased telomerase activity and comprehensive lifestyle changes: a pilot study. Lancet Oncol 2008;9(11):1048-57.
80. Zhang X, Zhao Q, Zhu W, Liu T, Xie SH, Zhong LX, et al. The association of telomere length in peripheral blood cells with cancer risk: a systematic review and meta-analysis of prospective studies. Cancer Epidemiol Biomarkers Prev 2017;26(9):1381-90.
81. The Telomeres Mendelian Randomization Collaboration. Association between telomere length and risk of cancer and non-neoplastic diseases: a Mendelian randomization study. JAMA Oncol 2017;3(5):636-51.
82. Weischer M, Nordestgaard BG, Cawthon RM, Freiberg JJ, Tybjarg-Hansen A, Bojesen SE. Short telomere length, cancer survival, and cancer risk in 47102 individuals. J Natl Cancer Inst 2013;105(7):459-68.

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Revisión

Current trends in the analytical determination of vitamin D

Tendencias actuales en la determinación analítica de vitamina D

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Key words:

Liquid chromatography-tandem Mass Spectrometry (LC-MS/MS). Vitamin D. Inmunoassay. Chromatography. Standardization.

Abstract

Vitamin D is a micronutrient that plays a large role in bone disease, and researchers are now discovering that it also does so in non-skeletal disease, thus making high-quality analytical determination necessary. To make this determination, a series of immunochemical and physical methods are used.

These methods present a series of different ways of handling samples as well as different methodologies that bring a series of advantages and limitations based on the scope of work in which the vitamin D analysis methodology is applied.

Although the Liquid Chromatography-tandem Mass Spectrometry (LC-MS/MS) is the gold standard method of analytical vitamin D determination, and is the only one to offer a more complete and accurate view of all metabolites of this vitamin, it is necessary to standardize all the analysis methodologies that allow accurate, reliable and quality analytical determination, since it is essential to obtain results that can reliably be extrapolated to the population, and that can be decisive in assessing a large number of pathologies.

Palabras clave:

Cromatografía líquida-espectrometría de masas en tándem (LC-MS/MS). Vitamina D. Inmunoensayo. Cromatografía. Estandarización.

Resumen

La vitamina D es un micronutriente que ejerce un gran papel en enfermedades óseas y actualmente se está descubriendo que también lo hace en enfermedades no óseas, por lo que una determinación analítica de calidad es necesaria.

Para realizar esta determinación se emplean una serie de métodos inmunoquímicos y físicos, los cuales van a presentar una serie de tratamientos diferentes de las muestras, así como diferentes metodologías que van a traer una serie de ventajas y limitaciones conforme al ámbito de trabajo en que se aplique la metodología de análisis de la vitamina D.

A pesar de que la cromatografía líquida-espectrometría de masas en tándem (LC-MS/MS) es el método gold standard de determinación analítica de la vitamina D, y de que es el que ofrece una visión más completa y precisa de todos los metabolitos de esta vitamina, es necesaria una estandarización de todas las metodologías de análisis que permitan una determinación analítica precisa, fiable y de calidad, ya que es imprescindible obtener unos resultados que sean extrapolables con fiabilidad a la población y que puedan ser determinantes para valorar un gran número de patologías.

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INTRODUCTION

Vitamin D is a fat-soluble vitamin of steroid nature (1). The denomination vitamin D refers to hormonal precursors characterized from the chemical perspective as open-ring steroids. Due to their great importance in the metabolic processes, two compounds are denominated: vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol), which can be contributed by the diet. Vitamin D_2 is present in plants, fungi and yeasts. Vitamin D_3, on the other hand, comes from animal products such as blue fish, eggs, and milk, but it is also formed in an endogenous process that begins with the photochemical transformation of 7-dehydrocholesterol upon exposing the skin to a narrow margin (295-300 nm) of ultraviolet B (UVB) radiation from the sun (2). This produces the appearance of previtamin D_3, which is subsequently isomerized to form vitamin D_3. Vitamins D_2 and D_3 are inactive and are mobilized in the blood bound to specific proteins, namely transcalciferin and vitamin D-binding protein (DBP) (3). In the liver, they are hydroxylated to form 25-hydroxy-vitamin D [25(OH) D], which is the species that is found in the greatest proportion in the blood. A subsequent hydroxylation that mainly takes place in the renal tubules gives rise to 1,25-dihydroxy-vitamin D [1,25$(OH)_2$D], which is the form of vitamin D that has metabolic activity. The inactivation pathways of vitamin D include an oxidative pathway, through which the compounds [25(OH)D] and [1,25$(OH)_2$D] create various oxidized derivatives, including both 26,23-lactone and calcitroic acid. Another pathway that inactivates vitamin D is epimerization followed by oxidation in C-24 (4).

The quantification of vitamin D found in biological samples presents recognized difficulties (5). This circumstance coincides with an increase in studies to evaluate the content of vitamin D (6,7) occurring over the last decade, which has been attributed to two factors: on the one hand, the prevalence of serious deficiencies of this vitamin in poor countries and, on the other, an increase in the use of vitamin D as a general marker of health status and because of its relationship with various pathologies (8). Traditionally, it was thought that the diseases associated with vitamin D deficiency were bone-related, as there is a widely documented causal association in scientific evidence between low vitamin D status and risk of developing rickets, osteomalacia and osteoporosis. Thus, this vitamin is an essential factor in bone metabolism and calcium homeostasis (9,10). However, new research in this field that is just beginning is focusing on the vitamin's role in the development or accentuation of non-skeletal diseases such as autoimmune disease, cardiovascular disease, infectious disease, as well as some types of cancers (10-16). Although it has been pointed out that vitamin D's involvement in these pathologies has been, in many cases, the result of extrapolation in epidemiological studies that may lack sufficient reliability (17), the idea that vitamin D supplementation could contribute to the treatment of the above-mentioned diseases has been maintained, and there has consequently been a remarkable increase in tests to determine the metabolites of [25(OH)D], which, although not the biologically active form of the vitamin, has served as a marker of vitamin D status in the blood in recent years (18). However, its measurement is only recommended in cases of bone diseases such as osteomalacia and osteoporosis, people with impairments in the absorption of fat produced by illnesses such as inflammatory bowel disease, cystic fibrosis, celiac disease, and bypasses; or by medications that interfere with vitamin D such as medicines that favor bone resorption or those that interfere with vitamin D metabolism (8,19). Given the scarce scientific literature that focuses on the influence of vitamin D in these non-skeletal diseases, the trends in recent years aim to clarify the role of vitamin D in these diseases, thus opening a wide range of research lines that can help clarify the vitamin's role in the etiopathogenesis of said diseases (1).

Serum concentrations of vitamin D do not depend on homeostatic control, but rather on lifestyle and environmental factors; and bodily values essentially come from two sources: on the one hand, the cutaneous synthesis of vitamin D, which is the result of solar radiation, and on the other, intake through diet. This intake is very poor since, in addition to being present in few foods in significant quantities, the intake of these foods is not usually widespread throughout the global population (20). In addition, a series of socio-cultural factors will intervene in these serum concentrations (21).

However, despite the need for a high-quality analytical determination of vitamin D and a greater control of vitamin D concentrations in the body, the number of analytical determinations of vitamin D has increased exponentially in the last decade. Such a rapid increase is due to a growing interest in the study of those mechanisms of action in which vitamin D intervenes. In addition, supplementation with high doses of vitamin D has increased in recent years, both on doctors' advice and through self-medication. Upon evaluating the tests that have been performed, we currently find that while many tests are justified, such as those done when suffering a traumatic fall that involves bone fracture or in pathologies such as osteoporosis, the number of tests that are done in an unjustified and inappropriate way has increased in those people who do not really need them. This includes those who complain of tiredness, fatigue, self-administration of vitamin D supplements, etc., in addition to tests which are not ordered by a specialist rather than the family doctor. These unjustified and inappropriate tests have increased considerably, thus increasing extra costs. Therefore, in those populations where there is doubt as to whether or not to make an analytical determination of vitamin D, it is important that food consumption frequency questionnaires be used, as well as an assessment of sun exposure, in order to estimate the person's overall vitamin D concentration, and thus avoid the excessive cost of these tests. This type of testing requires a more rational approach in its use, since this would avoid inappropriate expenditures both at the patient and the hospital level, and it would also lead laboratories to redirect their funds to other more necessary tests (19,22).

The controversy surrounding this issue is so great that there is no universal agreement among physicians, researchers and the public on the issues related to vitamin D and its analytical determination, nor on its influence on the etiopathogenesis of various diseases. Therefore, the need for quality research is paramount due to the aforementioned aspects, which cannot be avoided (23).

ANALYTICAL DETERMINATION OF VITAMIN D

The measurement of vitamin D is usually done in the serum by determining the amount of the metabolites [25(OH)D_2] and [25(OH)D_3], given their higher proportion in the blood. However, the need to evaluate the amount of other metabolites for a better idea about vitamin D status has been indicated. Table I shows the list of metabolites that have been determined simultaneously from a sample (24).

The main problem in the analytical determination of vitamin D is the wide range of methods used and the variations in the results due to problems with extraction and calibration. Therefore, today, there is a need to find an international method that calibrates measurement methods, as this will make the various studies in this field more comparable and reproducible, thus avoiding misinterpreting the large number of studies at the international level that are cited in the scientific literature. In line with this, the vitamin D standardization programs that are emerging (20) are worth mentioning. Through these programs, it is possible to improve clinical practice and public health worldwide (1).

Until international standardization is established, the determination of vitamin D levels should be reserved for special risk groups and types of disease (20). The methods for measuring the metabolites of vitamin D can be divided into two main groups: immunochemical methods (chemiluminescence immunoassays [CLIA], radioimmunoassay [RIA], enzymatic assays, and chemical binding assays) and physical detection methods (high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) and LC-MS/MS) (1,8).

Immunoassay techniques present several problems such as cross-reactivity due to polyreactive antibodies, the ability to analyze only one analyte at a time with no discrimination between them, the inability to achieve structural validation of the analyte, and a highly fluctuating sensitivity. Immunological techniques are generally not able to distinguish between [25(OH)D_2] and [25(OH)D_3] due to the cross-reactivity of the antibodies, and it is not possible to obtain the same information provided using chromatographic determination (25). In addition, immunological techniques have limited sensitivity and dynamic range, difficulties in the displacement of DBP, non-equimolar detection of [25(OH)D_2] and [25(OH)D_3], interference of heterophile antibodies, gel and clot activator interference in blood collection tubes, and a lack of adequate standardization. Furthermore, within the cross-reactivity to other circulating metabolites of vitamin D mentioned above, [24,25$(OH)_2D_3$] is the most predominant (1).

Table I. Vitamins D_2 and D_3 and their metabolites determined simultaneously in human serum using LC-MS/MS

Name	Abbreviation
Vitamin D_2	D_2
Vitamin D_3	D_3
25-hydroxyvitamin D_2	25(OH)D_2
25-hydroxyvitamin D_3	25(OH)D_3
24,25-dihydroxyvitamin D_2	24,25$(OH)_2D_2$
24,25-dihydroxiyvitamin D_3	24,25$(OH)_2D_3$
1,25-dihydroxyvitamin D_2	1,25$(OH)_2D_2$
1,25-dihydroxyvitamin D_3	1,25$(OH)_2D_3$
D_2 Sulfate	D_2-S
D_3 Sulfate	D_3-S
D_2 Sulfate 25-hydroxyvitamin	25(OH)D_2-S
D_3 Sulfate 25-hydroxyvitamin	25(OH)D_3-S

In recent years, due to the growing interest in the role of vitamin D in the body, the number of determinations requested has been increasing, giving rise to the need to move from the antiquated manual radioimunoassay to the automated immunoassay on random access analyzer platforms in the majority of clinical laboratories (20).

The reactive protein binding assay, although cheap and used in small samples, has the disadvantage of underestimation in low amounts and overestimation in high amounts. The RIA has the advantages that it is economical, fast and specific, determines small sample sizes, and is also specific (8).

As far as chromatographic techniques are concerned, they are less susceptible to the effects of the matrix than immunoassays (1). In the field of liquid chromatography, high-performance liquid chromatography (HPLC) is used, which is stable, reproducible, and discriminates between metabolites. However, it requires a larger sample size, requires a preparation step before chromatography, and sometimes the assay is subject to interference from other compounds measured in the ultraviolet spectrum, in addition to requiring a high level of technical expertise (8,25). Between liquid chromatography with ultraviolet detection (LC-UV), liquid chromatography with diode array detection (LC-DAD), and liquid chromatography-mass spectrometry (LC-MS), however, LC-MS provides better results than the two liquid chromatographic techniques listed above (25).

The gold standard method for the determination of vitamin D is LC-MS/MS. However, its high cost is an expense that many routine analysis laboratories cannot assume. It is also necessary to have a very specialized and qualified staff to carry out this determination. Therefore, the cheaper immunoassay is used, although it does not allow for the differentiation of vitamin D_2 and vitamin D_3 (20,25). In addition, LC-MS/MS requires expensive hardware and a laborious process that includes: pretreatment of the sample, calibration, chromatographic separation mode, and the selection of an internal standard (1).

LC-MS/MS provides multiple advantages including greater sensitivity, flexibility and specificity. This is fundamentally due to the use of internal standards that have a crucial role in the determination. In addition, it has the ability to accurately quantify multiple analytes that are of interest in a single assay, which speeds up and makes this determination very complete (25).

Unfortunately, no reference method or reference materials are available for the [1,25$(OH)_2$D] analysis to date (1). Vitamin D status is defined by the measurement of 25(OH)D, a term which refers to both the [25(OH)D_2] and [25(OH)D_3] circulating forms of the

vitamin. There are a number of reasons why the total [1,25(OH)$_2$D] concentration cannot be used as a vitamin D marker. Its short half-life of less than a day versus almost a month for [25(OH)D], the low concentrations of the final metabolite (picomole vs nanomole), and the fact that only a very small amount of [25(OH)D] is converted to [1,25(OH)$_2$D] give a false sense of vitamin sufficiency. It is likely that the quantitative applications of vitamin D metabolites in the HRMS will move from research to routine clinical laboratories in the near future, providing additional specificity in measurements. A multi-panel assay for the simultaneous measurement of vitamin D metabolites will improve future research on the optimal combination of vitamin D species for the assessment of vitamin D sufficiency, and will help us better understand the metabolism of vitamin D in both healthy and ill subjects (1).

HANDLING OF VITAMIN D SAMPLES

Methods for vitamin determination require a preconditioning of samples for analysis, including the separation of vitamins and their metabolites from complex matrices in biological fluids such as plasma and serum. In the literature, several procedures have been described for the preconditioning of samples, mainly for the separation of vitamins from the blood. To isolate these analytes from blood plasma, different techniques have been used, such as protein precipitation, liquid-liquid extraction (LLE) and solid-phase extraction (SPE). Deproteinization and LLE result in endogenous matrix compounds passing into the supernatant, which can affect the separation and determination of the analytes. Therefore, an SPE technique is applied for the additional purification of the sample. When analyzing samples containing vitamin D, a well-established and standardized pretreatment phase is necessary, which distinguishes those elements that should be disregarded from those that interest us when proceeding with our analysis (26).

The handling of the samples is very complex, as it influences the association between vitamin D and DBP protein, albumin, and the analyte-antibody balance (20). The main problem with the DBP protein is that it has 3 polymorphic forms, which are derived in 6 allelic forms. These different alleles circulate in more or less variable concentrations and have a different degree of affinity for the different metabolites of vitamin D, which could compromise the treatment method, which binds this DBP protein to the vitamin D metabolite (27). Vitamin D is a hydrophobic compound and sensitive to the matrix. However, vitamin D analytes are stable for 2 weeks at 30 °C but for 1 year (or longer) at -20 °C, and are not affected by up to four freeze-thaw cycles of the serum samples. Ultraviolet rays also do not influence the calcidiol content of a serum sample (21). The hydrophobic nature of vitamin D and the strong binding to its transporter (vitamin D binding protein), the different forms that circulate in the blood, and the question of standardization are among the most important factors that influence the measurement of this metabolite. Since [25(OH)D] is a lipophilic substance closely linked to DBP, this generates some technical problems. In addition, endogenous lipids can affect binding and chromatographic separation, since plasma and serum are extracted together (27).

The problem with immunoassays in the preparation of samples is that an antibody that is so specific to such a small antigen must be determined very clearly, in addition to the hydrophobicity of the vitamin and its binding protein (DBP), which would make oscillations in the amount of DBP present in the sample affect the immunoassay. In addition, many laboratories rely on commercial immunoassay kits, which have their own pretreatment protocol that differs between laboratories. All of this causes sensitivity and specificity to fluctuate since many factors must be controlled (28,29).

The LC-MS/MS method, which is the one most widely accepted, begins with the pretreatment of the sample to separate [25(OH)D] from DBP and to eliminate phospholipids and other interferences from the matrix that cause alterations in the ionization. Sample preparation is usually performed using protein precipitation, LLE, SPE, supported liquid extraction (SLE) or extraction plates coated with an immobilized absorption phase (1).

The quantification of [1,25(OH)$_2$D] is difficult due to its extremely low concentrations in the serum, as well as the co-existence of many other abundant vitamin D metabolites that can interfere with its measurement. Additionally, accurate quantification of [1,25(OH)$_2$D$_3$] using LC-MS/MS is a challenge due to its low serum concentrations and the lack of ionizable polar groups resulting in low ionization efficiency in Electrospray Ionization (ESI) and Atmospheric Pressure Chemical Ionization (APCI). In addition, specific care is needed to avoid potential interference from other dihydroxylated vitamin D metabolites (1).

LC-MS/MS methods differ in sample preparation aspects, chromatography, ionization source, and fragmentation patterns detected. Therefore, despite the accuracy of the method, these factors cause the results obtained to vary between different LC-MS/MS methods. LC-MS/MS also has several variants in laboratories, since different methodologies are added to improve aspects of the method itself, thus also making the results less comparable. The choice of one method or another also depends on staff experience, the objective to which it is directed, as well as the volume of the center where the determination is done. Therefore, the immunoassays that provide guideline measurements, which are not completely accurate, will be used in smaller laboratories for clinical use. In addition to being inexpensive, the staff in these laboratories are often not very specialized, so they are not prepared for a more complex test like chromatography. In contrast, very large clinical laboratories and academic institutions use LC-MS/MS methods given that their sensitivity and specificity mean that they are used in those at-risk populations where the accuracy of the method may be very important, such as in the pediatric population, for example. Along the same line, the method can also be chosen depending on the metabolite that you aim to determine, using a more specific test that determines the last precursor of vitamin D in pathologies in which you want to precisely analyze this vitamin such as rickets (28,29).

Otherwise, even when a good sample treatment is carried out, as well as an appropriate analytical method of vitamin D is chosen, vitamin D levels can be increased or decreased in the same person who maintains similar eating habits and of exposure to the

sun during the year. This is due to the variation of the exposure to sunlight in the different stages of the year. In populations in which vitamin D was measured in different seasons of the year, greater deficiency was found in the hottest stages, so we must take into account the seasonality of the year, since in hotter seasons people take more sun in places like the beach and with less protection, besides that it is convenient that at the time of asking about the habit of exposure to the sun, the latitude and the month of the year are taken into account (30,31).

The tendencies that will arise in the future will go on to establish a methodology to automate extraction, without requiring any intervention from human beings. This is due to the fact that when people handle the samples, they increase the probability of operator error and biological risks (6). Future challenges of the assay include moving to SPE to allow better sample cleaning and minimize the extraction steps to those that can be automated and try to generate less waste (8).

The absence of certified reference material for the analytical determination of [25(OH)D] is the most important factor that determines the inaccuracy in identifying individuals with vitamin D levels below the optimal threshold (27).

CONCLUSION

The trend in vitamin D analysis is on the rise as there is a need for its determination due to its relationship with a wide range of pathologies. Therefore, it is necessary to look for a methodology, according to each situation, that is cheap, easy to perform and accurate. The most accurate determination technique for the situation mentioned above would be LC-MS/MS chromatography. However, this technique is not easy to perform because, as described, it requires considerable experience and is not cheap. To solve this problem, a standardization of this technique would be adequate. Currently, a wide range of entities including laboratories use this technique together with other processes independently, which makes the method more expensive as there is no single universal methodology that allows for mass production to lower costs. Additionally, it is not reproducible, which is a key factor when interpreting the scientific literature. If we use different measurement instruments, handle samples differently, and leave the human error intrinsic to the manual and non-technological handling of samples up to chance, we shall yield a result that will be suitable within a certain range when evaluating and extrapolating a single study, but which is hardly comparable at the global level.

No one technique is better than another, it is simply more interesting than others depending on the aim of the study. If we want, on the one hand, to avoid excessive economic expenditures, obtain reliable data but work with a broader or narrower range of concentrations, and the vitamin D determination is to obtain a guiding idea, but the exact value is not crucial for our study, we will opt for immunoassay techniques like in clinical settings. On the other hand, if what we want is precision in the data, even if that entails more effort, money and experience, our choice has to be chromatographic techniques, like in field studies.

The future of this field is to continue developing variants of LC-MS/MS and to replace the immunoassay as data accuracy is crucial, even if it leads to other associated problems.

Another line that could be opened would be the handling of samples according to temperature. Since vitamin D can withstand many freeze-thaw cycles and is sensitive to certain environmental variables, working conditions could be established, such as handling both the sample and internal standard directly in a cold chamber as characteristics are maintained longer in a cold room. By doing the pretreatment there, all the samples would be handled at a constant temperature and under the same conditions as in the chromatographic technique, since working with them at room temperature causes the temperature to fluctuate as well as an increase in exposure to external agents, which means that at the time of treating the sample using chromatography, some confounding factors will not have been suppressed.

REFERENCES

1. Van den Ouweland J. Analysis of vitamin D metabolites by liquid chromatography-tandem mass spectrometry. Trends Analyt Chem 2016;84:117-30. DOI: 10.1016/j.trac.2016.02.005.
2. Higashi T, Shimada K, Toyo'oka T. Advances in determination of vitamin D related compounds in biological samples using liquid chromatography–mass spectrometry: A review. J Chromatogr B 2010;878:1654-61. DOI: 10.1016/j.jchromb.2009.11.026.
3. Combs G. The vitamins - Fundamental aspect in nutrition and health (3rd ed.). Amsterdam: Elsevier Academic Press, 2008.
4. Christakos S, Ajibade D.V, Dhawan P, Fechner A.J, Mady L.J. Vitamin D: Metabolism. Endocrinol. Metabol. Clin North Amer 2010;39:243-53.
5. Luque-García JL, de Castro MDL. Extraction of fat-soluble vitamins. J Chrom A 2001;935:3-11. DOI: 10.1016/S0021-9673(01)01118-9.
6. Singh RJ. Are clinical laboratories prepared for accurate testing of 25-hydroxy vitamin D? Clin Chem 2008;54:221-3. DOI: 10.1373/clinchem.2007.096156.
7. Babic N. Analytical methods and performance of the Immunoassay methods for determination of vitamin D in comparison to Mass Spectrometry. J Med Biochem 2012;31:333-8. DOI: 10.2478/v10011-012-0022-1.
8. Atef SH. Vitamin D assays in clinical laboratory: Past, present and future challenges. J Steroid Biochem Mol Biol 2018;175:136-7. DOI: 10.1016/j.jsbmb.2017.02.011.
9. DeLuca HF. Overview of general physiologic features and functions of vitamin D. Am J Clin Nutr 2004;80:1689-96. DOI: 10.1093/ajcn/80.6.1689S.
10. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266-81. DOI: 10.1056/NEJMra070553.
11. Reid IR. What diseases are causally linked to vitamin D deficiency? Arch Dis Child 2016;101:185-9. DOI: 10.1136/archdischild-2014-307961.
12. Bittenbring JT, Neumann F, Altmann B, Achenbach M, Reichrath J, Ziepert M, et al. Vitamin D deficiency impairs rituximab-mediated cellular cytotoxicity and outcome of patients with diffuse large B-cell lymphoma treated with but not without rituximab. J Clin Oncol 2014;32:3242-8. DOI: 10.1200/JCO.2013.53.4537.
13. Goshayeshi L, Saber H, Sahebari M, Rezaieyazdi Z, Rafatpanah H, Esmaily H. Association between metabolic syndrome, BMI, and serum vitamin D concentrations in rheumatoid arthritis. Clin Rheumatol 2012;31:1197-203. DOI: 10.1007/s10067-012-1995-3.
14. Norton R, O'Connell M. Vitamin D: Potential in the Prevention and Treatment of Lung Cancer. Anticancer Res 2012;32:211-21.
15. Plum LA, DeLuca HF. Vitamin D, disease and therapeutic opportunities. Nat Rev Drug Discov 2010;9:941-55. DOI: 10.1038/nrd3318.
16. Anderson JL, May HT, Horne BD, Blair TL, Hall NL, Carlquist JF, et al. Relation of vitamin D deficiency to cardiovascular risk factors, disease status, and incident events in a general population. Am J Cardiol 2010;106:963-8. DOI: 10.1016/j.amjcard.2010.05.027.
17. Sattar N, Welsh P, Panarelli M, Forouhi NG. Increasing requests for vitamin D measurement: costly, confusing, and without credibility. Lancet 2012;379:95-6. DOI: 10.1016/S0140-6736(11)61816-3.

18. Turpeinen U, Hohenthal U, Stenman UH. Determination of 25-hydroxyvitamin D in serum by HPLC and immunoassay. Clin Chem 2003;49:1521-4. DOI: 10.1373/49.9.1521.
19. Woodford HJ, Barrett S, Pattman S. Vitamin D: too much testing and treating? Clin Med 2018;18:196-200. DOI: 10.7861/clinmedicine.18-3-196.
20. Siggelkow H. Vitamin-D-Analytic. Diabetology 2016;12:248-53. DOI: 10.1007/s11428-016-0099-0.
21. Nikooyeh B, Samiee SM, Farzami MR, Alavimajd H, Zahedirad M, Kalayi A, et al. Harmonization of serum 25-hydroxycalciferol assay results from high-performance liquid chromatography, enzymeimmunoassay, radioimmunoassay, and immunochemiluminescence systems: A multicenter study. J Clin Lab Anal 2017;31. DOI: 10.1002/jcla.22117.
22. Rodd C, Sokoro A, Lix LM, Thorlacius L, Moffatt M, Slater J, et al. Increased rates of 25-hydroxy vitamin D testing: Dissecting a modern epidemic. Clin Biochem 2018;59:56-61. DOI: 10.1016/j.clinbiochem.2018.07.005.
23. Romagnoli E, Carnevale V, Biondi P, Minisola S. Vitamin D supplementation: when and how? J Endocrinol Invest 2014;37:603-7. DOI: 10.1007/s40618-014-0071-z.
24. Abu Kassim NS, Shaw PN, Hewavitharana AK. Simultaneous determination of 12 vitamin D compounds in human serum using online sample preparation and liquid chromatography-tandem mass spectrometry. J Chromatogr A 2018;1533:57-65. DOI: 10.1016/j.chroma.2017.12.012.
25. Kasalová E, Aufartová J, Krεmová LK, Solichová D, Solich P. Recent trends in the analysis of vitamin D and its metabolites in milk – A review. Food Chem 2015;171:177-90. DOI: 10.1016/j.foodchem.2014.08.102.
26. Karaźniewicz-Łada M, Główka A. A review of chromatographic methods for the determination of water-and fat-soluble vitamins in biological fluids. J Sep Science 2016;39:132-48. DOI: 10.1002/jssc.201501038.
27. Romagnoli E, Pepe J, Piemonte S, Cipriani C, Minisola S. Management of endocrine disease: Value and limitations of assessing vitamin D nutritional status and advised levels of vitamin D supplementation. Eur J Endocrinol 2013;169:R59-69. DOI: 10.1530/EJE-13-0435.
28. Babij N. Analytical methods and performance of the immunoassay methods for determination of vitamin din comparison to mass spectrometry. J Med Biochem 2012;31:333–8. DOI: 10.2478/v10011-012-0022-1.
29. Morris HA. Vitamin D Activities for Health Outcomes. Ann Lab Med 2014;34:181-6. DOI: 10.3343/alm.2014.34.3.181.
30. Kleine C, Obi Y, Streja E, Hsiung J, Park C, Holick MF, et al. Seasonal variation of serum 25-hydroxyvitamin D and parameters of bone and mineral disorder in dialysis patients. Bone 2019;124:158-65. DOI: 10.1016/j.bone.2019.03.003.
31. Aydın CG, Dinçel YM, Arıkan Y, Taş SK, Deniz S. The effects of indoor and outdoor sports participation and seasonal changes on vitamin D levels in athletes. SAGE Open Med 2019;7. DOI: 10.1177/2050312119837480.

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Revisión

Effect of water consumption on weight loss: a systematic review

Efecto del consumo de agua sobre la pérdida de peso: revisión sistemática

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Abstract

Water intake has been proposed for weight loss; however, the evidence of its efficacy is limited. The aim of this study was to systematically review the randomized clinical trials that assessed the effect of water consumption on weight with a follow up ≥ 12 weeks. A systematic query-based search was performed on PubMed, EBSCO, and Cochrane Library to identify eligible records that quantitatively measured body weight change after interventions. This review included six RCTs that reported different strategies for weight loss achievement: increasing daily water intake, replacement of caloric beverages with water, and premeal waterload. All the studies showed a weight loss effect after follow-up, ranged from -0.4 kg to -8.8 kg with a mean percentage of weight loss of 5.15%. The most effective intervention among the studies was the replacement of caloric beverages with water. The quality of the evidence for the primary outcome of weight loss was rated low to moderate. The main limitation of these results is the short-term follow up-period. In conclusion, despite 5.15% of weight loss, the low to moderate quality of evidence and the short term of follow-up are limitations to support evidence-based recommendations of water consumption for weight loss.

Key words:

Water consumption. Weight loss. Non-nutritive sweeteners. Obesity. Systematic review.

Resumen

El consumo de agua se ha propuesto como medida para la pérdida de peso; sin embargo, la evidencia de su eficacia es limitada. El objetivo de este estudio fue revisar sistemáticamente los ensayos clínicos aleatorizados que han evaluado el efecto del consumo de agua en el peso corporal con un periodo de seguimiento ≥ 12 semanas. Se realizó una búsqueda sistemática en cadena en PubMed, EBSCO y Cochrane Library para identificar estudios elegibles que midieran cuantitativamente el cambio de peso corporal después de sus intervenciones. Esta revisión incluye seis ECA que reportan diferentes estrategias para alcanzar la pérdida de peso: incremento del consumo diario de agua, reemplazo de bebidas calóricas por agua y sobrecarga con agua previa a las comidas. Todos los estudios mostraron un efecto de pérdida de peso después del seguimiento, con un rango de -0.4 kg a -8.8 kg y con un porcentaje promedio de pérdida de peso del 5.15%. La intervención más efectiva entre los estudios fue el reemplazo de bebidas calóricas por agua. La calidad de la evidencia para el resultado primario de pérdida de peso fue calificada de baja a moderada. La principal limitación de estos resultados es el corto periodo de seguimiento. En conclusión, a pesar de encontrarse una pérdida de peso del 5.15%, la calidad de la evidencia baja a moderada y el corto periodo de seguimiento son limitaciones para sustentar una recomendación basada en la evidencia sobre el consumo de agua para la pérdida de peso.

Palabras clave:

Consumo de agua. Pérdida de peso. Endulzantes no nutritivos. Obesidad. Revisión sistemática.

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INTRODUCTION

Over the past 50 years, the prevalence of obesity has increased to pandemic proportions all over the world (1), representing an important global health and economic problem (2). It was also considered, between 1975 and 2014, the most common nutritional disorder in the United States (2). The worldwide prevalence of obesity (BMI ≥ 30 kg/m²) increased from 3.2% in 1974 to 10.8% in 2014 among adult men, and from 6.4% to 14.9% in adult women over the same period (1,3).

Excess weight has been reported to be associated with various negative effects such as cardiovascular disease, hypertension, diabetes, cancer, and chronic renal disease, among others, and also with early mortality (2,4).

In response to the growing epidemic of obesity and obesity-related chronic diseases, over the last four years numerous guidelines and position statements have been published (5). Some authors have indicated that the fundamental goal in the treatment of overweight and obesity is weight loss, indicated to individuals with BMI ≥ 30 or ≥ 27 kg/m^2 in the presence of weight-related comorbidity (6).

Evidence-based treatments for weight loss include lifestyle intervention, pharmacotherapy, and bariatric surgery (6). However, there are inconsistent results regarding the effectiveness of some of these strategies (lifestyle intervention, pharmacotherapy) in the long-term maintenance of weight (7-8).

Water is essential for life (9). It comprises about 60% of human body weight and is critical for life; without water, humans can survive for just 2-4 days (10). Beverage consumption recommendations, motivated by the large increase in unhealthy weight patterns in the United States over the past 20 years, suggest water as the gold-standard beverage for optimal health (11).

Increasing water intake has been proposed as an important tool for reducing weight. However, the evidence of its efficacy is limited (12-13). Epidemiologic and clinical studies suggest that energy intake is significantly lower in water drinkers than in non-water drinkers, which may contribute to weight loss and consequently to obesity prevention (14-18).

Drinking water has been proposed to increase energy expenditure and rates of lipolysis (19-21). Some studies have concluded that drinking water, compared to intake of caloric beverages, lowers total energy intake (22-25). Absolute increases in drinking water may promote weight loss by altering metabolism and by a slight increase in satiety, thus promoting weight loss. Very few studies have been conducted to assess the long-term effects of drinking water on changes in body weight (13, 26).

A previous systematic review that analyzed the effect of water intake on body weight outcomes in an adult population, published in 2013, concluded that studies of individuals dieting for weight loss or maintenance suggest a weight-reducing effect of increased water consumption, whereas studies in general mixed-weight populations yielded inconsistent results (27). However, the weight loss effect was marked as low evidence because the quality of the studies was poor. In addition, the review included only one randomized clinical trial with a follow up of 12 weeks, one non-randomized trial, and a few more with observational periods of a few days, several of them cross-sectional in design.

Therefore, the aim of this review was to systematically summarize all the existing evidence from randomized clinical trials that evaluated the effect of water consumption on weight or body mass index in adult and adolescent populations with a follow-up equal or greater than 12 weeks.

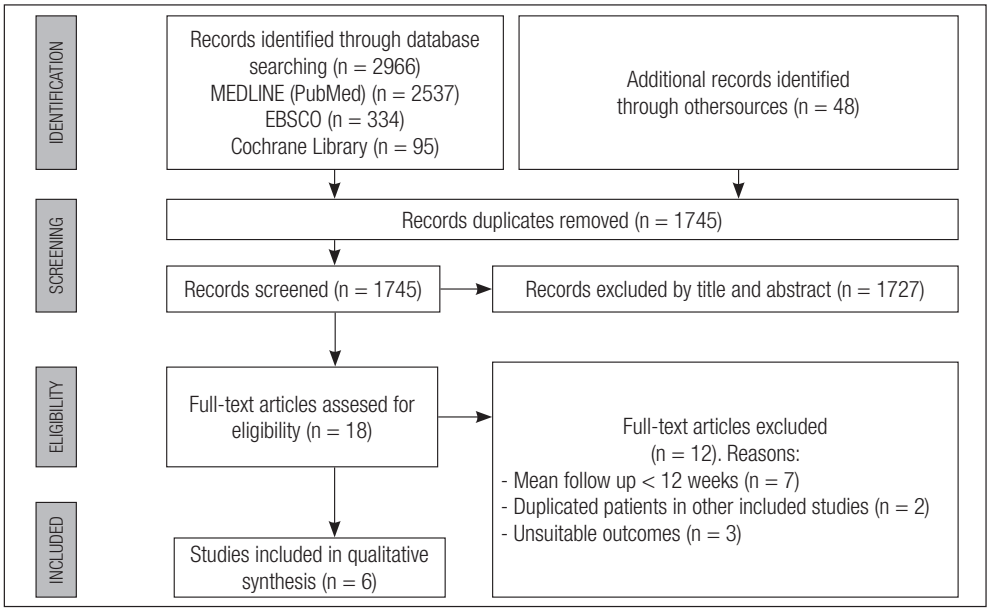

Figure 1.
Flow diagram of selected studies.

MATERIALS AND METHODS

This systematic review was conducted following the PRISMA guidelines.

IDENTIFICATION OF RECORDS

A systematic query-based PubMed search was performed to identify eligible records that quantitatively measured body weight change after interventions regarding water consumption. The search terms used were the following: ("water consumption OR "water intake" OR "drinking water" OR "beverages" OR "plain water") AND ("adults" OR "adolescents") AND ("body weight" OR "body mass index" OR "weight loss" OR "weight outcomes" OR "obesity" OR "overweight").

Searches using the keywords "water intake," "obesity," and "weight loss" were performed in EBSCO, Web of Science, and Google Scholar to identify additional publications. To maximize the number of studies assessing body composition outcomes, we included all studies found in the literature that met the inclusion criteria. The last search was conducted on March 8th, 2019.

The article selection process is presented in a flow diagram in figure 1.

INCLUSION/EXCLUSION CRITERIA

Randomized clinical trials of the effects of water consumption on body weight were selected, including the following criteria: 1. Any language full-text articles, adolescent and adult population above 12 years old; 2. Articles with a follow-up of at least 12 weeks; 3. Retention rate of at least 70%; 4. Studies that reported baseline and post-intervention measurements of body weight or BMI or both; and 5. Studies that reported the amount of water intake. Studies attending populations with comorbidities were included if these were related to overweight and obesity. We excluded published letters, comments, reviews, abstracts only, and duplicated studies.

SCREENING AND ELIGIBILITY

We identified 2,966 articles through the initial database research. Title screening was performed by one researcher to exclude clearly irrelevant and duplicated studies; 1,221 records were excluded. Screening on abstract was performed by three researchers, who excluded 1,727 records. Full-text screening of the remaining 18 records was initially performed by one researcher, and any eligible records with uncertain data were discussed with a second researcher. In total, 12 records were excluded. A total of 6 records were included.

DATA EXTRACTION

We used a standard data extraction method to collect the information of each study: author, year of publication, country, sample size, age interval and gender of the participants, mean follow-up, retention rate, weight loss, and BMI reduction outcomes reported on each study. Weight outcomes evaluated were body weight loss and body mass index reduction after intervention.

QUALITY ASSESSMENT

To assess the quality of the evidence, we used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system, which defines the quality of the evidence as high, moderate, low, or very low. The evidence was evaluated according to the primary outcome (weight loss).

RESULTS

STUDY CHARACTERISTICS

A total of six eligible publications were included, consisting of six RCTs. Table I summarizes the major characteristics of the studies included.

One study had an adolescent population with OW/OB without comorbidities (12), the other five included mixed (13,28-29) and only female populations (30-31) with OW/OB, and one of them included OW/OB with diabetes mellitus in both groups (31). Five of the studies reported statistical power and all studies reported a retention rate higher than 70% at 12 weeks of follow-up.

Different strategies to weight loss achievement were used: five of the studies included a weight loss program with hypocaloric diets, physical activity and/or behavioral programs. Two studies assessed the effect of increasing daily water intake (12,29), two the effect of replacing caloric beverages with water following lunch (30-31), and the remaining two studies evaluated the effect of 500 mL of water preload before all 3 daily meals and before the main meal (13,28).

All studies reported baseline and post-intervention weight, and four of them also reported BMI reduction (12,13,30,31). Other measurements were non-uniformly reported: four studies reported changes in waist circumference, lipid profile and fasting glucose (13,29-31); two of them reported A1C and insulin resistance indicators (30,31), and two reported body fat percentage (12,13).

PARTICIPANTS' CHARACTERISTICS

A total of 609 participants were included in this study. Total size samples ranged from 38 to 303 participants. Gender distribution was reported in all six studies, and there was a greater proportion of women (78.1%) than men (21.9%). Age at baseline ranged from 12 to 75 years. Baseline weight ranged from 83.90 to 93.03 kg, and BMI ranged from 32.0 to 34.2 kg/m^2.

Table I. Study characteristics and weight loss outcomes

Author, year (country)	Follow-up (weeks)	Retention rate (%)	Sample size: sex (age range in years)	Intervention	Weight change from baseline (kg)	p	BMI change from baseline (kg/m²)	p
Wong, 2017 (USA)	24	100	38: M/F (12 to 17)	IG: weight loss diet plus eight cups per day of water vs. CG: weight loss diet	IG: -0.4 CG: -0.6	0.90	IG: -0.6 CG: -0.4	0.71
Madjd, 2016 (Iran)	24	80	81: F (18 to 50)	IG: weight loss diet plus post lunch replacement of DB with water vs. CG: weight loss diet plus DB post-lunch daily	IG: -6.4 CG: -5.25	0.006	IG: -2.5 CG: -2.05	0.006
Peters, 2016 (USA)	52	73	303: M/F (21 to 65)	IG: weight loss behavioral program plus 710 mL of NSS per day vs. CG: weight loss behavioral program plus at least 710 mL of water per day	IG: -8.39 CG: -3.39	< 0.001		
Madjd, 2015 (Iran)	24	71	62: F (18 to 50)	IG: weight loss diet plus post lunch replacement of DB with water vs. CG: weight loss diet plus DB post-lunch daily	IG: -8.0 CG: -7.6	0.015	IG: -3.3 CG: -2.9	0.002
Parreti, 2015 (England)	12	92.8	84: M/F (56.5 mean)	IG: no weight loss diet plus 500 mL water preload 30 min before main daily meal vs. CG: no weight loss diet	IG: -2.4 CG: -1.2	0.028		
Dennis, 2010 (USA)	12	85.4	41: M/F (55 to 75)	IG: weight loss diet plus 500 mL water preload 30 before 3 daily meals vs. CG: weight loss diet	IG: -0.87 CG: -0.6	< 0.001	IG: -2.6 CG: -1.9	Not significant

OW: overweight; OB: obese; DM: diabete mellitus; IG: intervention group; CG: control group; DB: diet beverages; CB: caloric beverages; NSS: non-nutritive sweeteners.

CHANGE IN WEIGHT LOSS

Weight loss outcomes in the intervention groups, based on body weight in kgs, are shown in Table 1. Mean body weight at baseline and at end of follow-up was 89.33 kg and 84.55 kg, respectively. After the interventions all the studies showed a mean weight loss of -4.96 kg, ranging from -0.4 kg to -8.8 kg. The mean percentage weight loss was 5.15%. The most effective intervention among the studies was the replacing of caloric beverages with water, with weight loss ranging between 7.62% and 9.41% at 24 weeks of follow-up with a significant difference between groups (31). Interventions involving an increase in daily water intake were the least effective, with reductions that ranged from 0.46% to 2.98% at 24 (12) and 52 weeks of follow-up (29), respectively; differences between groups were reported only in the 52-week study. Premeal waterload showed a reduction that ranged from 2.6% to 7.8% at 12 weeks of follow-up. Both studies found significant differences between groups (13,28).

The study with the longest follow-up had 52 weeks, and reported a weight loss of 2.98% in the group with higher water intake (29).

GENERAL CHARACTERISTICS OF THE STUDIES INCLUDED

A RCT conducted by Dennis (13) studied the effects of water consumption on body weight. Participants were 55-75-year-old adults and included predominantly white men. The intervention group (IG) had a hypocaloric diet plus 500 mL of bottled water prior to each of the three daily meals, and the control group (CG) had a hypocaloric diet alone. After 12 weeks of follow-up a weight reduction of 7.8% ($p < 0.001$) was found in the IG, which was approximately 2 kg greater in the water group than in the CG. Weekly water intake compliance was 90%. There were differences in food and beverages energy density within groups but not between groups at the end of the study. No differences in mean ad libitum breakfast meal energy intake at the end of follow-up was found. Most male and white participants were included in the IG. The Institute for Public Health and Water Research funded the study.

Parretti et al (28) conducted a RCT to assess the efficacy of water preloading before meals as a weight loss strategy. All races, a nonspecific wide age range, and participants with comorbidities were included. The IG had 500 mL of water within 30 min prior to the main meals each day, without any specific diet, plus a

behavioral program. The CG received behavior counseling only. After 12 weeks of follow-up a change of -2.4 ± 3.4 kg was found in the IG. Twenty-seven percent of the participants lost at least 5% of their body weight; the change in CG was -1.2 ± 2.9 kg; a difference of -1.3 kg was reported between groups ($p = 0.028$). The mean difference in weight change between drinking water three times a day versus no water regimen a day was 3.6 kg (95% CI -7.0 to 0.2). Private funding was reported.

Madjd et al. (30) conducted a RCT to study the effect of replacing diet beverages (DBs) with water during a 24-week weight loss program with a hypocaloric diet, exercise, and behavioral support. Participants were 18-50-year-old women without other comorbidities. Subjects in the IG replaced their usual intake of DB with 250 mL of water after the main meal (lunch), and the CG was instructed to drink 250 mL of DB once a day after lunch, five times a week, and the resting days only water. In both groups no water or DBs were allowed during lunch. At the end of follow-up a weight loss of 8.8 ± 1.9 kg was reported in the IG, and of 7.6 ± 2.1 kg in the CG, with a 13.6% greater weight reduction in the IG ($p = 0.015$) group. A greater improvement in insulin sensitivity and cardiometabolic risk was found in both groups. The authors reported no conflicts of interest.

In 2016, Madjd et al. (31) replicated their previous study in type-2 diabetes female patients. With a larger sample and a retention rate of 80%, they found after 24 weeks of follow-up a reduction of 7.62% in body weight in the IG, compared to 1.16 kg in the CG ($p = 0.006$). A greater improvement in fasting plasma glucose and insulin sensitivity was reported in the IG. There was a greater reduction in energy intake in the IG compared with the CG. The authors reported no conflicts of interest.

Peters et al. (29) conducted a RCT to evaluate the effects of sweetened beverages with non-nutritive sweeteners (NNS) versus water (WG) in subjects enrolled in a one-year behavioral weight loss program. The sample consisted on 303 participants aged 21 to 65 years. The NNS group consumed 710 mL of NSS per day and the WG had 710 mL of water per day during the 52-week follow-up period. Both the NNS and water treatments were reported as non-equivalent: the NNS group had greater weight loss, -6.2 ± 7.65 kg ($p < 0.001$) when compared to the WG, with a reduction of 3.39 ± 6.33 kg. Forty-four percent of the participants in the NNS group archived a 5% weight reduction, compared to 25.5% in the WG. This study had the longest follow-up period and the largest sample. The authors reported private funding for the study.

Wong et al. (12) conducted a RCT in an adolescent population from 12 to 17 years of age. As an inclusion criterion the participants had to usually drink ≤ 4 cups of water per day. In addition to a standardized nutrition and behavioral intervention, the IG was encouraged to increase water intake to 8 cups per day, referred to as 8×8 (eight 8-oz glasses [1.92 L] of water per day), and the CG received no specific advice on drinking water but did receive the same nutritional and behavioral intervention. After 24 weeks of follow-up water intake was greater in the IG compared with the CG (1.6 cups per day, 95% CI, -0.2 to -3.0, $p = 0.03$), but the IG did not achieve the 8-cup-per-day goal. In addition, a significant reduction in BMI z score within groups, but not between groups, was found. Private funding was declared.

QUALITY OF THE EVIDENCE

The quality of the evidence was evaluated based on study design, study quality, consistency, directness, precision, and publication bias. All the studies reported they had calculated statistical power, retention rates were high, and no imbalance between intervention and control groups was found. Four studies reported their randomization procedures (12,28,30,31) and allocation concealment method (12,28,30,31), and followed an intention-to-treat principle [12,28,29,31]. While all the interventions tested the effect of water intake on weight reduction, the strategies used were different: two tested increase in water intake (12,29), two replacement of caloric beverages (30,31), and two premeal water load (13,28); and all the studies but one (28) included a weight loss diet. The length of the studies ranged from 12 to 52 weeks, and for weight loss longer-term weight assessments are needed. In five out of six studies the IG lost more weight than the control group. Four out of six studies had either industry funding or conflicts of interest with royalties out of a book promoting water intake. The quality of the evidence for the primary outcome of body weight loss was low to moderate.

DISCUSSION

In this systematic review we found that the overall reduction of the initial weight after a water consumption intervention in overweight and obese adults and adolescents was 5.15%, which ranged from 0.46% to 9.41%. However, the quality of the evidence for the effectiveness of water consumption interventions for weight loss ranged from low to moderate. Intervention strategies included increased water intake, replacement of caloric beverages, and premeal water load. Caloric beverage replacement was the most effective approach to weight loss achievement.

These results are consistent with a previous systematic review published in 2013, which included observational studies, non-randomized trials, and RCTs with short-term follow-up periods. Our review limited the studies to RCTs with a retention rate higher than 70% and a follow-up of at least 12 weeks. When compared to other RCTs assessing diet, physical activity, and pharmacological interventions, water consumption strategies show a quantitavely similar effect on weight reduction. However, the period of follow-up prevents long-term (more than a year) predictions regarding weight loss. Additionally, heterogeneous samples and low to moderate quality of the evidence are the main limitations of these results.

Public health programs and RCTs focusing on reducing energy intake from food usually give little value to fluid consumption, but the findings of this review indicate that the strength of the evidence for the effect of water intake, water replacement, or water load is low to moderate.

Among the strengths of this study are that all the studies included were well designed, randomized, controlled trials, had a follow-up of at least 12 weeks, and at least a 70% retention rate.

As for weaknesses, the studies included were heterogeneous, thus a meta-analysis could not be conducted, and the quality of the evidence for weight loss ranged from low to moderate. Other

adiposity indicators were not uniformly reported, and only one study with one year of follow-up was conducted.

CONCLUSIONS

Water consumption interventions in overweight and obese adults and adolescents resulted in a reduction of 5.15% of initial body weight. In this systematic review only six studies were included and the quality of the evidence for the effectiveness of weight loss ranged from low to moderate. Further high-quality studies with long-term follow-up are warranted to assess weight loss during more than one year.

REFERENCES

1. Blüher M. Obesity: global epidemiology and pathogenesis. Nat Rev Endocrinol 2019;15(5):288-98. DOI: 10.1038/s41574-019-0176-8.
2. Hall E, Crook E, Jones D, Wofford M, Dubbert P. Mechanisms of obesity-associatedcardiovascular and renal disease. AJMS 2002;324(3):127-37. DOI: 10.1097/00000441-200209000-00003.
3. Global Burden Disease. Health effects of overweight and obesity in 195 countries over 25 years. NEJM 2017;377(1):13-27. DOI: 10.1056/NEJMoa1614362.
4. Ryu S, Frith E, Pedisic Z, Kang M, Loprinzi P. Secular trends in the association between obesity and hypertension among adults in the United States, 1999–2014. 2019;62:37-42. DOI: 10.1016/j.ejim.2019.02.012.
5. Ryan D, Kahan S. Guideline recommendations for obesity management. Med Clin N Am 2018;102:49-63. DOI: 10.1016/j.mcna.2017.08.006.
6. Lahey R, Khan S. Trends in obesity and risk of cardiovascular disease. Curr Epidemiol Rep 2018;5(3):243-51. DOI: 10.1007/s40471-018-0160-1.
7. Lizarraga K, Bacardí M, Jiménez A. Do weight loss increase life expectancy? Systematic review. Nutr Hosp 2015;32(5):1919-25.
8. Camberos-Solis R, Jiménez-Cruz A, Bacardí-Gascón M, Culebras J. Long-term efficacy and safety of Roux-en-Y gastric bypass and gastric. Nutr Hosp 2010;25(6):964-70.
9. Walton J, O'Connor L, Flynn A. Cross-sectional association of dietary water intakes and sources, and adiposity: National Adult Nutrition Survey, the Republic of Ireland. European Journal of Nutrition 2019;58(3):1193-201. DOI: 10.1007/s00394-018-1635-z.
10. Daniels M, Popkin B. Impact of water intake on energy intake and weight status: a systematic review. Nutrition reviews 2010;68(9):505-21. DOI: 10.1111/j.1753-4887.2010.00311.x.
11. Popkin B, Armstrong L, Bray G, Caballero B, Frei B, Willet W. A new proposed guidance system for beverage consumption in the United States. Am J Clin Nutr 2006;83(3):529-42. DOI: 10.1093/ajcn.83.3.529.
12. Wong J, Ebbeling C, Robinson L, Feldman H, Ludwig D. Effects of advice to drink 8 cups of water per day in adolescents with overweight or obesity: a randomized clinical trial. JAMA Pediatr 2017;171(5):e170012. DOI: 10.1001/jamapediatrics.2017.0012.
13. Dennis E, Dengo A, Comber D, Flack K, Savla J, Devy K, et al. Water consumption increases weight loss during a hypocaloric diet intervention in middle-aged and older adults. Obesity 2010;18:300-7. DOI: 10.1038/oby.2009.235.
14. Bellisle F, Altenburg de Assis M, Fieux B, Preziosi P, Galan P, Guy-Grand B. Use of 'light' foods and drinks in French adults: biological, anthropometric and nutritional correlates. J Hum Nutr Diet 2001;14:191-206. DOI: 10.1046/j.1365-277X.2001.00289.x.
15. Williams CL, Strobino BA, Brotanek J. Weight control among obese adolescents: a pilot study. Int J Food Sci Nutr 2007;58:217-30. DOI: 10.1080/09637480701198083.
16. Husøy T, Mangschou B, Fotland T, Kolset SO, Nøtvik Jakobsen H, Tømmerberg I, Bergsten C, et al. Reducing added sugar intake in Norway by replacing sugar sweetened beverages with beverages containing intense sweeteners—a risk benefit assessment. Food Chem Toxicol 2008;46:3099-105. DOI: 10.1016/j.fct.2008.06.013.
17. Popkin B, Barclay D, Nielsen S. Water and food consumption patterns of U.S. adults from 1999 to 2001. Obes Res 2005;13:2146-52. DOI: 10.1038/oby.2005.266.
18. Tate DF, Lyons E, Stevens J, Erickson K, Polzien K, Diamond M, et al. Replacing caloric beverages with water or diet beverages for weight loss in adults: main results of the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial. Am J Clin Nutr 2012;95:555-563. DOI: 10.3945/ajcn.111.026278.
19. Boschmann M, Steiniger J, Hille U, et al. Water-induced thermogenesis. J Clin Endocrinol Metab 2003;88:6015-9. DOI: 10.1210/jc.2003-030780.
20. Berneis K, Ninnis R, Haussinger D, Keller U. Effects of hyper- and hypoosmolality on whole body protein and glucose kinetics in humans. Am J Physiol 1999;276:E188-95. DOI: 10.1152/ajpendo.1999.276.1.E188.
21. Keller U, Szinnai G, Bilz S, Berneis K. Effects of changes in hydration on protein, glucose and lipid metabolism in man: impact on health. Eur J Clin Nutr 2003;57(Suppl 2):S69-74. DOI: 10.1038/sj.ejcn.1601904.
22. Almiron-Roig E, Drewnowski A. Hunger, thirst, and energy intakes following consumption of caloric beverages. Physiol Behav 2003;79:767-73. DOI: 10.1016/S0031-9384(03)00212-9.
23. DellaValle DM, Roe LS, Rolls BJ. Does the consumption of caloric and non-caloric beverages with a meal affect energy intake? Appetite 2005;44:187-93. DOI: 10.1016/j.appet.2004.11.003.
24. Mattes RD. Dietary compensation by humans for supplemental energy provided as ethanol or carbohydrate in fluids. Physiol Behav 1996;59:179-87. DOI: 10.1016/0031-9384(95)02007-1.
25. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective observational analysis. Lancet 2001;357:505-8. DOI: 10.1016/S0140-6736(00)04041-1.
26. Stookey J, Constant F, Popkin B, Gardner C. Drinking water is associated with weight loss in overweight dieting women independent of diet and activity. Obesity 2008;16:2481-8. DOI: 10.1038/oby.2008.409.
27. Muckelbauer R, Sarganas G, Grüneis A, Müller-Nordhorn J. Association between water consumption and body weight outcomes: a systematic review. Am J Clin Nutr 2013;98:282-99. DOI: 10.3945/ajcn.112.055061.
28. Parretti H, Aveyard P, Blannin A, Clifford S, Coleman S, Roalfe A, et al. Efficacy of water preloading before main meals as a strategy for weight loss in primary care patients with obesity: RCT. Obesity 2015;23:1785-91. DOI: 10.1002/oby.21167.
29. Peters J, Beck J, Cardel M, Wyatt H, Foster G, Zhaoxing P, et al. The effects of water and non-nutritive sweetened beverages on weight loss and weight maintenance: a randomized clinical trial. Obesity 2016;24:297-304. DOI: 10.1002/oby.21327.
30. Madjd A, Taylor M, Delavari A, Malekzadeh R, McDonald I, Farshchi H. Effects on weight loss in adults of replacing diet beverages with water during a hypoenergetic diet: a randomized, 24-wk clinical trial. Am J Clin Nutr 2015;102:1305-12. DOI: 10.3945/ajcn.115.109397.
31. Madjd A, Taylor M, Delavari A, Malekzadeh R, McDonald I, Farshchi H. Beneficial effects of replacing diet beverages with water on type 2 diabetic obese women following a hypo-energetic diet: A randomized, 24-week clinical trial. Diabetes Obes Metab 2016. DOI: 10.1111/dom.12793.

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Revisión

Selenium concentration, dietary intake and risk of hepatocellular carcinoma – A systematic review with meta-analysis

Concentración de selenio, ingesta dietética y riesgo de carcinoma hepatocelular: revisión sistemática con metaanálisis

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Abstract

Aim: this study was performed to investigate the association between selenium concentrations, dietary intake, and the risk of hepatocellular carcinoma (HCC).

Methods: we identified eligible studies in PubMed and EMBASE databases, in addition to the reference lists of original studies and review articles on this topic, up to 1 Feb 2019. A summary of standardized mean differences (SMD) with 95% confidence intervals (CI) was calculated using a random-effects model. Heterogeneity between studies was assessed using Cochran Q and I^2 statistics.

Results: finally, a meta-analysis showed that dietary intake of selenium and tissue selenium concentration were not associated with HCC risk (dietary SMD = -0.11, 95% CI: -0.26 to 0.03; tissue SMD = -0.12, 95% CI: -0.56 to 0.33). However, samples from toenail, whole blood, and serum all showed an inverse association with HCC risk (toenail SMD = -0.53, 95% CI: -0.72 to -0.35; whole blood SMD = -2.21, 95% CI: -2.67 to -1.76; tissue SMD = -1.26, 95% CI: -1.71 to -0.81). Dose-response data from few studies showed that an extra increase in serum selenium was dramatically related with a lower risk of HCC (adjusted p-trend < 0.05). This study showed that selenium concentration in toenail, whole blood and serum was inversely associated with HCC risk.

Conclusion: increased concentration in serum selenium was related to a lower risk of HCC. However, these results based on dietary intake and tissue samples, which included few studies, did not reach statistical significance.

Key words:

Selenium. Selenoprotein. Hepatocellular carcinoma. Morbidity. Meta-analysis.

Resumen

Objetivo: este estudio se realizó para investigar la asociación entre las concentraciones de selenio, la ingesta dietética y el riesgo de carcinoma hepatocelular (CHC).

Métodos: identificamos estudios elegibles en las bases de datos PubMed y EMBASE, además de las listas de referencias de los estudios originales y artículos de revisión sobre este tema hasta el 1 de febrero de 2019. Se realizó un resumen de las diferencias medias estandarizadas (SMD) con intervalos de confianza (CI) del 95% utilizando un modelo de efectos aleatorios. La heterogeneidad entre estudios se evaluó utilizando las estadísticas de Cochran Q e I^2.

Resultados: por último, el metaanálisis mostró que la concentración de selenio en la ingesta dietética y de selenio tisular no estaban asociadas al riesgo de HCC (SMD dietética -0,11, IC 95%: -0,26 a 0,03; SMD tisular -0,12, IC 95%: -0,56 a 0,33). Sin embargo, las muestras de uña del pie, sangre entera y suero mostraron todas ellas una asociación inversa con el riesgo de CHC (SMD ungueal -0.53, IC 95%: -0.72 a -0.35; SMD de sangre entera -2.21, IC 95%: -2.67 a -1.76; SMD tisular -1.26, IC 95%: -1.71 a -0.81). Los datos de dosis-respuesta de pocos estudios mostraron que los incrementos del selenio sérico se relacionaban fuertemente con un menor riesgo de CHC (tendencia de p ajustada < 0.05). Este estudio demostró que la concentración de selenio en las uñas del pie, en sangre entera y en suero se asocian inversamente al riesgo de CHC.

Conclusión: el aumento de la concentración de selenio sérico se relacionó con menor riesgo de CHC. Sin embargo, los resultados de la ingesta dietética y los tejidos, que incluían pocos estudios, no alcanzaron la significación estadística.

Palabras clave:

Selenio. Selenoproteína. Carcinoma hepatocelular. Morbilidad. Metaanálisis.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is a major malignant tumor around the world, and particularly in China and Southeast Asia, with a poor 5-year survival rate. An estimated 782,500 new cases and 745,500 cancer-related deaths emerge every year, ranking HCC as the sixth cancer with more morbidity and the second in terms of cancer mortality (1). Hepatitis B virus (HBV) infection is the most important risk factor for HCC in Asia (2). The only one exception in Asia is Japan, where the prevalence of HCC has been closely associated with hepatitis C virus (HCV) infection (3). In western countries, however, HCV infection has been observed in about 60% of patients diagnosed with HCC (4,5).

Accompanied by infection with HBV or HCV, liver cirrhosis is also one of the most important risk factors in the development of HCC. Moreover, there are other confirmed risk factors, among which alcohol and aflatoxin stand out as most important (6,7). Food intake is also one of the most intensively studied risk factors closely related to HCC, most particularly coffee and tea (8), iron (9), red and white meats (10), some types of fat, and vitamin D (11). However, the results regarding the association of other dietary components with the risk of HCC are inconsistent.

Selenium has been shown to play important roles in multiple metabolic processes in the liver. Evidence from experimental studies suggested that dietary selenium intake might interact with selenoproteins and angiogenic cytokines in the hepatocarcinogenesis process, and high selenium concentrations could inhibit cancer progression (12-14). Low selenium intake was thought to increase susceptibility to HBV and HCV infection (15,16). Selenium deficiency has been observed in patients with liver cirrhosis and correlates well with severity of cirrhosis. This may create a vicious circle as deterioration in the homeostasis of selenium by severe cirrhosis may lead to greater oxidative stress and inflammation, which will aggravate the progression of cirrhosis. Selenium supplementation can suppress the progression of cirrhosis and the development of complications (17,18).

A previous meta-analysis including nine studies, performed by Zhang et al., suggested an inverse correlation between selenium concentration and risk of HCC (19). This study was limited by a small sample size and confined to two sample sources (blood and toenail). Recently, a large nested case-control study covering 132,765 people in China showed that no statistically significant association could be found between dietary intake of selenium and HCC risk (20). Furthermore, two studies concerning selenium concentration in HCC tissues showed almost the same concentration among tumor tissues, nontumor tissues, and normal livers (21,22). Therefore, we performed this update meta-analysis and dose-response review of all available evidence from observational studies following the PRISMA guidelines to clarify the association between selenium concentrations, dietary intake, and risk of HCC.

METHODS

DATA SOURCES AND SEARCH STRATEGY

Two of the authors (Y.G. and H.Z.) independently performed a literature search using PubMed and EMBASE databases for articles up to 1 Feb 2019. We searched the studies with the following text words and/or Medical Subject Heading (MeSH) terms: ("selenium") AND ("liver neoplasms" [MeSH] or "hepatocellular carcinoma" or "liver cancer").

STUDY SELECTION

We included studies that met all the following criteria: a) published as an original article; b) used a case-control, cross-sectional, nested case-control or cohort study design; c) explored selenium concentration in various samples including serum, whole blood, toenail, hair, tissue, and diet intake; d) a study endpoint was the morbidity or mortality of HCC; and e) the number of cases and controls, mean and standard deviation for both groups, estimated odds ratio (OR) or hazard rate (HR) with corresponding 95% confidence intervals (CIs) for cases versus controls, or the gradient concentrations versus lowest concentration were reported. Two authors (Y.G. and H.Z.) independently evaluated all the studies retrieved from the databases. We did not contact the authors for detailed information about the primary studies.

DATA EXTRACTION AND QUALITY ASSESSMENT

Three authors (Z.M., Z.Z. and B.H.) independently evaluated all the studies retrieved according to the prespecified selection criteria. Any discrepancies between reviewers were addressed by a joint reevaluation of the original article. The following information from each study was extracted using a standardized data collection form: the first author's last name, year of publication, geographic location, study design, number of cases, number of controls, quality of each study, types of samples, mean and standard deviation of selenium concentrations, the effect estimates with 95% CIs for cases versus controls, or the gradient concentrations versus lowest concentration. When crude or adjusted estimates were both presented in an individual study, we extracted the estimate adjusted for more confounding factors.

The quality of each study was evaluated independently by three reviewers using the Newcastle-Ottawa Scale (NOS). The NOS consists of three parameters of quality: selection, comparability, and outcome (cohort studies) or exposure (case-control studies). The NOS assigns a maximum of four points for selection, a maximum of two points for comparability, and a maximum of three points for exposure or outcome. Any discrepancies between reviewers were addressed by a joint reevaluation of the original article.

STATISTICAL ANALYSIS

We used the STATA 14.0 software (StataCorp, College Station, TX, USA) to conduct the meta-analysis of standardized mean differences (SMD) with 95% confidence intervals (CI), and to calculate the Cochran Q and I^2 statistics for heterogeneity across the studies. SMD was tested with an α level of 0.05, whereas an α level of 0.10 was used to examine Cochran's Q, as suggested by Higgins et al. To investigate the sources of heterogeneity across these studies, we carried out heterogeneity tests and sensitivity analyses. In heterogeneity tests, we used the Cochran Q and I^2 statistics (23), which were used to test the differences obtained between studies due to chance. For the Q statistic, a p-value of less than 0.10 was considered representative of statistically significant heterogeneity. The I^2 statistic is the proportion of total variation contributed by between-study variation. It has been suggested that I^2 values of 25%, 50%, and 75% be assigned to low, moderate, and high heterogeneity, respectively (24). We conducted a sensitivity analysis to estimate the influence of each individual study on the summary results by repeating the random-effects meta-analysis after omitting one study at a time. We evaluated the role of several potential sources of heterogeneity by subgroup analyses according to study design, geographical locations, study quality, and sample sizes.

Dose-response data were reported in five studies (20,25-28). Data from different sources of selenium concentration varied from each other, and the baseline concentrations of selenium in the serum differed a lot between the studies performed by Yuan (26), by Hughes (25), and by Yu (28), so they could not be pooled together in one dose-response meta-analysis, and we could only report the dose-response data from a single study.

Funnel plots and Egger's test were performed to test for evidence of publication bias (29). In the presence of a publication bias, we used the "trim and fill" method to correct such bias (30).

RESULTS

DATA SOURCES AND SEARCH STRATEGY

The detailed steps of our literature search are presented in figure 1. In brief, a total of 296 citations were obtained for a review of their titles and abstracts. Of these 296 citations, 279 were not relevant. The full texts of the remaining 17 studies were retrieved for review. Two studies were retrieved by hand searching the references of included studies. These two studies were both indexed in ResearchGate, not in PubMed or Embase. Meanwhile, one study was excluded because of being reported as an abstract without any detailed data (31).

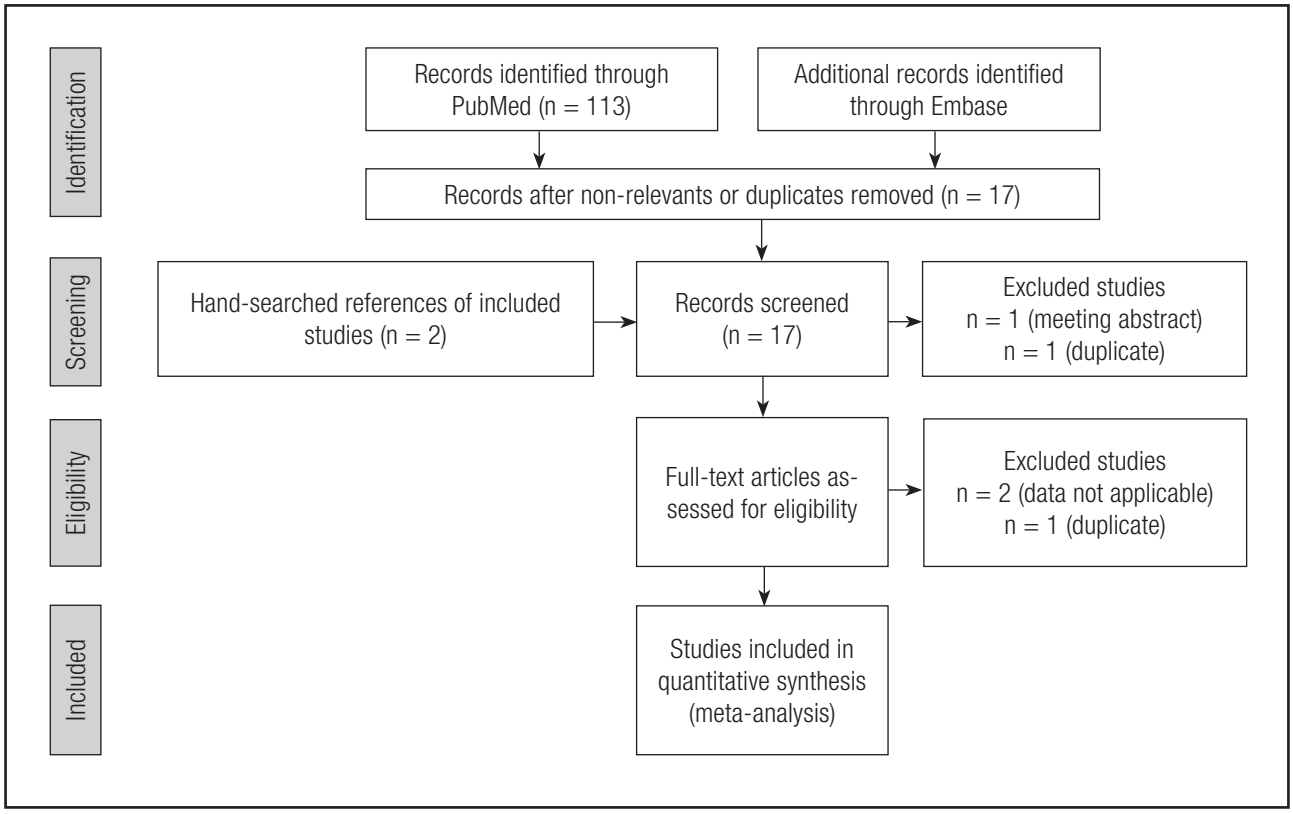

Figure 1.
Flow chart showing the selection process of the studies included in the meta-analysis.

One article (32) was duplicate with its updated one (33), and we included the latter. Two studies investigating tissue samples were excluded (22,34) due to lack of detailed data. Finally, 14 studies were included in the final meta-analysis (Fig. 1).

STUDY CHARACTERISTICS

Fourteen articles that met our inclusion criteria for this meta-analysis were published between 1994 and 2017. There were three nested case-control studies (20,25,27) and eleven retrospective case-control studies (21,26,28,33,35-41). Nine articles described the association between serum selenium concentration and HCC risk (25,26,28,33,36,37,39-41), two described the association between whole blood selenium concentration and HCC risk (35,38), one reported the association between tissue selenium concentration and HCC risk (21), one reported the association between toenail selenium concentration and HCC risk (27), and the last one dealt with dietary intake selenium concentration (20). The average score for the quality assessment of included studies was 7.5. Dose-response data with the graded concentrations versus the lowest concentration were presented in five studies (20,25-28) (Table I).

META-ANALYSIS

A well-designed case-control study conducted by Yuan et al. showed that no independent effect of serum selenium concen-

Table I. Characteristics of the 14 studies included

Author (Refs.)	Year/ Location	Study design	Cases (n)	Controls (n)	Sample source	Selenium level (X ± SD)		NOS
						Case	Control	
Ma (20)	2017/China	NCC (women) NCC (men)	192 344	72,593 59,636	Dietary μg/d	40.8 ± 14.5 49.1 ± 17.2	44.2 ± 17.3 50.0 ± 19.0	9
Tashiro (21)	2003/Japan	CC	23	123	Tissues μg/g	1.51 ± 1.26	1.66 ± 1.26	7
Sakoda (27)	2005/China	NCC	166	394	Toenail ppm	3.1 (1.5-3.6) 2.55 ± 0.78 *	3.5 (1.7-4.4) 3.05 ± 1.0 *	8
Bettinger (35)	2013/Germany	CC	10	10	Whole blood μg/L	84.7 ± 16.4	117.5 ± 15.7	6
Wang (38)	2002/China	CC	51	50	Whole blood μg/L	180 ± 20	280 ± 60	7
Hughes (25)	2016/Europe	NCC	106	106	Serum μg/L	71.3 (41.3-105.9) 73.6 ± 19.64 †	85.2 (55.3-117.5) 86.4 ± 18.91 †	9
Kim (36)	2012/Korea	CC	30	120	Serum ug/L	67.47 ± 14.30	108.38 ± 29.5	7
Madiha (41)	2010/Egypt	CC	20	10	Serum μg/L	47.3 ± 10.5	67.3 ± 7.55	7
Yuan (26)	2006/China	CC	213	1087	Serum μg/dL	10.9 (p = 0.58) ‡	10.9	9
Lin (37)	2006/China	CC	18	50	Serum μg/L	108.5 ± 21.8	129.0 ± 21.5	7
Yu (28)	1999/China	CC	69	138	Serum μg/L	131.6 ± 30.9	150.2 ± 35.2	8
Lin (39)	1998/China	CC	51	19	Serum μg/L	106.0 ± 17.7	126.4 ± 10.1	7
Buljevac (40)	1996/Croatia	CC	10	248	Serum g/L	42.00 ± 10.59	66.79 ± 9.13	7
Casaril (33)	1994/Italy	CC	23	19	Serum ng/mL	78.35 ± 19.78	96.09 ± 22.03	7

*NOS: Newcastle-Ottawa Scale; CC: case-control study; NCC: nested case-control study; SD: standard deviation. * SD was calculated from the interquartile range between the parentheses; when sample sizes are large and the distribution of the outcome is similar to the normal distribution, the width of the interquartile range is approximately 1.35 standard deviations; † SD was calculated from the 5th and 95th percentiles between the parentheses; ‡ Only the mean and p-value were available.*

tration on HCC risk was observed. However, only mean and p-value was provided, without standard deviation. A meta-analysis of 13 studies in a random-effects model found that the selenium concentration of all samples was inversely associated with the risk of HCC (standardized mean difference (SMD) = -1.02, 95% CI: -1.34 to -0.70; test for heterogeneity $p < 0.001$, $I^2 = 94.0\%$) (Fig. 2A). Heterogeneity across studies was extremely high. A subgroup analysis of different samples showed that dietary intake selenium and tissue selenium concentrations were not associated with HCC risk (dietary intake SMD = -0.11, 95% CI: -0.26 to 0.03; tissue SMD = -0.12, 95% CI: -0.56 to 0.33). However, samples from toenail, whole blood and serum all showed an inverse association with HCC risk (toenail SMD = -0.53, 95% CI: -0.72 to -0.35; whole blood SMD = -2.21, 95% CI: -2.67 to -1.76; tissue SMD = -1.26, 95% CI: -1.71 to -0.81) (Fig. 2).

In a sensitivity analysis, the overall homogeneity and effect size was calculated by removing one study at a time. The direction of the effect did not change when any study was excluded, supporting the stability of low selenium concentration in all samples related to an increase in HCC risk (Fig. 2B).

We subsequently conducted a subgroup systematic review and meta-analysis according to geographical location, study quality, study design, and sample size. A statistically significant relation was observed in various regions – Asia, -0.77 (-1.11, -0.43); Europe, -1.52 (-2.52, -0.52); Africa, -2.07 (-3.01, -1.14). When assessing study quality, the inverse association was observed in both high- and low-quality groups – NOS ≥ 8, -0.38 (-0.61, -0.14); NOS < 8, -1.49 (-2.06, -0.93). As regards study design, both nested case-control studies and case-control studies showed a positive result – NCC, -0.34 (-0.60, -0.08); CC, -1.39 (-1.91, -0.86). Sample size for cases ranged from 10 to 536, and this might be an important confounder for risk of HCC. When we confined the meta-analysis to sample sizes with a cut-off point of 50, a positive association was also found in both groups – more than 50, -0.71 (-1.06, -0.37); less than 50, -1.42 (-2.10, -0.74) (Table II).

PUBLICATION BIAS

The shape of the funnel plots for studies examining the association of selenium concentration, dietary intake, and HCC risk seemed asymmetrical [Begg's test (p = 0.155), Egger's test (p = 0.022)], indicating that there might be a potential publication bias (Fig. 2C). However, a trim-and-fill analysis with a linear estimator and random-effects model showed no trimming and unchanged data.

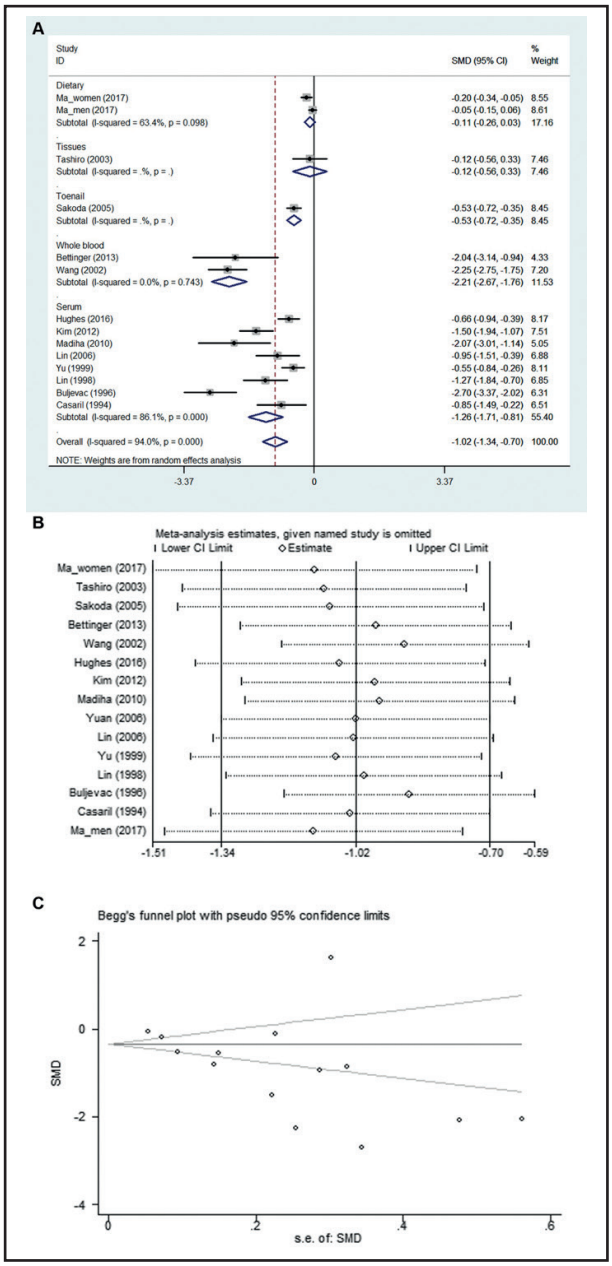

Figure 2.
A. Forest plot examining the association of selenium levels in various samples and hepatocellular carcinoma risk. SMD: standardized mean deviation. B. Sensitivity analysis by removing one study at a time and calculating the overall homogeneity and effect size. C. Funnel plots examining the association of selenium levels in various samples and hepatocellular carcinoma risk. Begg's test (p = 0.155), Egger's test (p = 0.022). SMD: standardized mean deviation.

DOSE-RESPONSE DATA

Dose-response data were presented in five studies. The study by Ma et al. showed that dietary intake selenium was not associated with HCC risk. The study by Sakoda et al. revealed that toenail selenium was lower in HCC cases than in controls (p = 0.03); however, getting to a higher quartile of toenail selenium was not compatible with a significant trend in risk (p-trend = 0.06). Yuan's study showed a negative result (p-trend = 0.24, adjusted p-trend = 0.27). Hughes' study suggested that an extra increase in serum selenium (by 20 µg/L) was dramatically related to a lower risk of HCC (adjusted p-trend = 0.016, OR = 0.41, 95% CI: 0.23 to 0.72), whereas Yu's study showed that an increase in serum sele-

Table II. Subgroup analysis of selenium levels in various samples and hepatocellular carcinoma risk

Subgroup	References	SMD (95% CI)	Tests for heterogeneity	
			I^2 (%)	p-value
Geographical region				
Asia	20, 21, 27, 28, 36-39	-0.77 (-1.11, -0.43)	94.2	< 0.001
Europe	25, 33, 35, 40	-1.52 (-2.52, -0.52)	91.1	< 0.001
Africa	41	-2.07 (-3.01, -1.14)	NA	NA
Study quality				
NOS ≥ 8	20, 25, 27, 28	-0.38 (-0.61, -0.14)	88.9	< 0.001
NOS < 8	21, 33, 35-41	-1.49 (-2.06, -0.93)	87.8	< 0.001
Study design				
NCC	20, 25, 27	-0.34 (-0.60, -0.08)	90.4	< 0.001
CC	21, 28, 33, 35-41	-1.39 (-1.91, -0.86)	89.5	< 0.001
Sample size				
More than 50	20, 25, 27, 28, 38, 39	-0.71 (-1.06, -0.37)	94.5	< 0.001
Less than 50	21, 33, 35-37, 40, 41	-1.42 (-2.10, -0.74)	88.2	< 0.001
Overall	20, 21, 25, 27, 28, 33, 35-41	-1.02 (-1.34, -0.70)	94.0	< 0.001

nium by 12 µg/L was significantly related with a lower risk of HCC (adjusted p-trend = 0.036, OR = 0.937, 95% CI: 0.882 to 0.996).

DISCUSSION

In this collaborative meta-analysis, the results showed that samples obtained from toenail, whole blood, and serum were inversely associated with HCC risk (toenail SMD = -0.53, 95% CI: -0.72 to -0.35; whole blood SMD = -2.21, 95% CI: -2.67 to -1.76; tissue SMD = -1.26, 95% CI: -1.71 to -0.81); however, the results from the analysis of dietary intake and tissues, which included few studies, did not reach statistical significance. Obvious heterogeneity was observed when all studies were included, but the omission of each one study made little or no difference. Dose-response data including few studies revealed that an increased concentration in serum selenium was related with a lower risk of HCC (Hughes' study, by 20 µg/L, OR = 0.41; Yu's study, per 12 µg/L, OR = 0.937); however, no positive trend was observed in samples from dietary intake and toenail. Some marginal publication bias might have existed in this meta-analysis [Begg's test (p = 0.155), Egger's test (p = 0.022)], but the trim-and-fill analysis showed that the results remained unchanged.

It was surprising that the dietary intake of selenium was not associated with risk for HCC in the only study included; however, several confounding factors should be considered in the interpretation of Ma's study. First, food and trace element intakes were complicated, and they interacted with each other. It is impossible to adjust for all nutrition factors and trace elements in individual studies. Second, the commonly used Food Frequency Questionnaire (FFQ) was not accurate in assessing the actual amount of dietary intake, and it might be easily interfered with by recall bias. Third, Ma's study did not calculate the daily intake of any potential multi-mineral supplement (such as Centrum® produced by Pfizer), which represented a relevant source of the trace element.

The liver is commonly known as an important organ in the metabolism of trace elements. However, selenium concentration was shown to be almost the same among tumor tissues, non-tumor tissues, and normal livers. The result might not be robust and stable. First, important confounding factors (dietary intake, HBV and/or HCV infection, cirrhosis, diabetes status, and BMI) were not controlled for between case and control groups. Second, sample size was too small, and further study was still needed to address this problem.

High selenium concentrations in toenail, whole blood, and serum samples were related to a lower risk of HCC, and the protective effect seemed to be strengthened by increasing levels in serum concentration. The biological functions of selenium are mainly mediated by selenium-containing proteins (selenoproteins), which contain at least one selenocysteine (Sec). Although the identification and functions of many selenoproteins remain unknown, there has been significant progress in characterizing some selenoproteins and in understanding their physiological functions. Single-nucleotide polymorphisms (SNPs) in selenoprotein genes can alter the concentration and function of selenoproteins. SNPs in selenoprotein genes have been reported to be associated with risk for various cancers. Polymorphisms of the glutathione peroxidase 1 (GPx-1) gene, which codes for a selenium-containing protein, have been implicated in the development of head and neck, lung, and breast cancers (42,43). Polymorphisms in the GPx2, GPx4 and selenoprotein P (SePP) genes have been found to be associated with colorectal cancer (44,45), whereas 15 kDa selenoprotein (Sep15) gene polymorphisms may increase lung cancer risk in smoking individuals (46). Selenoprotein S (SEPS) polymorphisms might influence susceptibility to gastric cancer (47). Polymorphisms in the genes coding for SEPP and mitochondrial superoxide dismutase have synergic effects in the development of prostate cancer (48). A novel study investigating the underlying pathway showed that decreased selenium concentrations resulted in accumulation of lipid peroxides. This led to enhanced activator protein 1 (AP-1) activation, and consequently to elevated expression of vascular endothelial growth factor (VEGF) and interleukin 8 (IL-8), which accelerated the growth of HCC (49).

Based on a compelling preclinical rationale, selenium supplementation might be considered as a promising treatment for cancer patients with low selenium concentrations. A multicenter, double-blind cancer prevention trial (Nutritional Prevention of Cancer Study Group, NPC trial) showed that selenium treatment (200 micrograms daily) significantly reduced total cancer incidence and the incidences of lung, colorectal, and prostate cancers (50). A follow-up study continued to show a significant protective effect on the overall incidence of prostate cancer; however, the effect was restricted to those with low serum levels of selenium (51). In another randomized, placebo-controlled trial, selenium supplementation (200 μg daily) did not prevent colorectal adenomas. However, the recurrence of adenoma can be reduced by 18% with selenium supplementation (52). The above results were inconsistent with two novel phase-III trials (ECOG 5597 and the SELECT study). Selenium supplementation (200 μg daily) in patients with resected stage-I non-small-cell lung carcinoma had no benefit over placebo in the prevention of second primary tumors (ECOG 5597) (53). Similarly, neither selenium (200 micrograms daily from L-selenomethionine) nor vitamin E, alone or in combination, could reduce the risk of prostate cancer (54). Scientists and clinicians should reconfirm the role of selenium supplementation in more individualized trials before new public health recommendations can be made.

There are several strengths to the present study – a) only nine studies covering toenail and blood samples were included in previous meta-analyses. The present study included 14 studies after a comprehensive and systematic search of the literature, which covered selenium concentrations in dietary intake, tissue, toenail, and blood samples. With the available evidence and an enlarged number of studies to date, we have enhanced statistical power to detect any associations between selenium concentration and the risk of HCC; b) although few studies were included, we presented the dose-response data showing that an increase in serum selenium concentrations was significantly related with lower risk of HCC (3). The analysis process was normative. We performed sensitivity analyses and subgroup analyses to investigate heterogeneity across studies, and a further trim-and-fill analysis to verify the results concerning publication bias.

This meta-analysis has limitations that affect interpretation of the true results. First, all studies in this meta-analysis used a nested case-control study or case-control study design, which is more susceptible to recall and selection biases. Second, there is substantial heterogeneity across studies. Heterogeneity was likely due to unmeasured confounding factors and to misclassified exposure to selenium and/or selenium species, including HBV and HCV infection, cirrhosis, alcohol consumption, smoking, DM, and BMI. Individual studies were adjusted for these potential confounders in an inconsistent way. Third, we did not have sufficient information to perform a subgroup analysis, which might affect the stability of the results due to heterogeneity across studies. Dose-response data were reported in only five studies. Data from different sources of selenium concentration varied from each other, so they could not be present without being pooled together in one dose-response meta-analysis.

CONCLUSIONS

Our meta-analysis of observational studies provided evidence that selenium concentration in toenail, whole blood, and serum was inversely associated with HCC risk. Increasing concentrations in serum selenium were related with a lower risk of HCC. However, the results obtained for dietary intake and tissues, which included few studies, did not reach statistical significance. Given the small number of studies included in this meta-analysis, its limited details, and the non-randomized or controlled study designs, further prospective cohort studies with a larger sample size and a more accurate assessment of baseline characteristics, in addition to being well-controlled for confounders, are needed to confirm the effect of selenium concentration on HCC risk.

REFERENCES

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015;2:87-108.
2. Beasley RP. Hepatitis B virus. The major etiology of hepatocellular carcinoma. Cancer 1988;10:1942-56.
3. Shiratori Y, Shiina S, Imamura M, Kato N, Kanai F, Okudaira T, et al. Characteristic difference of hepatocellular carcinoma between hepatitis B- and C- viral infection in Japan. Hepatology 1995;4(Pt 1):1027-33.
4. Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular carcinoma incidence, mortality, and survival trends in the United States from 1975 to 2005. J Clin Oncol 2009;9:1485-91.
5. El-Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterology 2007;7:2557-76.
6. Purohit V, Rapaka R, Kwon OS, Song BJ. Roles of alcohol and tobacco exposure in the development of hepatocellular carcinoma. Life Sci 2013;1:3-9.
7. Magnussen A, Parsi MA. Aflatoxins, hepatocellular carcinoma and public health. World J Gastroenterol 2013;10:1508-12.
8. Montella M, Polesel J, La Vecchia C, Dal Maso L, Crispo A, Crovatto M, et al. Coffee and tea consumption and risk of hepatocellular carcinoma in Italy. Int J Cancer 2007;7:1555-9.
9. Kew MC. Hepatic iron overload and hepatocellular carcinoma. Liver Cancer 2014;1:31-40.
10. Fedirko V, Trichopolou A, Bamia C, Duarte-Salles T, Trepo E, Aleksandrova K, et al. Consumption of fish and meats and risk of hepatocellular carcinoma: the European Prospective Investigation into Cancer and Nutrition (EPIC). Ann Oncol 2013;8:2166-73.
11. Fedirko V, Duarte-Salles T, Bamia C, Trichopoulou A, Aleksandrova K, Trichopoulos D, et al. Pre-diagnostic circulating vitamin D levels and risk of hepatocellular carcinoma in European populations: A nested case-control study. Hepatology 2014;60:1222-30.
12. Kasaikina MV, Turanov AA, Avanesov A, Schweizer U, Seeher S, Bronson RT, et al. Contrasting roles of dietary selenium and selenoproteins in chemically induced hepatocarcinogenesis. Carcinogenesis 2013;5:1089-95.
13. Moustafa ME, Carlson BA, Anver MR, Bobe G, Zhong N, Ward JM, et al. Selenium and selenoprotein deficiencies induce widespread pyogranuloma formation in mice, while high levels of dietary selenium decrease liver tumor size driven by TGFalpha. Plos One 2013;2:e57389.
14. Liu JG, Zhao HJ, Liu YJ, Liu YW, Wang XL. Effect of two selenium sources on hepatocarcinogenesis and several angiogenic cytokines in diethylnitrosamine-induced hepatocarcinoma rats. J Trace Elem Med Biol 2012;4:255-61.
15. Rayman MP. Selenoproteins and human health: insights from epidemiological data. Biochim Biophys Acta 2009;11:1533-40.
16. Bellinger FP, Raman AV, Reeves MA, Berry MJ. Regulation and function of selenoproteins in human disease. Biochem J 2009;1:11-22.
17. Nangliya V, Sharma A, Yadav D, Sunder S, Nijhawan S, Mishra S. Study of trace elements in liver cirrhosis patients and their role in prognosis of disease. Biol Trace Elem Res 2015;1:35-40.
18. Burk RF, Hill KE, Motley AK, Byrne DW, Norsworthy BK. Selenium deficiency occurs in some patients with moderate-to-severe cirrhosis and can be corrected

by administration of selenate but not selenomethionine: a randomized controlled trial. Am J Clin Nutr 2015;5:1126-33.
19. Zhang Z, Bi M, Liu Q, Yang J, Xu S. Meta-analysis of the correlation between selenium and incidence of hepatocellular carcinoma. Oncotarget 2016;47:77110-16.
20. Ma X, Yang Y, Li HL, Zheng W, Gao J, Zhang W, et al. Dietary trace element intake and liver cancer risk: Results from two population-based cohorts in China. Int J Cancer 2017;5:1050-9.
21. Tashiro H, Kawamoto T, Okubo T, Koide O. Variation in the distribution of trace elements in hepatoma. Biol Trace Elem Res 2003;1:49-63.
22. Miyata S. Trace elements in hepatocellular carcinoma--comparison between hepatoma tissue and non-hepatoma liver tissue. Nihon Shokakibyo Gakkai Zasshi 1986;9:2091.
23. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;11:1539-58.
24. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;7414:557-60.
25. Hughes DJ, Duarte-Salles T, Hybsier S, Trichopoulou A, Stepien M, Aleksandrova K, et al. Prediagnostic selenium status and hepatobiliary cancer risk in the European Prospective Investigation into Cancer and Nutrition cohort. Am J Clin Nutr 2016;2:406-14.
26. Yuan JM, Gao YT, Ong CN, Ross RK, Yu MC. Prediagnostic level of serum retinol in relation to reduced risk of hepatocellular carcinoma. J Natl Cancer Inst 2006;7:482-90.
27. Sakoda LC, Graubard BI, Evans AA, et al. Toenail selenium and risk of hepatocellular carcinoma mortality in Haimen City, China. Int J Cancer 2005;4:618-24.
28. Yu MW, Horng IS, Hsu KH, Chiang YC, Liaw YF, Chen CJ. Plasma selenium levels and risk of hepatocellular carcinoma among men with chronic hepatitis virus infection. Am J Epidemiol 1999;4:367-74.
29. Sterne JA, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. J Clin Epidemiol 2001;10:1046-55.
30. Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000;2:455-63.
31. Yang DH, Liu WW, Yuan AL. Changes in blood selenium level and glutathione peroxidase activity and their clinical significance in primary liver cancer and benign liver diseases. Zhonghua Nei Ke Za Zhi 1988;10:612-4.
32. Corrocher R, Casaril M, Bellisola G, Gabrielli G, Hulpe M, Garofoli E, et al. Reduction of liver glutathione peroxidase activity and deficiency of serum selenium in patients with hepatocellular carcinoma. Tumori 1986;6:617-9.
33. Casaril M, Corso F, Bassi A, Capra F, Gabrielli GB, Stanzial AM, et al. Decreased activity of scavenger enzymes in human hepatocellular carcinoma, but not in liver metastases. Int J Clin Lab Res 1994;2:94-7.
34. Okuno T, Shimamura Y, Mizuno M, Miyata J, Miyake T, Itokawa Y, et al. Trace elements in hepatoma tissue. Trace Elements Med. 1988.
35. Bettinger D, Schultheiss M, Hennecke N, Panther E, Knüppel E, Blum HE, et al. Selenium levels in patients with hepatitis C virus-related chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma: a pilot study. Hepatology 2013;6:2543-4.
36. Kim IW, Bae SM, Kim YW, Liu HB, Bae SH, Choi JY, et al. Serum selenium levels in Korean hepatoma patients. Biol Trace Elem Res 2012;1:25-31.
37. Lin CC, Huang JF, Tsai LY, Huang YL. Selenium, iron, copper, and zinc levels and copper-to-zinc ratios in serum of patients at different stages of viral hepatic diseases. Biol Trace Elem Res 2006;1:15-24.
38. Wang CT, Chang WT, Pan TM, Wang RT. Blood concentrations of selenium, zinc, iron, copper and calcium in patients with hepatocellular carcinoma. Clin Chem Lab Med 2002;11:1118-22.
39. Lin TH, Tseng WC, Cheng SY. Direct determination of selenium in human blood plasma and seminal plasma by graphite furnace atomic absorption spectrophotometry and clinical application. Biol Trace Elem Res 1998;1-3: 133-49.
40. Buljevac M, Romic Z, Vucelic B, Banic M, Krznaric Z, Plesko S. Serum selenium concentration in patients with liver cirrhosis and hepatocellular carcinoma. Acta Med Croatica 1996;1:11-4.
41. Madiha AE, Wafaa ME, Radwa SS, Naglaa A, Mervat G. Serum levels of selenium, zinc, copper and iron in patients with post viral hepatitis liver cirrhosis and hepatocellular carsinoma. Al-Azhar Assiut Medical Journal 2010; 8.
42. Hu Y, Benya RV, Carroll RE, Diamond AM. Allelic loss of the gene for the GPX1 selenium-containing protein is a common event in cancer. J Nutr 2005;12(Suppl):3021S-4S.
43. Hu YJ, Diamond AM. Role of glutathione peroxidase 1 in breast cancer: loss of heterozygosity and allelic differences in the response to selenium. Cancer Res 2003;12:3347-51.
44. Bermano G, Pagmantidis V, Holloway N, Kadri S, Mowat NA, Shiel RS, et al. Evidence that a polymorphism within the 3'UTR of glutathione peroxidase 4 is functional and is associated with susceptibility to colorectal cancer. Genes Nutr 2007;2:225-32.
45. Al-Taie OH, Uceyler N, Eubner U, Jakob F, Mork H, Scheurlen M, et al. Expression profiling and genetic alterations of the selenoproteins GI-GPx and SePP in colorectal carcinogenesis. Nutr Cancer 2004;1:6-14.
46. Jablonska E, Gromadzinska J, Sobala W, Reszka E, Wasowicz W. Lung cancer risk associated with selenium status is modified in smoking individuals by Sep15 polymorphism. Eur J Nutr 2008;1:47-54.
47. Shibata T, Arisawa T, Tahara T, Ohkubo M, Yoshioka D, Maruyama N, et al. Selenoprotein S (SEPS1) gene -105G>A promoter polymorphism influences the susceptibility to gastric cancer in the Japanese population. BMC Gastroenterol 2009;9:2.
48. Cooper mL, Adami HO, Gronberg H, Wiklund F, Green FR, Rayman MP. Interaction between single nucleotide polymorphisms in selenoprotein P and mitochondrial superoxide dismutase determines prostate cancer risk. Cancer Res 2008;24:10171-7.
49. Rohr-Udilova N, Sieghart W, Eferl R, Stoiber D, Björkhem-Bergman L, Eriksson LC, et al. Antagonistic effects of selenium and lipid peroxides on growth control in early hepatocellular carcinoma. Hepatology 2012;4:1112-21.
50. Clark LC, Combs GJ, Turnbull BW, Slate EH, Chalker DK, Chow J, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. JAMA 1996;24:1957-63.
51. Duffield-Lillico AJ, Dalkin BL, Reid ME, Turnbull BW, Slate EH, Jacobs ET, et al. Selenium supplementation, baseline plasma selenium status and incidence of prostate cancer: an analysis of the complete treatment period of the Nutritional Prevention of Cancer Trial. Bju Int 2003;7:608-12.
52. Thompson PA, Ashbeck EL, Roe DJ, Fales L, Buckmeier J, Wang F, et al. Selenium Supplementation for Prevention of Colorectal Adenomas and Risk of Associated Type 2 Diabetes. J Natl Cancer Inst 2016:108.
53. Karp DD, Lee SJ, Keller SM, Wright GS, Aisner S, Belinsky SA, et al. Randomized, double-blind, placebo-controlled, phase III chemoprevention trial of selenium supplementation in patients with resected stage I non-small-cell lung cancer: ECOG 5597. J Clin Oncol 2013;33:4179-87.
54. Lippman SM, Goodman PJ, Klein EA, Parnes HL, Thompson IM Jr, Kristal AR, et al. Designing the Selenium and Vitamin E Cancer Prevention Trial (SELECT). J Natl Cancer Inst 2005;2:94-102.

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