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Nutrición Hospitalaria

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SOCIEDAD ESPAÑOLA DE NUTRICIÓN CLÍNICA Y METABOLISMO

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Economía de la salud, una disciplina necesaria en nutrición clínica

Health economics, a necessary discipline in clinical nutrition

La desnutrición relacionada con la enfermedad (DRE) constituye un verdadero reto para los sistemas sanitarios (1). Ello se debe a la elevada prevalencia que exhibe en los hospitales, a su impacto sobre el curso clínico de la enfermedad y la recuperación de los pacientes, así como a los elevados costes económicos que genera (1,2).

El estudio PREDyCES (2) caracterizó la prevalencia de DRE en nuestros hospitales y puso de manifiesto su notable impacto en el coste sanitario del proceso, siendo el escenario más desfavorable aquel en el que esta afecta a un paciente inicialmente normonutrido. El paciente quirúrgico no constituye una excepción, ni en términos de prevalencia, que estableció en el 17 % el estudio PREDyCES, pero que puede llegar al 65 % en los casos de cirugía del tracto digestivo superior, ni en términos económicos.

En las últimas décadas el gasto sanitario viene creciendo de forma progresiva (3), circunstancia que podría sustentarse en el aumento de la demanda sanitaria y el incremento de los costes de los elementos que conforman la oferta de procedimientos (4).

Actualmente, nos encontramos en un momento especialmente sensible en lo que a gasto sanitario se refiere. La pandemia de COVID-19 vapuleó, y continúa sacudiendo, terriblemente la estructura social, el modelo económico de nuestro país e indudablemente, las instituciones sanitarias. La elevada demanda asistencial generada en las distintas olas sufridas se ha traducido en un incremento notable de los costes sanitarios, siendo quizás más necesario que nunca que los profesionales sanitarios tomemos consciencia de la relevancia de incorporar a nuestras habilidades conceptos básicos, y no tan básicos, relacionados con la economía de la salud.

La economía de la salud se erige, por tanto, como una herramienta imprescindible para el adecuado análisis estratégico en materia de gestión de costes y asignación de recursos, tratando de ofrecer el mayor grado de bienestar posible a partir de los recursos disponibles (5). En los últimos años, los estudios de análisis de costes en el campo de la nutrición clínica están adquiriendo una importancia creciente, como demuestra la curva de la tasa de publicaciones de los últimos 20 años en bases de datos especializadas en ciencias de la salud como es el caso de PubMed.

En este número de *Nutrición Hospitalaria* se incluye la publicación de un estudio observacional y prospectivo centrado en pacientes quirúrgicos ingresados en el servicio de Cirugía Vascular de un hospital universitario de carácter terciario de nuestro país (6). Aunque el tamaño muestral no es elevado y solo utilizan una herramienta de cribado para la valoración nutricional, tiene interés al analizar los costes derivados de la DRE en dos escenarios clínicos bien definidos: el paciente que ingresa en situación de alto riesgo nutricional y aquel cuyo estado nutricional empeora durante la hospitalización. En este último grupo se observó un incremento estadísticamente significativo en las complicaciones hospitalarias, así como de todas las variables analizadas relacionadas con los costes (gasto antibiótico, farmacéutico y hospitalario total).

Resultados como estos nos brindan la oportunidad de identificar aquellos factores que favorecen el desarrollo o perpetúan la DRE en nuestros hospitales y, a partir de ellos, proponer acciones destinadas a mejorar la calidad del proceso integral de atención nutricional. Los puntos más importantes serían: implicar a los equipos directivos

en la lucha contra la DRE, proporcionar a los equipos sanitarios una formación continuada de calidad en nutrición clínica, implementar herramientas de cribado nutricional universales al ingreso, desarrollar protocolos de diagnóstico y tratamiento nutricional, así como mejorar la coordinación entre profesionales sanitarios, estandarizar un plan de monitorización y, finalmente, registrar adecuadamente la DRE, así como los procedimientos realizados que permita su correcta codificación y asignación de costes.

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ARÁN

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Trabajo Original

Paciente crítico

Factors associated with enteral nutrition and the incidence of gastrointestinal disorders in a cohort of critically ill adults

Factores asociados con la nutrición enteral y la incidencia de trastornos gastrointestinales en una cohorte de enfermos críticos adultos

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Abstract

Introduction: adults in intensive care commonly receive enteral nutrition (EN). Data describing the conditions associated with EN in critically ill patients are limited.

Objective: to describe the incidence of gastrointestinal disorders and to identify conditions associated with the use of EN.

Methods: a prospective cohort, single-center study of critically ill adults. The patients were followed daily for the first 10 days of hospitalization in the intensive care unit (ICU) or until ICU discharge or death. Clinical, nutritional variables and gastrointestinal disorders were compared between patients who did and did not receive EN. Univariate and multivariate regression identified the conditions associated with EN with the proposed variables.

Results: of the 157 included adults, 62 % received EN. The EN group had higher APACHE II (23.6 ± 7.6 vs. 15 ± 7.2, $p < 0.001$) and SOFA scores on the day of ICU admission [7 (5-10.5) vs. 4 (2-6); $p < 0.001$], and higher ICU mortality (32 % vs. 10 %, $p = 0.002$). Diarrhea and need for gastric decompression were more frequent in the EN group (39.7 % vs. 11.7 %, $p < 0.001$ and 34 % vs. 13.3 %, $p = 0.004$, respectively). The multivariate analysis showed that neurological deficit (OR: 16.7 [95 % CI: 5.9-46.9]; $p < 0.001$), previous enteral tube feeding (OR: 45.1 [95 % CI: 5.3-380]; $p < 0.001$), and SOFA score on the day of ICU admission (OR: 1.2 [95 % CI: 1.01-1.3]; $p = 0.03$) were associated with EN.

Conclusions: conditions related to the severity of critically ill patients, such as higher SOFA scores, greater neurological deficit, and prior enteral tube feeding, were more commonly associated with EN. Diarrhea and need for gastric decompression were more frequent in patients who received EN.

Keywords:

Critical care. Enteral nutrition. Gastrointestinal motility. Gastrointestinal intubation. Risk factors. Complications.

Resumen

Introducción: los adultos en cuidados intensivos comúnmente reciben nutrición enteral (NE). Los datos que describen las condiciones asociadas con la NE en pacientes críticos son limitados.

Objetivo: describir la incidencia de trastornos gastrointestinales e identificar las condiciones asociadas con el uso de la NE.

Métodos: estudio prospectivo de cohortes en un solo centro, de adultos en estado crítico. Se monitoreó a los pacientes diariamente en los primeros 10 días de hospitalización en la unidad de cuidados intensivos (UCI) o hasta el alta o la muerte en la UCI. Se compararon las variables y los trastornos gastrointestinales entre los pacientes que recibieron y no recibieron NE. La regresión univariada y multivariada identificó las condiciones asociadas con la NE con las variables propuestas.

Resultados: de los 157 adultos incluidos, el 62 % recibieron NE. El grupo con NE tuvo puntuaciones APACHE II (23,6 ± 7,6 frente a 15 ± 7,2; $p < 0,001$) y SOFA más altas en el día de la admisión en la UCI [7 (5-10,5) frente a 4 (2-6); $p < 0,001$] y mayor mortalidad en la UCI (32 % *vs.* 10 %, $p = 0,002$). La diarrea y la necesidad de descompresión gástrica fueron más frecuentes en el grupo con NE (39,7 % *vs.* 11,7 %; $p < 0,001$ y 34 % *vs.* 13,3 %, $p = 0,004$, respectivamente). El análisis multivariado mostró que el déficit neurológico (OR: 16,7 [IC 95 %: 5,9-46,9]; $p < 0,001$), la alimentación anterior por sonda enteral (OR: 45,1 [IC 95 %: 5,3-380]; $p < 0,001$) y la puntuación SOFA en el día de la admisión en la UCI (OR: 1,2 [IC 95 %: 1,01-1,3]; $p = 0,03$) presentaban asociación con la NE.

Conclusión: las condiciones relacionadas con la gravedad de los pacientes críticos, como las puntuaciones SOFA más altas, el mayor déficit neurológico y la alimentación anterior por sonda enteral, se asociaron más con la NE. La diarrea y la necesidad de descompresión gástrica fueron más frecuentes en los pacientes que recibieron NE.

Palabras clave:

Cuidados críticos. Nutrición enteral. Motilidad gastrointestinal. Intubación gastrointestinal. Factores de riesgo. Complicaciones.

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INTRODUCTION

In Europe, 27.9 % to 34.4 % of the patients admitted to general hospitals receive enteral nutrition (EN) therapy (1). A multicenter survey on the prevalence of hospital malnutrition found that only 5.6 % of patients receive EN in Latin America (2). A French study evaluating macronutrients delivered in an intensive care setting found that up to 78 % of its sample of 51 patients received EN (3). A 2008 Brazilian study of 907 elderly patients in intensive care found that 40 % received EN (4). In a study on the prevalence of drug-enteral nutrition interaction in a Brazilian intensive care unit (ICU), Reis et al. (5) found that 29 % of hospitalized patients received EN. A previous study by our group (6) found that the majority of ICU patients (59 %) did not receive EN. In fact, there have been no recent censuses on the subject, and consistent data about the number of critically ill patients who receive EN are unavailable, especially in Brazil.

Moreover, little is known about the conditions that facilitate or hinder the use of EN, i.e., that determine whether this therapy is fitting for some patients but not others. Some authors have tried to explain this. Patel et al. (7), in a phase-3 single-center pilot clinical trial, enrolled 31 patients who were on mechanical ventilation and had septic shock (using vasopressors), comparing patients on early EN vs. those who did not receive it. No differences were identified between the groups regarding baseline clinical characteristics except for age (years), which was higher in the early EN group (64 ± 14 vs. 56 ± 16; $p = 0.02$). The authors also found that the early EN group spent less time on mechanical ventilation [27 (24-28) vs. 14 (0-26) ventilator-free days; $p = 0.009$] and less time in the ICU (25 [14-27] vs. 12 [0-22] ICU-free days; $p = 0.014$).

Studies indicate that one limitation of EN in patients on vasopressors is the risk of intestinal ischemia. A recent review of nine studies reported large variability (from 0.3 % to 8.5 %) in the incidence of intestinal ischemia in this patient profile (8). Although the incidence of intestinal ischemia secondary to EN is low, it contributes to significant morbidity and high mortality rates, ranging from 46 % to 100 % (9).

Recent guidelines (10,11) indicate that hemodynamically stable critically ill patients who receive early EM survive longer. On the other hand, in patients on vasoactive drugs, mechanical ventilation or sedatives, there may be alterations in blood flow and peripheral vascular perfusion, affecting gastrointestinal motility and gastric emptying (12). Under such conditions, gastrointestinal disorders could additionally limit the use of EN (13).

Although some studies (14-16) show that up to 60 % of critically ill patients have gastrointestinal motility disorders (vomiting, diarrhea, increased gastric residue, and constipation), little is known about the role of EN in these disorders. Two studies have reported an association between EN and gastrointestinal disorders. In 37 Spanish ICUs, Montejo (16) evaluated the effect of a management protocol for preventing diet discontinuation and gastrointestinal disorders, including only patients on EN (n = 400). This author reported that gastrointestinal disorders were frequent (increased gastric residue [39 %], constipation [15.7 %], diarrhea [14.7 %], abdominal distention [13.2 %], vomiting [12.2 %] and regurgitation [5.5 %]), pointing out that patients with gastrointestinal complications received a lower volume of EN than those without gastrointestinal complications (63.1 ± 1.2 % vs. 93.3 ± 0.3 %; $p < 0.001$), had longer hospital stays (20.6 ± 1.2 vs. 15.2 ± 1.3 days; $p < 0.01$) and higher mortality (31 % vs. 16.1 %; $p < 0.001$). Nassar et al. (17) studied 106 surgical patients in a Brazilian ICU and found that constipation was common (69.9 %), as well as that early EN (within 24 hours of ICU admission) was a protective factor against constipation (OR: 0.16; 95 % CI: 0.05-0.45) (17). Other authors (15) have reported that gastrointestinal disorders are related to poor clinical outcomes. A multicenter study including patients (n = 377) from 40 ICUs in several European countries found that the number of concurrent gastrointestinal symptoms is an independent risk factor for 28-day ICU mortality (OR: 3.18; 95 % CI: 1.08-9.40; $p = 0.035$) (15). However, the causal relationship between EN and these gastrointestinal complications is still not clear, nor is their impact on hard outcomes.

Given the lack of robust evidence about the conditions that favor EN, as well as about how critically ill patients are affected by gastrointestinal disorders, the aim of this study was to describe the incidence of gastrointestinal disorders and to identify conditions associated with the use of EN in a cohort of critically ill patients.

METHODS

DESIGN, SETTING, AND POPULATION

At the end of 2016, a prospective cohort study was conducted at the ICU of a large public university hospital in southern Brazil to assess the incidence of and factors associated with constipation (6). Adults (aged ≥ 18 years) who remained in the ICU for a period ≥ 3 days were included. Adults who had constipation or diarrhea on admission, or who had preoperative bowel preparation with enemas, a colostomy, who were admitted from another ICU or were readmitted to the ICU during the current hospitalization were excluded.

DATA COLLECTION

At the start of the study, the first 10 ICU patients were included, who were followed up until ICU discharge or death, at which point new patients were admitted as participants. The patients were followed daily during the first 10 days of ICU stay by previously trained nurses who used a standardized instrument developed for the study, that consisted of variables related to previous and current clinical history, interventions and therapeutic support, nutritional support, and daily Acute Physiology and Chronic Health Evaluation (APACHE II) and Sepsis-related Organ Failure Assessment (SOFA) scores. For each gastrointestinal disorder, a criterion was adopted, as described below, according to the literature. Constipation was defined as no bowel movement for three consecutive days (17). Diarrhea was considered three or more

episodes of liquid or semi-liquid stools per day (18). Vomiting was defined as the occurrence of any visible regurgitation of gastric content (19). Abdominal pain, distension, and the need for gastric decompression were determined through clinical assessment by the care team, and were recorded in the patients' charts.

The study was conducted in accordance with the Declaration of Helsinki guidelines, and the hospital's research ethics committee approved the research protocol.

STATISTICAL ANALYSIS

Data were tabulated and analyzed using the SPSS 20.0 software. A descriptive analysis was performed according to the variables' characteristics and distribution, and the assumptions of the statistical tests. Continuous variables were expressed as mean ± SD or median [interquartile range] as indicated. Categorical variables were expressed as absolute and relative frequency. The analysis considered two groups: a) patients who received EN for at least 24 hours during their ICU stay, and b) patients who did not receive EN, i.e., who received their diet orally or parenterally, or who fasted during their ICU stay. Comparisons between groups were performed using the chi-square test with residual analysis adjusted for categorical variables, and Student's *t*-test for continuous variables. Cox regression with log-rank test was used to estimate the hazard ratio (HR), and Kaplan-Meier analysis between the EN and non-EN groups and gastrointestinal disorders, adjusted for ICU stay. The gastrointestinal disorders included in this analysis were those that were significantly different in the univariate analysis.

To identify conditions associated with EN, a multivariate regression was performed with robust variance and binary outcomes to calculate the odds ratio, adjusted for confounders. The variables for the multivariate regression were selected from the univariate analysis, considering $p < 0.20$; p values < 0.05 were considered statistically significant.

RESULTS

Of all ICU patients admitted during the study period (n = 2,651), 346 were potentially eligible. Of these, 157 were included, with 10 patients monitored at a time (Fig. 1).

The EN group had a more severe profile: they had a higher mean APACHE II score (23.6 ± 7.6 vs. 15 ± 7.2, $p < 0.001$) and a higher mean SOFA score on the day of ICU admission [7 (5-10.5) vs. 4 (2-6); $p < 0.001$], were admitted to the ICU for sepsis and neurological reasons (35.1 % vs. 10 % and 20.6 % vs 3.3 %, $p < 0.001$, respectively), and had higher ICU mortality (32 % vs. 10 %, $p = 0.002$).

Of all the included patients, 95 % had at least one gastrointestinal disorder during the study period. The most frequent disorders were constipation (75.9 %), abdominal distension (41.4 %), and diarrhea (28.7 %). Univariate analysis showed that any gastrointestinal disorder was more frequent in the EN group (97.9 % vs. 90 %, $p = 0.02$). In isolation, diarrhea and the need for gastric decompression were more frequent in the EN group (39.7 % vs. 11.7 %, $p < 0.001$ and 34 % vs. 13.3 %, $p = 0.004$, respectively). There were no significant differences between groups for the other variables (Table I).

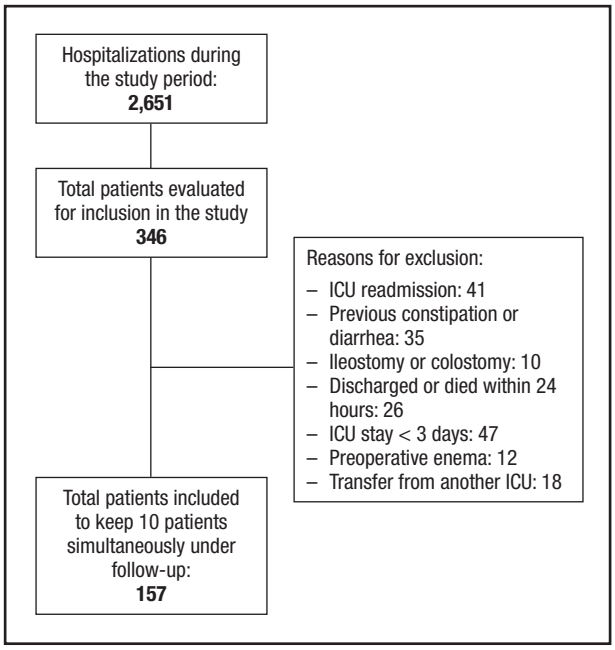

Figure 1.
Study flow chart.

The risk of diarrhea (HR = 3.8, 95 % CI = 1.7-8.7) and the need for gastric decompression (HR = 2.8, 95 % CI = 1.3-6.0) was higher in the EN group. No difference in the risk of abdominal distension (HR = 1.6, 95 % CI = 0.9-2.7) was found between the groups, according to cumulative survival (Fig. 2).

The following conditions were independently associated with EN: neurological deficit (Glasgow Scale ≤ 9 or RASS Scale ≤ -2), prior enteral tube feeding, and SOFA score on the day of ICU admission (Table II). For each one-point increase in SOFA score, the use of EN increased by 20 %.

DISCUSSION

In a cohort of critically ill patients, the present study found that conditions associated with EN included neurological deficit, previous enteral feeding, and high SOFA scores. We also found that gastrointestinal motility disorders are extremely common in critically ill patients, with constipation and abdominal distension being most frequent. Moreover, the incidence of diarrhea and need for gastric decompression with a nasogastric tube was more frequent in the EN group than the non-EN group.

Although it is already known that the use of EN is more related to patients with neurological involvement, as they have a higher

Table I. Demographic and clinical characteristics

	All (n = 157)	EN (n = 97)	Non-EN (n = 60)	p
Age (years)	58.3 ± 15.2	58.7 ± 16	57.6 ± 13.9	0.66
Male	84 (53.5)	52 (61.9)	32 (53.3)	0.97
APACHE II	21.5 ± 8.4	23.6 ± 7.6	15 ± 7.2	< 0.001
SOFA	6 [4-9]	7 [5-10.5]	4 [2-6]	< 0.001
Reason for ICU admission				
Sepsis	40 (25.5)	34 (35.1)	6 (10)	
Neurological	22 (14)	20 (20.6)	2 (3.3)	
Respiratory	24 (15.3)	19 (19.6)	5 (8.3)	
Cardiological	12 (7.6)	6 (6.2)	6 (10)	< 0.001
Gastroenterological	5 (3.2)	4 (4.1)	1 (1.7)	
Postoperative	43 (27.4)	6 (6.2)	37 (61.7)	
Other	11 (7)	8 (8.2)	3 (5)	
Previous diseases				
Arterial hypertension	76 (48.4)	49 (50.5)	27 (45)	0.50
Diabetes	37 (23.6)	22 (22.7)	15 (25)	0.73
Cancer	29 (18.5)	21 (21.6)	8 (13.3)	0.19
COPD	15 (9.6)	10 (10.3)	5 (8.3)	0.68
Renal disease	23 (14.6)	17 (17.5)	6 (10)	0.19
Heart failure	11 (7)	7 (7.2)	4 (6.7)	0.89
Ischemic heart disease	14 (8.9)	6 (6.2)	8 (13.3)	0.12
Stroke	14 (8.9)	12 (12.4)	2 (3.3)	0.05
Diverticulitis or Crohn's disease	5 (3.2)	3 (3.1)	2 (3.3)	0.93
Nutritional status				
BMI				
< 18.5 (%)	20 (12.9)	16 (16.8)	4 (6.7)	
≥ 18.5 and < 25 (%)	49 (31.6)	30 (31.6)	19 (31.7)	0.295
≥ 25 and < 30 (%)	45 (29)	25 (26.3)	20 (33.3)	
≥ 30 (%)	41 (26.5)	24 (25.3)	17 (28.3)	
Gastrointestinal disorders				
Presence of any disorder (%)	149 (95)	95 (97.9)	54 (90)	0.02
Constipation (%)	119 (75.9)	74 (76.3)	45 (75)	0.85
Abdominal distension (%)	65 (41.4)	46 (47.4)	19 (31.7)	0.05
Diarrhea (%)	45 (28.7)	38 (39.7)	7 (11.7)	< 0.001
Vomiting (%)	41 (26.1)	25 (25.8)	16 (26.7)	0.90
Need for gastric decompression (%)	41 (26.1)	33 (34)	8 (13.3)	0.004
Abdominal pain (%)	20 (12.7)	14 (14.4)	6 (10)	0.41
ICU death	37 (23.6)	31 (32)	6 (10)	0.002

Values expressed as mean ± standard deviation, frequency (%) or median [25th percentile-75th percentile]. EN: enteral nutrition; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sepsis-related Organ Failure Assessment; ICU: intensive care unit; COPD: chronic obstructive pulmonary disease.

risk of dysphagia (20), no study was designed with the direct objective of evaluating the conditions associated with EN.

Since no study has directly identified the conditions associated with the use of EN in critically ill patients, it is impossible to draw any direct comparisons with our findings. However, indirect comparisons with studies designed for other purposes might be useful. For example, a prospective Spanish study (21) assessed the profile and costs of home EN, following patients for three years. Although the patient profile differed from ours, neurological deficits were also frequent (62 %) in their sample.

Likewise, the prolongation of and failure to resolve neurological conditions in critically ill patients requires that these patients

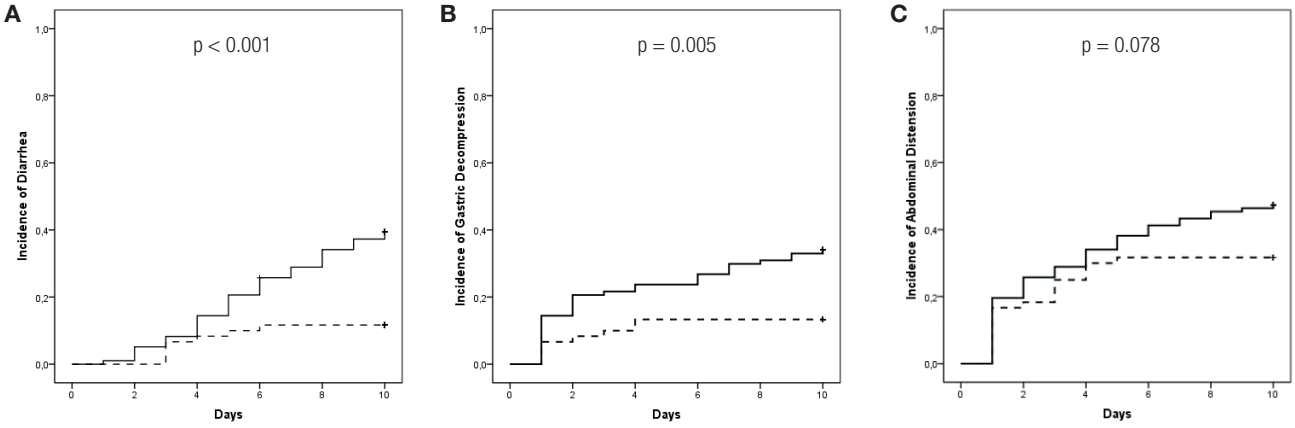

Figure 2.

Comparison of diarrhea (A), gastric decompression (B), and abdominal distension incidence (C) between patients who received enteral nutrition (solid line) and those who did not (dotted line).

Table II. Multivariate analysis for predictors of enteral nutrition use

Variable	Crude OR	Adjusted OR	p
Neurological deficit	20.7 (8.4-51.2)	16.7 (5.9-46.9)	< 0.001
Prior enteral tube feeding	23.9 (3.2-181.3)	45.1 (5.3-380)	< 0.001
SOFA score	1.3 (1.2-1.5)	1.2 (1.01-1.3)	0.03

OR: odds ratio; SOFA: Sepsis-related Organ Failure Assessment.

become repeat users of EN (22). Thus, we verified that the previous use of enteral tube feeding was a condition frequently associated with EN on our cohort.

Patients with higher SOFA scores are more likely to not eat when alone (23), but no study showed a direct association with this clinical variable. Studies with objectives different from ours (21,23) indirectly describe a high SOFA score among patients with EN. To evaluate the effects of early EN on clinical outcomes, Khalid et al. (24) analyzed data from critically ill patients (n = 1,174) in a number of U.S. hospitals, divided into early or late EN groups. They found that the early EN group had higher APACHE II (23 ± 7 vs. 25 ± 8; $p = 0.002$) and SAPS II scores (52 ± 15 vs. 55 ± 16; $p < 0.001$). Although all patients in their study received EN at some point (early or late), there is some similarity between their results and ours regarding the association between SOFA score and EN use.

Critically ill patients undergo catabolic stress and systemic inflammatory response, which alter the morphology and function of the gastrointestinal tract (13), resulting in a higher incidence (> 60 %) of gastrointestinal disorders in ICU patients due to impaired motility, digestion, or absorption processes (14,15). An even higher rate of disorders was identified in the present cohort (95 %), which could be related to the fact that we included any type of gastric alteration (constipation, diarrhea, nausea, vomiting or abdominal distension).

Although, according to the literature, gastrointestinal disorders are frequent in critically ill patients, the reported incidence varies (16,17), including much lower rates than we identified. There are different explanations for this variability. The first of these refers to the set of signs and symptoms included in the studies, as well as lack of consensus about how to define these events. While Nassar et al. (17) define constipation as no bowel movement for three consecutive days, Nguyen et al. (25) described it using a strict concept that combined bowel movement frequency with clinical manifestations, which they called "impaired gastrointestinal transit". Variations in participant profile could also lead to different incidence rates. A multicenter study by Blaser et al. (15) evaluated patients on mechanical ventilation and, besides the disorders considered in our study, they considered gastrointestinal bleeding and abdominal hypertension. According to these authors, 60.2 % of their sample had at least one gastrointestinal disorder in the first week of ICU treatment. An older study reported higher rates of gastrointestinal disorders: in 1999, Montejo (16) evaluated 400 patients from 37 Spanish ICUs, finding that 62.8 % had gastrointestinal disorders. However, only critically ill patients on EN were assessed, and the included hospitals' protocol was to avoid discontinuing EN and prevent the occurrence of gastrointestinal disorders.

There is also great variation in the literature when dealing exclusively with the incidence of constipation in critically ill patients

(9 % [26] to 96 % [27]). In the present study the incidence of constipation was 75.9 % according to the previously used definition of no bowel movements for three consecutive days. Using the same definition, Nassar et al. (17) found a constipation incidence of 69.9 % in 106 surgical patients in a Brazilian ICU, which was similar to our finding in a different patient profile. In a retrospective U.S. cohort that included 83 patients with burns over more than 20 % of their body surface area, on mechanical ventilation in an ICU, late evacuation was defined as no evacuation after six days of ICU treatment, and the reported incidence was 36.1 % (28). Although there is large variability in the reported incidence rates, constipation is a common problem in critically ill patients.

In addition to frequent constipation, we found that abdominal distension affected 41 % of the patients in this study, with 10 days of follow-up. In a Chinese prospective cohort of 470 adults in 14 ICUs, with a median length of stay of 14 (11.0-14.3) days, abdominal distension occurred in 44.8 % of the patients (29). On the other hand, in a multicenter study, Blaser et al. (15) found a lower rate than ours (20.7 %), although their patients were followed for less time in the ICU (7 days).

Comparing gastrointestinal disorders between EN and non-EN patients, we found that diarrhea and the need for gastric decompression were more frequent in the EN group. In Montejo (16) and Heyland et al. (30), the main gastrointestinal complication found among critically ill patients on EN was increased gastric residue, which we also found. The incidence of diarrhea in the EN group was 39.7 %, which was significantly higher than in the non-EN group. A retrospective Australian cohort (n = 50) of critically ill patients on EN included stool volume in the definition of diarrhea, reporting an incidence of 78 %, which was higher than ours (31). However, their definition differed from ours, and the volume considered in their study was based on the subjective assessment of the nursing staff.

Despite being a finding already reported in other studies (32), monitoring the incidence of diarrhea during the infusion of EN allows care practices to be reviewed, since among the causes of this disorder are the composition of enteral formulas (high osmolarity or low amount of dietary fiber increase the risk), the characteristics of their administration, including the position of the enteral tube (gastric or jejunal, with no consensus on the benefit of a gastric tube in preventing diarrhea), and the mode of infusion (use of an infusion pump decreases the risk of diarrhea when compared to gravitational dripping) (33). Also, it is necessary to observe the risks of microbial contamination of the EN formulas used, as well as contamination of the enteral tube lumen, due to inadequate handling practices and lack of care with diet administration devices (34).

Although we found no difference in the incidence of constipation between the EN and non-EN groups, some authors have detected a difference. Nassar et al. (17) reported that early EN (within 24 hours of ICU admission) was associated with a lower incidence of constipation (OR: 0.16; 95 % CI: 0.05-0.45). In another study, late EN (OR: 3.42; 95 % CI: 1.88-6.22; $p < 0.001$), sedatives (OR: 3.07; 95 % CI: 1.71-5.52; $p < 0.001$) and surgery (OR: 1.86; 95 % CI: 1.01-3.42; $p = 0.047$) were independent risk factors for delayed bowel movement (35).

Our study was initially designed to assess the incidence of gastrointestinal disorders and their determinants in ICU patients, not to compare the relationship between these events and the risk of EN. Thus, other variables that could be predictors of EN may have been overlooked in our cohort. On the other hand, our study design was robust, with methodological care taken throughout its planning, implementation, data analysis and interpretation, and it provides information that is scarce in the literature.

CONCLUSION

Our data indicate that the conditions associated with EN in critically ill patients were neurological deficit, prior enteral tube feeding, and higher SOFA scores. Gastrointestinal disorders were very common, especially constipation and abdominal distension. Among the critically ill patients who received EN, there was a higher incidence of diarrhea and need for gastric decompression.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Paciente crítico

Beneficios de un programa de formación y de un algoritmo clínico de soporte nutricional mixto para mejorar la nutrición del paciente crítico: estudio antes-después

Benefits of an education program and a clinical algorithm in mixed nutritional support to improve nutrition for the critically ill patient: a before-and-after study

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Resumen

Introducción: la nutrición óptima del paciente crítico es clave para su recuperación.

Objetivos: promover la formación y difusión del conocimiento acerca del soporte nutricional mixto (SNM) mediante un algoritmo clínico entre los intensivistas para mejorar el estado nutricional de los pacientes críticos.

Métodos: estudio antes-después con la participación de 19 unidades de cuidados intensivos (UCI) polivalentes en 10 comunidades autónomas. Cinco miembros del comité científico formaron a los formadores mediante presentaciones orales y el algoritmo de SNM. Los formadores fueron responsables de la formación de los intensivistas en sus propias UCI. El cuestionario de 30 ítems fue completado por 179 y 105 intensivistas antes y después de la intervención, respectivamente.

Resultados: se observó un aumento del conocimiento en seis (20 %) preguntas específicas relacionadas con el SNM. En 11 ítems (36,6 %), el conocimiento adecuado sobre diferentes aspectos del soporte nutricional que ya estaban presentes antes de la formación se mantuvieron, y en cinco ítems (16,7 %) hubo un aumento de la tasa de respuestas correctas. En cuatro ítems (13,3 %), las respuestas correctas no mejoraron y en otros cuatro (13,3 %), los porcentajes de respuestas correctas disminuyeron.

Conclusiones: el algoritmo de SNM ha logrado una sólida consolidación de los principales conceptos de esta estrategia. Algunos aspectos referentes a cómo manejar al paciente desnutrido, cómo identificarlo y qué tipo de nutrición pautar desde el inicio del ingreso en la UCI, los aportes nutricionales en situaciones especiales y el seguimiento de posibles complicaciones como la realimentación, son áreas que requerirían estrategias formativas adicionales.

Palabras clave:

Algoritmo clínico.
Nutrición enteral.
Nutrición parenteral.
Paciente crítico.
Soporte nutricional mixto.

Abstract

Introduction: optimal nutrition in the critically ill patient is a key aspect for recovery.

Objectives: to promote training in and knowledge of mixed nutrition support (MNS) by means of a clinical algorithm among intensivists for improving the nutritional status of critically ill patients.

Methods: a before-and-after study with the participation of 19 polyvalent intensive care units (ICUs) in 10 autonomous communities. Five members of the scientific committee trained the trainers by means of oral presentations and a clinical algorithm on MNS. Then, trainers were responsible for explaining the algorithm to local intensivists in their ICUs. The 30-item study questionnaire was completed before and after the intervention by 179 and 105 intensivists, respectively.

Results: a clear improvement of knowledge was found in six (20 %) specific MNS-related questions. In 11 items (36.6 %), adequate knowledge on different aspects of nutritional support that were already present before the intervention were maintained, and in five items (16.7 %) an improvement in the rate of correct responses was recorded. There were no improvements in correct responses for four items (13.3 %), and for four (13.3 %) additional items the percentage of correct responses decreased.

Conclusions: the use of the MNS algorithm has achieved a solid consolidation of the main concepts of MNS. Some aspects regarding how to manage the malnourished patient, how to identify them and what type of nutrition to guide from the beginning of admission to the ICU, nutritional contributions in special situations, and the monitoring of possible complications such as refeeding are areas for which further training strategies are needed.

Keywords:

Clinical algorithm.
Critical patient.
Enteral nutrition.
Parenteral nutrition.
Mixed nutritional support.

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INTRODUCCIÓN

La terapia nutricional en el paciente crítico es un elemento clave en su recuperación. Numerosos estudios, incluyendo revisiones sistemáticas y metaanálisis, han proporcionado evidencia sólida de que una provisión óptima de nutrientes y el establecimiento temprano de un balance calórico adecuado por abordaje enteral o parenteral se asocian con una evolución favorable, con disminución de la morbilidad y la mortalidad (1-4). Por el contrario, diferentes estudios han confirmado el papel de la desnutrición y del balance energético negativo como factores de riesgo de mortalidad, complicaciones, disminución de los días libres de ventilación mecánica y mayor duración de la estancia en la UCI y en el hospital, con peores resultados funcionales y de recuperación a largo plazo (5-8).

Respecto al momento de inicio y la vía de administración, la nutrición enteral (NE) es la vía de preferencia (9-11), recomendándose la nutrición parenteral (NP) cuando existen contraindicaciones para la vía enteral o cuando se espera que los pacientes críticos no vayan a recibir una dieta oral completa durante 3 o más días consecutivos (12,13). En un ensayo multicéntrico prospectivo, aleatorizado y controlado de 2388 pacientes críticos para evaluar las diferencias entre la NE precoz y la NP precoz, no hubo diferencias en la mortalidad a 30 y 90 días, ni en la duración del soporte de órganos, ni en las complicaciones infecciosas, ni en la duración de la estancia en la UCI y en el hospital (14). Sin embargo, en otro ensayo aleatorizado y controlado de 2410 pacientes con ventilación mecánica y tratamiento con fármacos vasoactivos por shock, la NE precoz isocalórica no disminuyó la mortalidad ni el riesgo de infecciones secundarias, pero se asoció a un mayor riesgo de complicaciones digestivas en comparación con la NP isocalórica parenteral (15). Asimismo, en una revisión sistemática con metaanálisis de 18 ensayos aleatorizados y controlados, con 3347 pacientes, se observó que la NE en comparación con la NP no afectaba a la mortalidad global, pero disminuía el riesgo de complicaciones infecciosas y la estancia en la UCI (16).

El retraso en el inicio de la NE, sin embargo, comporta un aumento de la mortalidad y de las complicaciones infecciosas (9). A pesar de la importancia del inicio temprano de la NE, su implementación en la práctica clínica es subóptima, con retrasos de varios días hasta alcanzar los requerimientos nutricionales recomendados (17). El soporte nutricional mixto (SNM), basado en la NE precoz suplementada con alimentación parenteral, es una estrategia efectiva y segura para alcanzar un aporte calórico óptimo más precozmente que con la NE (18). Asimismo, permite disminuir el número de complicaciones y puede mejorar la supervivencia (19,20), por lo que es una estrategia a tener en cuenta a la hora de planificar el aporte nutricional en los pacientes críticos en los que la vía enteral es insuficiente, pudiéndose evitar la sobrealimentación mediante una prescripción cuidadosa, idealmente basada en el gasto energético medido por calorimetría indirecta (21). En la práctica clínica, sin embargo, algunos estudios han alertado acerca de las deficiencias presentes en las prácticas de tratamiento nutricional en el marco del soporte integral del paciente crítico (22-24).

Con el propósito de promover la formación y difusión del conocimiento acerca del soporte nutricional mixto entre los intensivistas de nuestro país, se diseñó un estudio antes-después basado en la aplicación de un algoritmo clínico de actuación para adecuar el manejo del paciente tratado con soporte nutricional mixto. Con ello, además, se podría optimizar el arsenal terapéutico disponible en la UCI.

MATERIAL Y MÉTODOS

DISEÑO

El proyecto ALGORITMIA consistía en un estudio de intervención antes-después basado en un programa educativo y en la aplicación de un algoritmo clínico de actuación en el ámbito del soporte nutricional mixto, contando con la participación de los servicios de medicina intensiva polivalentes de una serie de hospitales públicos de tercer nivel de diferentes comunidades autónomas del país. El objetivo principal del estudio era dotar a los médicos intensivistas participantes de los conocimientos necesarios de SNM para mejorar su implementación y mejorar, consecuentemente, el estado nutricional de los pacientes críticos. Los objetivos secundarios eran los siguientes: a) evaluar el nivel de conocimiento de las guías de práctica clínica sobre el manejo de la nutrición clínica en los pacientes críticos; y b) determinar aquellos aspectos en los que había mayor incertidumbre en el manejo del SNM en el paciente crítico. Por tratarse de un programa formativo, no era necesario obtener la aprobación por un comité de ética.

FASES Y DESARROLLO DEL PROYECTO

El proyecto constaba de dos fases. En la primera, de marzo a diciembre de 2017, se establecieron el comité científico, el equipo técnico y la selección del panel de formadores. En la segunda, de marzo a diciembre de 2018, el panel de formadores procedió a la formación en el algoritmo clínico de actuación de SNM, a la puesta en práctica del algoritmo en los servicios de medicina intensiva correspondientes y a la cumplimentación del cuestionario del estudio antes y después de la estrategia formativa. Finalmente, de enero a abril de 2019 se procedió al análisis de los datos recogidos en el cuestionario y a la presentación de los resultados al grupo de trabajo.

El comité científico estaba formado por un grupo de cuatro expertas especialistas en medicina intensiva y una experta especialista en endocrinología y nutrición. Trabajando en colaboración, y tras hacer una revisión de la literatura para actualizar la evidencia disponible en el campo de la nutrición del paciente crítico, desarrollaron un programa formativo para optimizar el abordaje y manejo del SNM en pacientes críticos. Este programa, en formato "formación de formadores", estaba integrado por cinco presentaciones orales con PowerPoint en formato presencial, de unos 20 minutos de duración y cada una de ellas desarrollada por una de las autoras. Los temas de las presentaciones eran los siguientes: abordaje

de la NE, controversias en NP, tolerancia gastrointestinal de la nutrición, déficit en el aporte nutricional y SNM. En cada una de las presentaciones se incluían datos de los estudios sobresalientes recientemente publicados en la literatura, y los pormenores fisiopatológicos, clínicos y diagnósticos y terapéuticos que cada una de las formadoras consideraba de interés. Asimismo, las expertas enseñaron a los formadores el algoritmo clínico de implementación del SNM, sus bases científicas y su aplicación práctica (Tabla I). Además, desarrollaron un cuestionario sobre el conocimiento del manejo y el abordaje del SNM para poder valorar el impacto del programa formativo en el colectivo de la medicina intensiva. El cuestionario del proyecto ALGORITMIA constaba de 30 ítems en forma de enunciados o preguntas con cinco opciones de respuesta, de las cuales solo se podía elegir una. Asimismo, solamente una opción era la correcta. El detalle del cuestionario se describe en la tabla III. Los formadores fueron los encargados de pasar los cuestionarios en sus servicios antes de la formación y tras unos meses de haber implementado el algoritmo.

Los formadores dispusieron de una página web de acceso restringido donde podían encontrar el algoritmo, las presentaciones

Tabla I. Algoritmo clínico de actuación en el soporte nutricional mixto

Día 1	**Evaluación individual** Situación hemodinámica controlada (1) Ingesta oral no posible > 3 días (2) Valoración nutricional: (3-5) – NUTRIC Score ≥ 5 – Considerar enfermos en riesgo de Realimentación	Objetivo nutricional (6-9) – 20-25 kcal/kg/día y – 1,2-2,5 g proteínas/kg/día
	Iniciar nutrición enteral (si no hay contraindicación) (10-14) 10-20 mL/h en las siguientes 24 h	
	Nutrición	**Monitorización**
Día 2	**Aumento gradual de la nutrición enteral** (15-17)	**Tolerancia gastrointestinal** (27-34)
	– Objetivo: alcanzar el 80 % de los requerimientos – Si hay tolerancia gastrointestinal, incrementar según el protocolo habitual en las siguientes 24-48 h	– Monitorizar: • Presión intraabdominal, distensión abdominal o dolor > descartar patología abdominal • Diarrea > descartar *Clostridium difficile* • Vómitos, regurgitaciones > comprobar sonda nasogástrica • Estreñimiento • Residuo gástrico (> 500 mL) – Optimizar/valorar: • Sedación • Procinéticos • Fibra • Laxantes • Sonda transpilórica • Tipo de dieta enteral
Día ≥ 3	**Evaluación del objetivo calórico-proteico** (18-20)	**Tolerancia metabólica** (35)
	¿Se ha alcanzado menos del 60 % del objetivo calculado? – Incluir aporte: propofol, suero glucosado, líquidos de diálisis y módulos de proteína **Soporte nutricional mixto** (21-23) – Iniciar nutrición parenteral para suplementar las calorías y proteínas necesarias para alcanzar el 100 % del objetivo calórico-proteico – Evitar la sobrenutrición	– Monitorizar: • Glucosa: 140-180 mg/dL • Triglicéridos: < 400 mg/dL • Función hepática • Función renal • Ionograma • Balance nitrogenado
	Incrementar la nutrición enteral en función de la tolerancia gastrointestinal, promover la ingesta oral y reducir acorde con la nutrición parenteral (24-26)	

Los números entre paréntesis corresponden al soporte bibliográfico de cada punto. El listado de los artículos se incluye en la Bibliografía.

de las cinco expertas y una calculadora electrónica para facilitar el cálculo de los requerimientos calórico-proteicos alcanzados con la NE, y ayudar a llevar a cabo la formación en sus respectivos servicios y la óptima implementación del algoritmo.

ANÁLISIS ESTADÍSTICO

Los datos correspondientes a los cuestionarios de antes y después de la formación y de la aplicación del algoritmo fueron incluidos en una base de datos por personal independiente al proyecto, estando el acceso a los resultados restringido al comité científico. Se efectuó un análisis descriptivo.

RESULTADOS

En total, 19 médicos intensivistas (uno por UCI) recibieron la formación presencial y distribuyeron los cuestionarios entre los miembros de sus respectivos servicios. Las UCI participantes estaban situadas en 10 comunidades autónomas (Andalucía, Cataluña, Castilla y León, Extremadura, Galicia, País Vasco, Aragón, Madrid, Comunidad Valenciana e Islas Canarias). El cuestionario fue completado por 179 intensivistas antes de la aplicación del algoritmo de soporte nutricional mixto, y por 105 después de la implementación del mismo.

Las variaciones en los porcentajes de respuestas correctas e incorrectas para cada ítem del cuestionario antes y después de la formación y aplicación del algoritmo se describen en la tabla II. Los cambios observados para cada una de las respuestas correctas del cuestionario se resumen en la tabla III. Tal como se muestra en la figura 1, en todos los ítems del cuestionario, excepto en cuatro (ítems 1, 3, 16 y 24), hubo incrementos en los porcentajes de encuestados que eligieron la respuesta correcta después de la formación y aplicación del algoritmo. En algunos casos, la variación fue muy notable (un aumento del 35 % en el ítem 4, del objetivo nutricional inicial del paciente normonutrido de 20-25 kcal/kg/día – 1,2-2,5 g proteína/día, o del 29 % en el ítem 11, del volumen de residuo gástrico patológico de 500 cc en una medición). En otros aspectos, los porcentajes de respuestas correctas antes de la intervención eran ya buenos (del 90 % o superiores), por lo que en estos casos (ítems 1, 9, 13, 17, 20 y 30) las tassas de mejoría fueron inferiores al 10 % (Fig. 1), pero aun así se consiguió una mejora.

En relación con los conocimientos del SNM, específicamente en los ítems 6, 7, 25, 26, 27, 28 y 30 del cuestionario (20 % del total) se observaró un incremento del porcentaje de respuestas correctas tras la formación. De forma similar, también mejoró el conocimiento sobre la indicación de inicio de la NP (ítem 5). Por otra parte, en 11 ítems del cuestionario (7, 9, 13, 15, 17, 18, 19, 20, 21, 22, 23), correspondiente al 36,7 %, se mantuvieron los buenos conocimientos sobre el soporte nutricional que ya se tenían.

Respecto a los parámetros o índices a utilizar para valorar el riesgo nutricional, hubo una disminución del 2 % en el porcentaje de respuestas correctas (alto riesgo definido por un NRS 2000 > 5 y/o NUTRIC Score ≥ 5), pero hubo un incremento del 22 % al 46 % en la elección del NUTRIC Score, que es un índice específico para pacientes críticos. El porcentaje de encuestados que acertaron en la elección del pliegue tricipital como parámetro que no es un buen indicador de malnutrición fue tan solo del 17 % antes de la formación, disminuyendo después a un 15 %, aunque la opción de los valores de albúmina antes del ingreso aumentó del 17 % al 41 %. Por otra parte, también se observó un incremento considerable, del 57 % al 79 %, en la consideración de que la NE no se debe suspender tras haberse iniciado. En este sentido, el manejo de la diarrea tras el inicio de la NE parece haber mejorado tras la formación y aplicación del protocolo, lo cual se podría traducir en una menor retirada de la NE tras la aparición de la diarrea. Por otra parte, destacaba un escaso conocimiento de las emulsiones lipídicas de la NP, con porcentajes en la elección de la respuesta correcta del 28 % al 31 %.

DISCUSIÓN

La implementación de una intervención formativa asociada a la aplicación de un algoritmo clínico de actuación ha logrado mejorar el conocimiento de los intensivistas sobre diferentes aspectos del SNM en los pacientes críticos. Cabe destacar la adecuada capacidad en términos de cuándo hay que iniciar el SNM (ítem 6), con un 69 % de aciertos iniciales que tras la formación aumentan al 83 %. Ello se ve reforzado por el aumento del 88 % al 96 % de respuestas correctas en la indicación del SNM a partir del tercer día de ingreso si no se tolera la nutrición enteral de forma completa. De igual forma, la respuesta al caso clínico planteado (ítem 27) es correcta antes de la intervención en un 82 % de los casos, incrementándose después hasta el 92 %, fijando la idea en los encuestados de que, si aparecen complicaciones de tolerancia gastrointestinal y no se alcanzan los requerimientos nutricionales (sumando NE, por sonda gástrica y propofol), hay que iniciar el SNM. Asimismo, destaca un conocimiento excelente de cómo monitorizar al paciente con SNM (ítem 30) antes (91 %) y después de la formación (97 %). En este sentido, el objetivo primario del estudio —proporcionar los conocimientos necesarios sobre el SNM para optimizar el estado nutricional de los pacientes críticos— se ha alcanzado plenamente.

Respecto a la implementación de las recomendaciones de las guías de práctica clínica (11,13), se ha confirmado un conocimiento excelente por la detección de la opción de respuesta incorrecta de la estabilidad de los biomarcadores y que estos no se afectan por la síntesis y degradación proteica, con un 90 % de aciertos iniciales que aumentan al 96 % tras la formación. Sin embargo, el conocimiento de la puntuación NUTRIC (Nutrition Risk in Critically Ill) como instrumento de cribado nutricional, y de la puntuación ≥ 5 para los pacientes de alto riesgo (25,26), era claramente insuficiente. Asimismo, hay un cierto desconocimiento de los indicadores de malnutrición del paciente crítico (ítem 3), lo que probablemente se deba a que algunos de ellos, como el pliegue tricipital, no se usan habitualmente en las UCI. También llama la atención el aumento de los participantes que, tras la formación, creían que los valores de albúmina sérica antes del ingreso en la UCI no son

Tabla II. Variaciones en los porcentajes de respuesta para cada ítem del cuestionario en función de las cinco opciones antes y después de la formación y aplicación del algoritmo de soporte nutricional mixto

Ítem del cuestionario	Opciones de respuesta									
	a		b		c		d		e	
	Antes %	Después %	Antes %	Después %	Antes %	Después %	Antes %	Después %	Antes %	Después %
1	3	1	1	0	4	0	90	99	2	0
2	6	1	8	4	46	44	9	4	22	46
3	8	5	17	8	40	30	17	15	17	41
4	1	1	35	70	6	2	31	17	25	10
5	1	0	5	1	16	6	76	93	0	0
6	3	1	18	15	7	0	69	83	1	0
7	7	4	41	19	21	40	27	31	1	1
8	48	43	4	1	25	32	11	12	4	5
9	2	2	3	1	2	0	0	0	92	95
10	42	19	1	2	6	4	35	59	11	13
11	7	4	12	9	44	73	13	4	22	9
12	1	0	42	56	28	31	2	1	22	9
13	1	0	0	0	1	0	1	1	96	97
14	3	0	9	6	57	79	3	0	2	1
15	3	1	2	1	2	0	2	2	89	94
16	47	38	3	1	35	51	2	0	9	7
17	3	1	2	0	2	1	91	97	1	0
18	88	92	1	0	1	3	6	1	2	1
19	1	0	1	0	4	5	8	7	84	88
20	1	0	1	0	0	1	0	0	96	98
21	8	15	6	3	8	0	23	31	46	45
22	1	0	0	1	1	0	1	0	96	97
23	1	0	0	0	0	1	2	2	94	96
24	4	2	1	0	0	1	44	42	47	54
25	3	0	3	1	1	0	2	2	88	96
26	1	0	6	2	1	2	15	15	76	78
27	1	0	7	1	82	92	1	1	6	1
28	8	4	0	1	1	0	1	0	83	93
29	39	25	1	1	46	68	6	2	2	2
30	1	0	0	1	1	1	3	0	91	97

En sombreado las opciones de respuesta correctas.

útiles como marcador de malnutrición. El conocimiento inicial del objetivo nutricional, con un concepto claro de 20-25 kcal/kg/día iniciales y 1,2-1,5 g de proteína/día, era deficiente, con un 35 % de respuestas correctas que aumenta al 70 % tras la formación. En el paciente desnutrido, el inicio precoz de la NP también se consolida con un aumento del 76 % al 93 % tras la formación. Iniciar el SNM a las 24-48 h del ingreso en el paciente desnutrido no es una buena práctica, ya que puede ocasionar sobrenutrición. En este punto destaca una mala comprensión, aunque con cierta mejoría (21 % que se incrementa al 40 %).

Otros conceptos bien entendidos tras la formación incluyen el volumen residual patológico, el que no se debe suspender la NE frente a un episodio de diarrea de 48 h de duración, y la composición de la dieta a tener en cuenta frente a una complicación.

Tabla III. Resultados del cuestionario antes y después de la formación y aplicación del algoritmo de soporte nutricional mixto para las opciones correctas de cada ítem

Ítems del cuestionario y respuesta correcta	Antes %	Después %
1. En la valoración del estado nutricional del paciente crítico, qué afirmación consideras que no es adecuada: – Los biomarcadores se mantienen estables y no se afectan por la síntesis y degradación proteica	90	99
2. La valoración del riesgo nutricional debería realizarse en todos los pacientes críticos al ingreso en la unidad. Para ello existen diferentes parámetros e índices que podemos utilizar. Seleccione la respuesta correcta: – Los pacientes con alto riesgo nutricional se definen por un NRS 2002 > 5 y/o NUTRIC Score ≥ 5	46	44
3. ¿Cuál de los siguientes parámetros no es un buen indicador de malnutrición al ingreso del paciente crítico? – Pliegue del tríceps	17	15
4. ¿Cuál es el objetivo nutricional inicial en el paciente crítico normonutrido? – 20-25 kcal/kg/día – 1,2-2,5 g de proteína/día	35	70
5. Paciente varón de 70 años, ingresado previamente en Medicina Interna para estudio de síndrome tóxico (peso habitual, 65 kg), que se diagnostica de neoplasia gástrica. Actualmente presenta una talla 165 cm y 55 kg de peso. En el postoperatorio precoz presenta shock séptico por peritonitis secundaria a dehiscencia de sutura, siendo reintervenido y trasladado a la UCI con ventilación mecánica. ¿Qué soporte nutricional indicarías? – Tras la estabilización hemodinámica, y dada la desnutrición previa del paciente, se iniciaría nutrición parenteral	76	93
6. ¿En qué momento está recomendado iniciar el soporte nutricional mixto en el paciente crítico? – A partir del tercer día si no se ha conseguido superar el 60 % del objetivo calórico, y a lo largo de la estancia si durante 2 días consecutivos no se ha logrado superar el 60 % del objetivo calórico (ambas ciertas)	69	83
7. La vía enteral es la de elección para la nutrición en todo paciente crítico siempre que sea posible; sin embargo, existen situaciones en las que esta vía no es posible o no cubre los requerimientos totales del enfermo, en cuyo caso será necesaria la utilización de la nutrición parenteral. De los supuestos siguientes, señale en cuál la nutrición parenteral total o el soporte nutricional mixto NO está indicado: – Está indicado iniciar la nutrición mixta (parenteral + enteral) en aquellos pacientes desnutridos al ingreso en UCI en los que, a las 24-48 horas del ingreso, los requerimientos calórico-proteicos no han sido cubiertos por la nutrición enteral.	21	40
8. ¿Cómo debería ser la emulsión lipídica de la nutrición parenteral en un paciente crítico ingresado en la UCI por shock séptico secundario a neumonía? – Debemos utilizar formulaciones que contengan un menor contenido en omega 6, por su efecto proinflamatorio	25	32
9. En el seguimiento nutricional del enfermo crítico: ¿Qué parámetros nos pueden ayudar a monitorizar la nutrición del paciente crítico? – Balance nitrogenado, prealbúmina, albúmina, déficit calórico-proteico (todas ciertas)	92	95
10. ¿Qué es cierto con respecto al síndrome de realimentación? – Son pacientes con más de 7 días de ingreso con una ingesta pobre o nula	35	59
11. ¿Qué volumen de residuo gástrico consideramos patológico? Responda qué hace habitualmente en su unidad – 500 cc en una medición	44	73
12. ¿Cuál de las siguientes medidas se utiliza para mejorar el vaciado gástrico en los pacientes portadores de sonda nasogástrica? – Optimización de los niveles de glucemia	28	31
13. La administración del volumen de nutrición enteral prescrito continúa siendo un reto en las unidades de cuidados intensivos. ¿Cuál de las siguientes le parece una medida a aplicar para optimizar la administración de la nutrición enteral en su unidad? – Utilización de un protocolo de nutrición, implicación de todo el personal médico, enfermería y auxiliares en el manejo de la nutrición, mantener un registro de la nutrición administrada diariamente, conocer las complicaciones asociadas a la administración de la nutrición enteral y anticipar tratamientos para evitarlas (todas ciertas)	96	97
14. En caso de iniciar la nutrición enteral, qué no deberíamos hacer (señalar la respuesta incorrecta): – Suspender la nutrición enteral	57	79

(Continúa en página siguiente)

Tabla III (Cont.). Resultados del cuestionario antes y después de la formación y aplicación del algoritmo de soporte nutricional mixto para las opciones correctas de cada ítem

Ítems del cuestionario y respuesta correcta	Antes %	Después %
15. Ante una complicación, ¿qué parámetros de la composición de la dieta tendrías en cuenta? – Diarrea: fibra insoluble; estreñimiento: fibra soluble e insoluble; vómitos: osmolaridad de la dieta; hiperglucemia: cantidad de hidratos de carbono (todas ciertas)	89	94
16. ¿Cuál de las siguientes NO sería una medida a adoptar ante un paciente bajo nutrición enteral que presenta un episodio de diarrea de 48 horas de evolución? – Suspender la nutrición enteral temporalmente e iniciar nutrición parenteral u otro soporte nutricional	47	38
17. ¿Cuál sería el mejor abordaje por enfermería para cumplir con los objetivos nutricionales del paciente con nutrición enteral? – Establecer una alimentación por volumen, modificando el ritmo de infusión de forma dinámica; recoger en una gráfica el volumen pautado-volumen entregado (ambas ciertas)	91	97
18. En cuanto a la monitorización del soporte nutricional, es falso que: – No se puede monitorizar objetivamente	88	92
19. Tras el cálculo de los requerimientos del paciente, la prescripción médica del producto de nutrición enteral adecuado con la velocidad de perfusión calculada – No es necesario preocuparse más por el soporte nutricional del paciente; no se han de tener en cuenta los aportes externos como el propofol, los sueros glucosados o los líquidos de diálisis con citrato, ya que van variando durante la estancia en la UCI y sería muy complicado monitorizarlos; las suspensiones ocasionales de la perfusión de nutrición enteral por motivos de pruebas radiológicas o analíticas, o de intervenciones quirúrgicas son mínimas y no afectan de forma sustancial al aporte final; las complicaciones gastrointestinales relacionadas con la nutrición enteral no suelen ser frecuentes y, en caso de aparición, tienen soluciones eficaces y rápidas (todas son falsas)	84	88
20. ¿Cuál de las siguientes consideras que sería una consecuencia de la malnutrición en el paciente crítico? – Aumento de la tasa de infecciones nosocomiales; mayor tiempo de ventilación mecánica; mayor costo sanitario y estancia hospitalaria; impacto sobre la calidad de vida con incremento de la comorbilidad y mayor tasa de reingresos hospitalarios (todas ciertas)	96	98
21. Respecto a las calorías no nutricionales, señale la respuesta FALSA: – Una infusión de dextrosa al 5 % a 21 mL/hora aporta 400 kcal en 24 horas	23	31
22. En la monitorización del aporte nutricional, ¿cuál de las siguientes acciones se deben considerar en el cálculo del aporte? – Los módulos de proteínas; la sueroterapia utilizada; si reciben fármacos que contienen lípidos como el propofol; la utilización de citrato en la terapia continua de reemplazo renal (todas se deben considerar)	96	97
23. El aporte nutricional es un pilar fundamental del tratamiento del paciente crítico, por eso debemos insistir en el aporte y debemos considerar: – Evitar el déficit nutricional por suspensión de la dieta; la nutrición enteral es la más fisiológica pero no siempre es posible (ambas ciertas)	94	96
24. El déficit de aporte nutricional viene dado por las siguientes situaciones, excepto una: – Alimentación dinámica por volumen	44	42
25. ¿En qué caso estaría justificado el soporte nutricional mixto? – A partir del tercer día de ingreso si no se tolera nutrición enteral de forma completa	88	96
26. Paciente varón de 41 años, ingresado en la UCI por traumatismo craneoencefálico tras una precipitación hace una semana. Permanece sedoanalgesiado. Peso 75 kg. Mide 170 cm. Requerimientos calculados: 20 kcal/kg → 1500 kcal; 25 kcal/kg → 1875 kcal. Se inició la nutrición enteral hace 5 días con dieta hipercalórica e hiperproteica e inicio de procinéticos hace 2 días, alcanzando diariamente entre 800-1000 kcal/día por residuos gástricos elevados y suspensiones temporales de la perfusión de nutrición enteral. ¿Qué estrategia de soporte nutricional nos hemos de plantear a continuación? – Colocación de una sonda pospilórica; inicio de nutrición parenteral, manteniendo la nutrición enteral, para alcanzar los requerimientos (ambas ciertas)	76	78

(Continúa en página siguiente)

Tabla III (Cont.). Resultados del cuestionario antes y después de la formación y aplicación del algoritmo de soporte nutricional mixto para las opciones correctas de cada ítem

Ítems del cuestionario y respuesta correcta	Antes %	Después %
27. Paciente de 75 kg en el que al 5.º día de estancia en la UCI con estabilidad hemodinámica, al analizar la gráfica, objetivamos que presenta un volumen residual gástrico > 500 cc pese a los procinéticos, y que en los dos días anteriores su ingesta se ha limitado a 800 kcal (suma de nutrición enteral + sonda gástrica + propofol). ¿Cuál sería su actitud? – Bajar el ritmo de nutrición enteral, mantener los procinéticos, añadir soporte nutricional mixto hasta alcanzar objetivos	82	92
28. Para el soporte nutricional mixto, el aporte de nutrición parenteral debe ser: – Individualizado, pudiendo escoger cualquier tipo de nutrición parenteral que se ajuste a los requerimientos (tricameral, estandarizada en campana o a la carta)	83	93
29. ¿Cuál de estas no es una complicación de la sobrenutrición en el paciente crítico? – Aumento de la capacidad fagocítica de los neutrófilos.	46	68
30. Una vez iniciado el soporte nutricional mixto: ¿Qué debemos hacer a continuación? – Realizar analíticas de control con función hepática y renal, ionograma y parámetros nutricionales; monitorización diaria del aporte calórico y proteico, teniendo en cuenta la nutrición enteral, la nutrición parenteral, los sueros y posibles fármacos; ajustar el aporte en bolsa de nutrición de forma diaria en función del punto anterior, revalorando siempre su posible retirada (las tres son ciertas)	91	97

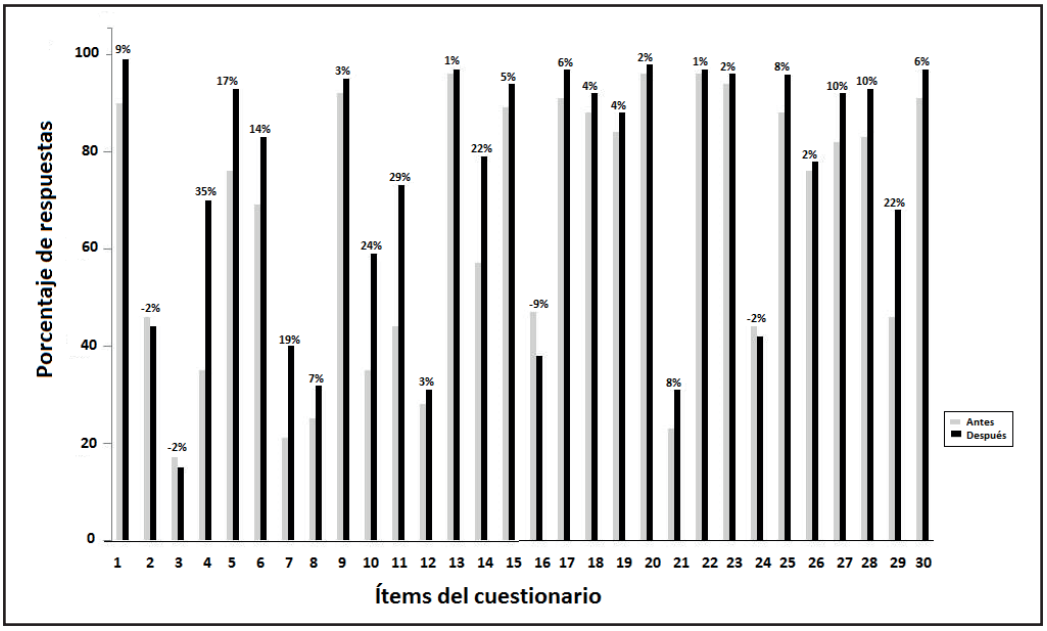

Figura 1.

Variación de los porcentajes de respuestas correctas para cada ítem del cuestionario tras la formación e implementación del algoritmo de soporte nutricional mixto.

Con respecto a la monitorización del soporte nutricional, la misión de la enfermería y la transversalidad del proceso, así como la importancia de monitorizar la nutrición del paciente crítico, son cuestiones bien fijadas (ítems 17, 18 y 22) con un muy buen porcentaje de respuestas correctas que, además, mejora tras la formación.

Se ha observado un mal conocimiento del síndrome de realimentación, con porcentajes de respuestas correctas del 35 %

y el 59 % antes y después de la formación, respectivamente. En este aspecto, un 42 % de los encuestados creían que dicho síndrome cursa con niveles altos de fosfato en sangre, porcentaje que disminuye al 19 % tras la formación. En este sentido, un 39 % de los participantes opinaba que la hipofosfatemia no es una complicación de la sobrenutrición del paciente crítico, aunque este porcentaje disminuyó (25 %) tras la formación. Las respuestas correctas sobre que el aumento de la capacidad fagocítica de los neutrófilos no es una complicación de la sobrenutrición aumentaron del 46 % al 68 %.

Los resultados de este estudio son difíciles de comparar, ya que se han publicado escasos trabajos de intervención en el ámbito de la nutrición del paciente crítico. En un estudio prospectivo liderado por la enfermería y efectuado en 42 pacientes ingresados en una UCI de un hospital de Oslo, asignados a un grupo de intervención (n = 21) y a un grupo control (n = 21), se evaluaba la aplicación de un algoritmo nutricional con el objetivo diana de 30 kcal/kg/día y un soporte nutricional implementado a las 24 h del ingreso en la UCI, comparándose los datos recogidos en los dos grupos del estudio durante 2 meses antes y 2 meses después de la intervención (27). Los pacientes asignados al grupo de intervención recibieron significativamente mayores cantidades de nutrientes que los pacientes del grupo de control, así como mayor proporción de nutrientes en forma de NE, con mejoría en las prácticas de aspiración del contenido gástrico y la tasa de incremento de la NE. En otro estudio prospectivo efectuado en el Servicio de Medicina Intensiva de Hospital Universitario 12 de Octubre de Madrid, diseñado en tres fases (observación, elaboración de propuestas y difusión, y análisis de la implantación del proceso de mejora) y con la participación de 110 pacientes en la primera fase y 119 en la tercera, se incrementó el aporte proteico y la utilización de la nutrición enteral, pero sin diferencias en el tiempo de inicio o la duración de la misma (13). A diferencia de nuestro trabajo, ninguno de estos dos estudios tenía como objetivo el SNM. En una revisión descriptiva reciente de Lambell y cols. (28) sobre la terapia nutricional en el paciente crítico tampoco se aborda el SNM, pero se presentan datos de estudios interesantes sobre nutrición en subgrupos específicos (pacientes desnutridos, obesos, no ventilados mecánicamente), así como tras al alta de la UCI.

Los resultados del presente estudio deben interpretarse teniendo en cuenta algunas limitaciones, como la disminución del número de participantes que completaron la encuesta tras la intervención, lo que podría deberse a la rotación del personal, a la carga asistencial o a los meses asignados para completar la encuesta. Ello, por otra parte, reforzaría aun más las mejoras obtenidas. Los datos no se han analizado estadísticamente y, por tanto, las estimaciones de los efectos cuantitativos son meramente descriptivas. Tampoco se puede excluir el sesgo de información en función de la habilidad docente de cada formador. No obstante, el carácter multicéntrico del estudio, con la participación de 19 UCI distribuidas en diferentes territorios del país, ofrece una aproximación real a la problemática del SNM en el paciente crítico.

En resumen, la formación y el diseño del algoritmo de actuación en el SNM han logrado una sólida consolidación de los principales conceptos de esta estrategia. Algunos aspectos referentes a cómo manejar al paciente desnutrido, cómo identificarlo y qué tipo de nutrición pautar desde el inicio del ingreso en la UCI, los aportes nutricionales en situaciones especiales y el seguimiento de posibles complicaciones como la realimentación, son áreas en las que convendría insistir para diseñar estrategias formativas específicas.

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ARÁN

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Trabajo Original

Pediatría

Are Spanish children drinking enough and healthily? An update of the Liq.in[7] cross-sectional survey in children and adolescents

¿Beben los niños y adolescentes españoles lo suficiente y de forma saludable? Actualización del estudio transversal Liq.in[7] en niños y adolescentes

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Abstract

Introduction: insufficient and/or unhealthy total fluid intake (TFI), especially in the early stages of life, may have a negative impact on health.

Objective: to assess the current patterns of fluid consumption in children and adolescents in Spain, including drinking occasions and locations (e.g., at home or at school), and to compare TFI with adequate intake (AI) of water from fluids as recommended by the European Food Safety Agency (EFSA).

Methodology: a Spanish cross-sectional study was performed assessing TFI from all sources of fluid consumption according to drinking occasions during the day and location, using a validated liquid intake 7-day record (Liq.in[7]). Data collection occurred between April and May, 2018. A sample of 146 (63 % boys) children (4-9 years old) and adolescents (10-17 years old) was included. Parents reported such information when children were under 16 years.

Results: a high proportion of children and adolescents did not meet EFSA-derived reference values for fluid intake (73 % and 72 %, respectively). Forty percent of children and about 50 % of adolescents consumed at least one serving of sugar-sweetened beverage (SSB) per day, while about 20 % consumed only one or less servings of water per day. Consumption during the main meals was most important for both children and adolescents (representing 50 % and 54 % of TFI, respectively), and was mainly driven by water (62 %). Consumption at home in children (70 % of TFI) was made of water (47 %). In the same way, at school, water contributed to half intake. However, adolescent girls at school drink more SSBs (41 %) than water (34 %), the former being the most consumed fluid. At other locations, adolescent boys also drink more SSBs (51 %) than either water (29 %) or milk and derivatives (10 %).

Conclusion: the drinking habits of Spanish young populations are far removed from current recommendations because of a low fluid intake, specifically water, and a high proportion of SSB consumption in children and adolescents. Interventions to ensure that EFSA TFI recommendations are met are of special importance for children and adolescents, with — according to our results — a special focus on male adolescents.

Keywords:

Total fluid intake. Children and adolescents. European Food Safety Authority.

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Resumen

Introducción: la ingesta total de líquidos insuficiente o poco saludable, especialmente en las primeras etapas de la vida, puede tener un impacto negativo sobre la salud.

Objetivo: evaluar el patrón actual de consumo de líquidos en niños y adolescentes en España, incluyendo el número de veces y los lugares para beber, y comparar la ingesta total de líquidos con la ingesta adecuada establecida por la Agencia Europea de Seguridad Alimentaria (EFSA).

Metodología: estudio transversal que evaluó la ingesta total de líquidos utilizando un registro validado de ingesta de líquidos de 7 días (Liq.in7). Se realizó entre abril y mayo de 2018, incluyendo una muestra de 146 niños de 4 a 9 años y adolescentes de 10 a 17 años españoles (63 % varones). Los padres detallaron dicha información en caso de que los niños fueran menores de 16 años.

Resultados: una alta proporción de niños y adolescentes no cumplían con los valores de referencia de la EFSA para la ingesta de líquidos (73 % y 72 %, respectivamente). El 40 % de los niños y aproximadamente el 50 % de los adolescentes consumían al menos una porción (250 ml) de bebidas azucaradas por día, y el 20 % consumían una porción o menos de agua al día. Durante las comidas principales se consumía la mayor cantidad de líquidos tanto en los niños como en los adolescentes (representando el 50 % y el 54 % de la ingesta total de líquidos, respectivamente), principalmente agua (62 %). El consumo de los niños en el hogar (70 % de la ingesta total de líquidos) también consistía principalmente en agua (47 %). Del mismo modo, en la escuela, el agua contribuía a la mitad de la ingesta. Sin embargo, los adolescentes en el instituto bebían más bebidas azucaradas (41 %) que agua (34 %). En otros lugares, los adolescentes varones también bebían más bebidas azucaradas (51 %) que agua (29 %) o leche y derivados (10 %).

Conclusión: de acuerdo con nuetros resultados, la población joven española no cumple las recomendaciones actuales tanto por presentar una baja ingesta total de líquidos como por realizar un alto consumo de bebidas azucaradas. Es importante que las intervenciones que intenten mejorar la ingesta de líquidos en los niños y adolescentes basen sus objetivos en alcanzar los valores de referencia de la EFSA con un enfoque especial, según nuestros resultados, consistente en mejorar los comportamientos de ingesta de líquidos en los adolescentes varones.

Palabras clave:

Ingesta total de líquidos. Niños y adolescentes. Autoridad Europea de Seguridad Alimentaria.

INTRODUCTION

Water is the most basic requirement of all living beings, ensuring the maintenance of normal physical and cognitive functions (1). Insufficient fluid intake has been associated with adverse health effects in adults (2), (El-Sharkawy, 2015, Acute and chronic effects of hydration status on health;Perrier, 2020 #42)and with cognitive impairment in children (3). Childhood is an important period for the adoption of healthy habits, including those related to total fluid intake (TFI), as adopting healthy dietary habits during childhood can facilitate their maintenance through adulthood (4). Besides, drinking sugar-sweetened beverages (SSBs) instead of water has been widely associated with an increase in body fat, and classified as one of the most important risk factors for overweight and obesity during childhood (5-7).

Age- and sex-specific reference values for an adequate intake (AI) of water have been established by the European Food Safety Authority (EFSA) (8). Specifically, the EFSA AI for total water (i.e., water coming from both foods and beverages) is set at 1600 mL/day for boys and girls aged 4-8 years, and at 1900 mL/day for girls and 2100 mL/day for boys aged 9-13 years. Adolescents over 14 years of age are considered as adults, with AIs set at 2000 and 2500 mL/day for women and men, respectively. Although EFSA AIs are based on total water, it is estimated that roughly 20 % of water intake comes from solid foods, while the majority, or roughly 80 %, comes from beverages and drinking water. Thus, it is possible to approximate the AI for water from fluids as 80 % of the dietary reference values mentioned above. These reference values only apply in moderate environmental temperatures and at moderate physical activity levels, so specific conditions must be carefully considered.

Unfortunately, some studies have shown that a high proportion of children and adolescents do not drink enough to meet an adequate water intake (9). A cross-sectional survey conducted in 13 countries worldwide determined that more than fifty percent of the whole study population were at risk of inadequate fluid intake (10). Moreover, a survey performed in children and adolescents in Latin America, Europe, and Asia concluded that plain water accounted for less than half of TFI, and indicated a prevalent consumption of caloric fluids including juices (11). A recent study in 27 cities in China concluded that only 45 % and 36 % of children and adolescents met the AIs for total fluid intake set by the Chinese Nutrition Society (12), and ranked SSB consumption among the top three sources of fluid intake, together with water and milk (13). Another study performed in Indonesia observed that water was the most frequently consumed drink; however, 24 % of children and 41 % of adolescents consumed at least one serving of SSB per day (14) (national cross-sectional survey). Another study conducted in Latin America, whose participants were children and adolescents, also observed that water and SSBs were the most commonly consumed beverages in this population (15) (national cross-sectional survey). Finally, in a very recent review (16), 12 out of 24 studies reported a mean/median water/fluid intake below recommended levels, while 4 out of 13 studies reporting hydration status indicated under-hydration based on urine osmolality (greater than 800 mOsm.kg^{-1}).

While what children drink is well documented, far less is known about their fluid intake patterns, including the beverages preferred at different moments of consumption during the day, and the beverages chosen for consumption inside or outside the home. Understanding how fluid consumption may differ throughout the day or as a function of location could help drive policy initiatives to encourage healthier drinking habits. As few studies in Spain have focused on the patterns of fluid consumption in young population groups, the aim of our study was to assess the current patterns of fluid consumption among children and adolescents in Spain, including drinking occasions and locations (e.g., at home or at school), and to compare their TFI with the adequate intake (AI) of water from fluids as recommended by the European Food Safety Agency (EFSA).

METHODOLOGY

DESIGN AND STUDY POPULATION

The present analysis reports on a cross-sectional survey in Spain, which was part of a recurring, multinational fluid intake survey campaign using the Liq.In^7 questionnaire. The objective of this survey was to assess all sources of fluid consumption, including water and different types of beverages, and their association with other lifestyle variables. The recruitment of participants and further details of the populations included in this analysis have been previously described (17). Briefly, a subsample of 167 (63 % boys) children and adolescents (4-17 years old) were included between April and May, 2018. Participants were recruited via an existing dataset and contacted electronically using a quota-based sampling for age, sex and Nielsen areas, in relation to the total country population and confirmed by the National Statistical Institute (18). Recruitment was limited to one individual per household. Participants who had a parent or a caregiver who was illiterate, or working in a company advertising, marketing, doing market research for, manufacturing, distributing or selling different types of beverages were excluded from participation, as these individuals might be more aware of their fluid intake. Taking medication or suffering from a medical condition (dialysis, heart diseases, etc.) requiring restricted fluid intake, and following a specific diet were also exclusion criteria. Coupons for free products were offered to parents or caregivers for taking part in the study. Each child's parent or caregiver consented to participate via an online questionnaire, and all data were recorded anonymously.

ASSESSMENT OF FLUID INTAKE AND OTHER VARIABLES

Participants or their parents reported all their fluid intake by completing the Liq.In^7 questionnaire, a 7-day fluid-specific record previously validated for accuracy and reliability (19), every time they drank something (any drink; e.g., water, beverages, cold and hot drinks, alcohol) for a period of 7 continuous days. For children and adolescents under the age of 16 years a single parent was responsible for completion of the questionnaires. The participants or their parents could fill in the questionnaire up to 48 hours from the actual time of drinking.

The Liq.In^7 record is structured according to different times of day from awakening, mealtimes (breakfast, lunch, dinner), in-between meal times (morning, just before lunch, afternoon, evening, just before going to bed), until bedtime. The participant or their parent received instructions to report everything they drank at any moment of the day with the following details: fluid type, volume consumed, size of the container used when they were drinking, where the beverage was consumed, and whether food was also consumed, but the specific type of food was not reported.

In addition to the fluid intake assessment, other variables and lifestyle indicators were also evaluated, such as socioeconomic characteristics, region, habitat (urban or rural classification), and parental education level.

CLASSIFICATION AND ANALYSIS OF FLUID TYPES

The included fluid items were: water (tap water, filtered tap water, natural mineral water, sparkling natural mineral water, fountain water); hot beverages (coffee, coffee with milk, espresso with a drop of milk, cappuccino, tea and other infusions and hot beverages); milk and derivatives (milk, milkshakes, milkshakes with juice, liquid yogurt, other milk drinks); sugar-sweetened beverages (SSB) (carbonated soft drinks (CSD), juice-based drinks including nectar, nectar without added sugar, water with juice, other juice drinks, functional beverages including energy drinks, sport drinks, functional water, flavored water, ready-to-drink (RTD) tea and coffee); 100 % fruit juices; artificial/non-nutritive sweetened beverages (A/NSB) (light/zero/sugar-free drinks); other beverages (beverages based on soluble cereals). Total fluid intake was defined as the sum of all these categories. For the analysis, 100 % of fruit juices, A/NSBs, alcoholic beverages, and other beverages were combined under 'other fluid types'.

Individual mean daily TFI was compared with the EFSA-derived AI for water coming from fluids (8). The number of individuals drinking ≤ 1 serving (250 mL) of SSB per week, 2-6 servings of SSB per week and ≥ 1 serving of SSB per day was analyzed. These cut-offs are based on meta-analyses showing that such amounts of SSB are associated with potential risks for the development of metabolic diseases (6,7,20).

STATISTICAL ANALYSIS

Participants who did not complete the full 7-day record, or who reported a mean daily total fluid intake below 400 mL or higher than 4 L/day for children below the age of 14 years, and higher than 6 L/day for children aged 14 to 17 years, were excluded from the present analysis (n = 21). The demographic and anthropometric characteristics of the study population are presented as either mean and standard deviation (21) for continuous variables, or as number and percentage for dichotomous variables. Intake data are skewed, therefore TFI are presented as median and percentiles; mean and standard error of the mean (SEM) are provided for completeness. The intake of different fluid types is also presented as median, 25th and 75th percentiles. The intakes of each fluid type according to drinking occasions and locations are presented as percentage of TFI.

Drinking occasions were classified into three categories: 1) meals, meaning that the act of drinking occurred during a main meal (breakfast, lunch or dinner); 2) snack, meaning that the act of drinking occurred with food but outside a main meal; 3) outside meal, meaning that the act of drinking occurred outside a main meal and without any food (a stand-alone drinking occasion). Locations were classified into three categories: 1) at home, 2) at school

(including cafeterias), and 3) other locations such as restaurants/bars/pubs, transportation, a friend's or acquaintance's home, sports venue, shopping center, street, park, hotel, hospital, etc.

Wilcoxon's signed-rank test was used to compare medians of total fluid intake between sexes. Statistical analyses were performed using the Statistical Package for the Social Sciences software, version 22.0 (SPSS, Inc., Chicago, IL, USA).

RESULTS

SAMPLE DESCRIPTION

Table I shows the characteristics of the sample. In both age categories, girls were underrepresented as compared to boys (42 % and 33 %, respectively, for subjects aged 4-9 years and 10-17 years). The mean ages of the two groups were 6.4 ± 1.8 years for children and 13.2 ± 2.3 years for adolescents. The distribution of the sample across the geography of Spain was aligned with the current population density map of the country, with Andalusia, the Mediterranean area, and areas around Madrid and Barcelona being those most represented. More than half of the sample in both age categories had parents with university degrees.

DAILY TOTAL FLUID INTAKE

The reported TFIs per age group and sex are shown in table II; there were no significant differences by sex or by age. Total median (25^{th}-75^{th} percentiles) values for the two age categories were

Table I. Descriptive characteristics of the survey population (n = 146), by age

	4-9 years		10-17 years	
*Sample size**	*65 (44 %)*		*81 (56 %)*	
Females	27	42 %	27	33 %
Males	38	58 %	54	67 %
Age†	6.4	1.8	13.2	2.3
*Parental educational level**				
University Bachelor/Graduate Degree	16	25 %	15	19 %
Elementary Baccalaureate	4	6 %	10	12 %
Postgraduate Degree	27	42 %	33	41 %
Higher Baccalaureate/Preparatory	9	14 %	15	19 %
Primary education	1	2 %	2	2 %
Vocational training	8	12 %	6	7 %
Preferred not to answer	0	0 %	0	0 %
*Regional areas**				
Area 1: Catalonia-Aragon	1	2 %	2	2 %
Area 2: Levante	15	23 %	17	21 %
Area 3: South	15	23 %	14	17 %
Area 4: Center	2	3 %	7	9 %
Area 5: North-Center	9	14 %	16	20 %
Area 6: Northwest	5	8 %	1	1 %
Area 7: Metropolitan Area of Barcelona	6	9 %	12	15 %
Area 8: Metropolitan Area of Madrid	12	18 %	12	15 %
*Annual Household Income**				
Under € 10 000	5	8 %	1	1 %
€ 10 000 to € 15 000	3	5 %	3	4 %
€ 15 001 to € 20 000	9	14 %	6	7 %
€ 20 001 to € 30 000	16	25 %	25	31 %
€ 30 001 to € 40 000	10	15 %	12	15 %
€ 40 001 to € 60 000	14	22 %	18	22 %
more than € 60 000	4	6 %	4	5 %
Preferred not to answer	4	6 %	12	15 %

**Data are expressed as numbers (percentage for categorical variables). †Data are expressed as mean ± SD for continuous variables.*

Table II. Daily total fluid intake (mL/day) among children (4-9 years) and adolescents (10-17 years) by sex

Age group	Sex	TFI Mean ± SEM	Percentiles							Sex differences*	Age differences†
			5	10	25	50	75	90	95		
4-9 years	Total	1184 ± 67	555	609	758	1109	1424	1936	2124	NS	NS
	Females	1133 ± 85	584	614	748	1108	1339	1934	2058		
	Males	1220 ± 99	519	580	782	1124	1477	1985	2591		
10-17 years	Total	1321 ± 68	518	690	849	1181	1773	2206	2299	NS	
	Females	1374 ± 128	520	714	849	1181	1805	2087	3055		
	Males	1294 ± 80	499	650	790	1177	1682	2249	2343		

*TFI: total fluid intake; SEM: standard error of the mean; NS: not statistically significant. *Wilcoxon's test was performed to compare medians between sexes. †Wilcoxon's test was performed to compare medians between age groups.*

1109 (758-1424) and 1181 (849-1773) mL/day for subjects aged 4-9 years and 10-17 years, respectively.

COMPARISON WITH EFSA REFERENCE VALUES

Figure 1 shows the proportion of participants consuming ≤ 50 %, 50-75 %, 75-100 %, and ≥ 100 % of the AI of water from fluids derived from the EFSA AI for total water (22). Seventy-two percent of children and 73 % of adolescents failed to meet the TFI AIs derived from the EFSA reference values. Among children, females were less likely to meet the AIs than males (22 % and 32 %, respectively), while the opposite was observed among adolescents, with females more likely to achieve the EFSA AI of water from fluids than adolescent males (41 % and 20 %, respectively). One third of adolescent males consumed ≤ 50 % of the AI of water from fluids, compared to 11 % for adolescent females.

DAILY INTAKE OF DIFFERENT FLUID TYPES

Median daily intake of the different fluid types is shown in table III by age category and sex. Water was the most commonly consumed beverage, both in males and females, across both age

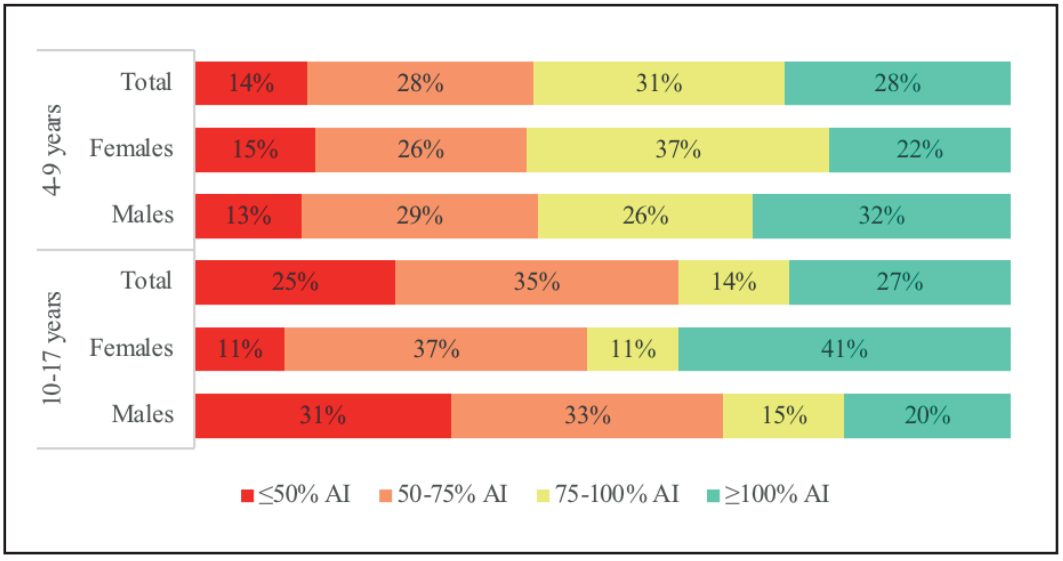

Figure 1.

Percentage (%) of participants according to adherence to EFSA AI recommendations for water from fluids among children (4-9 years) and adolescents (10-17 years). AI: adequate intake.

AIs for water from fluids were derived from the EFSA AIs for total water, assuming that 80 % of total water comes from water and other beverages: thus, the AIs for water from fluids were set at 1.28 L/d for girls and boys aged 4-8 years; 1.52 and 1.68 L/d for girls and boys, respectively, aged 9-13 years; and 1.6 and 2.0 L/d for girls and boys, respectively, aged 14 years and older.

Table III. Median (P25-P75) daily intake (mL/day) of different fluid types by gender among children (4-9 years) and adolescents (10-17 years)

	4-9 years							10-17 years						
	Total			Females		Males		Total			Females		Males	
	Median	P25	P75	Median	P25	Median	P25	Median	P25	P75	Median	P25	Median	P25	P75
Water	*470*	*319*	*691*	*448*	*249*	*485*	*346*	*496*	*308*	*805*	*684*	*259*	*477*	*326*	*765*
Tap water	94	0	453	71	0	156	0	118	0	519	71	0	130	0	575
Bottled water	198	23	465	249	0	192	32	159	0	431	177	0	145	22	401
Milk & derivatives	*311*	*201*	*441*	*274*	*219*	*332*	*163*	*236*	*118*	*380*	*248*	*151*	*200*	*103*	*373*
SSB	*170*	*71*	*311*	*189*	*107*	*156*	*65*	*236*	*130*	*392*	*237*	*133*	*208*	*122*	*405*
CSD	0	0	41	0	0	0	0	47	0	94	47	0	47	0	94
Juice-based drinks	107	47	203	107	47	114	44	141	0	202	141	9	124	0	197
Flavored water	0	0	0	0	0	0	0	0	0	45	0	0	0	0	47
Functional beverages	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RTD tea & coffee	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hot beverages	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*84*	*0*	*0*	*0*	*0*	*88*
Other fluid types	12	0	94	0	0	41	0	47	0	141	24	0	47	0	218

SEM: standard error of the mean; SSB: sugar-sweetened beverages; CSD: carbonated, sweetened drinks; RTD: ready-to-drink.

groups, representing 470 (319-691) mL/day in children and 496 (308-805) mL/day in adolescents. Water was followed by milk and derivatives, and by SSBs in both age groups. Together, these three categories accounted for an average of 95 % and 88 % of TFI in children and adolescents, respectively. Median intake of other fluid types is the combination of 100 % fruit juices, A/NSB and other beverages to make reading easy because the volume consumed of each of this specific fluid types was very low.

Table IV shows that most of the children and adolescents drank 2 or more servings of SSB per week (89 % and 95 %, respectively), and that 40 % of children and almost 50 % of adolescents drank ≥ 1 serving per day. When comparing males and females, a higher proportion of males drank 1 or more than 1 serving of SSB per day in both age groups. Around 20 % of both children and adolescents drank less than 1 serving of water per day, with a higher proportion of females consuming less than 1 serving compared to males.

FLUID INTAKE ACCORDING TO DRINKING OCCASIONS

The volume and contribution of the different fluid types to TFI according to occasions are shown in figure 2, while the median intakes are shown in table V.

Fluid intake during meals

In both children and adolescents, the largest proportion of TFI was consumed during main meals (representing 50 % and 54 % of TFI, respectively). During main meals, water was the main contributor to TFI regardless of age or sex (62 % overall). There was no significant difference in the volume of water consumed at main meals between children (288 (195-514) mL/day) and adolescents (401 (243-625) mL/day). In children, water consumption tended to be a larger contributor for males compared to females (66 % and 60 %, respectively); while in adolescents, water consumption was a larger contributor for females compared to males (68 % and 58 %, respectively).

When focusing on SSB contribution, juice-based drinks were the most popular drinks in children at all drinking occasions compared to other types of SSB. In adolescents, juice-based drinks remained the first contributor to SSB, but we observed an increase of CSD contribution when compared to children, with a similar contribution of juice-based drinks during meals (6 %).

Fluid intake during snack occasions

Overall, 25 % of TFI occurred during snack occasions (27 % and 23 % of the TFI among children and adolescents, respectively). In contrast to meals, where water was the dominant beverage, the consumption of milk and derivatives (54 % and 41 % of TFI, respectively) dominated during snack occasions, representing a

Table IV. Percentage (%) of children (4-9 years) and adolescents (10-17 years) by category of SSB consumption, and percentage consuming less than one serving of water daily

	Gender	SSB			Water
		0-1 serving/week	2-6 serving/week	≥ 1 serving/day	< 1 serving/day
4-9 years	Total	7 (11 %)	32 (49 %)	26 (40 %)	12 (18 %)
	Females	2 (7 %)	15 (56 %)	10 (37 %)	7 (26 %)
	Males	5 (13 %)	17 (45 %)	16 (42 %)	5 (13 %)
10-17 years	Total	4 (5 %)	37 (46 %)	40 (49 %)	14 (17 %)
	Females	1 (4 %)	15 (56 %)	11 (41 %)	6 (22 %)
	Males	3 (6 %)	22 (41 %)	29 (54 %)	8 (15 %)

SSB: sugar-sweetened beverages.

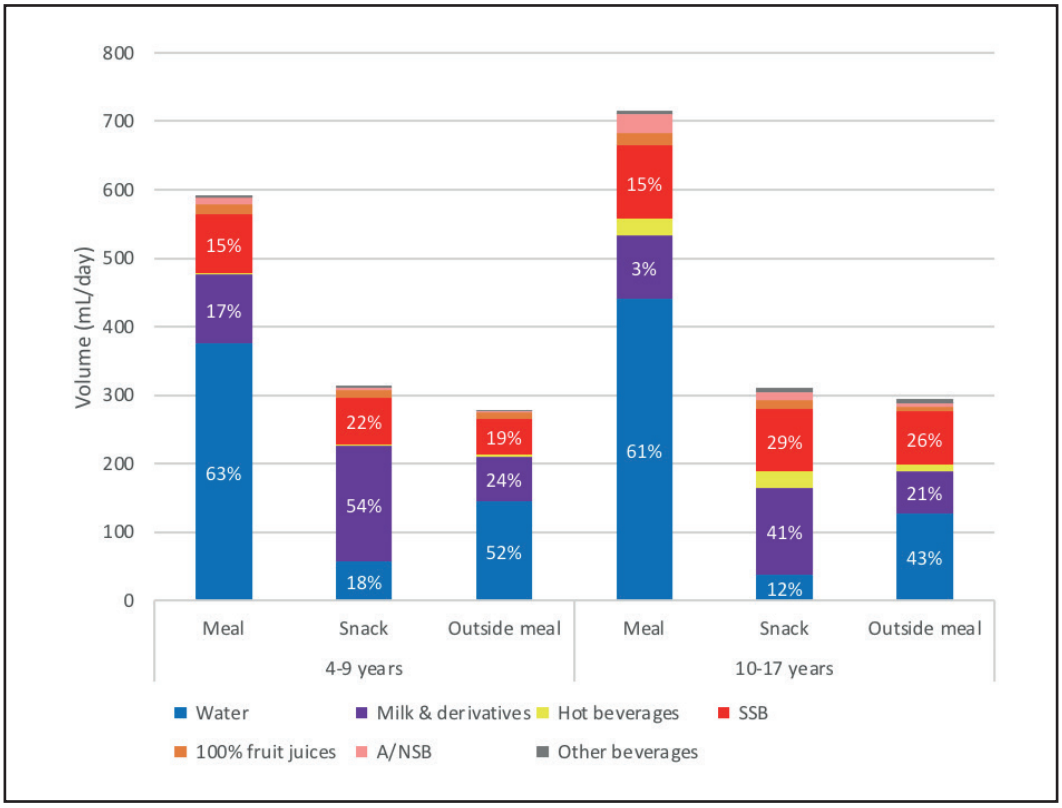

Figure 2.

Volume (mL/day) and contribution (%TFI) of each beverage group to total fluid intake per drinking occasion in children (4-9 years) and adolescents (10-17 years). SSB: sugar-sweetened beverages; A/NSB: artificial/non-nutritive sweetened beverages.

higher contribution to TFI than SSB (22 % and 29 %, respectively) and water (18 % and 12 %, respectively).

Fluid intake outside of meal occasions

Beverages consumed outside of meals represented 24 % and 22 % of TFI among children and adolescents, respectively. Outside meals, water was the main contributor to TFI for both age groups. As during main meals, milk and derivatives, and SSB were the following main contributors to TFI. We observed sex differences among adolescents, with milk and derivatives playing a larger role in females than in males. Specifically, in females, milk and derivatives and SSB had a similar contribution to TFI (29 % and 26 %, respectively), while in males SSB contributed to 27 % and milk and derivatives to 17 % of TFI.

Table V. Median (P25-P75) intake (mL/day) of different fluid types according to drinking occasions among children (4-9 years) and adolescents (10-17 years)

	4-9 years								10-17 years							
	Meal			Snack			Outside meal		Meal			Snack			Outside meal	
	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75
Water	288	195	514	18	0	86	118	33	213	401	243	625	0	0	47	47	0	160
Tap water	78	0	242	0	0	18	0	0	117	83	0	395	0	0	0	0	0	47
Bottled water	106	0	339	0	0	47	31	0	101	118	0	377	0	0	4	0	0	68
Milk & derivatives	47	0	147	130	31	260	24	0	83	47	0	141	71	0	177	0	0	91
SSB	47	0	129	36	0	94	36	0	71	71	0	148	47	0	130	36	0	119
CSD	0	0	9	0	0	0	0	0	0	0	0	47	0	0	0	0	0	0
Juice-based drinks	0	0	71	29	0	71	12	0	47	0	0	50	0	0	71	0	0	47
Flavored water	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Functional beverages	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RTD tea & coffee	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hot beverages	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other fluid types	0	0	12	0	0	37	0	0	0	0	0	53	0	0	36	0	0	22

SSB: sugar-sweetened beverages; CSD: carbonated, sweetened beverages; RTD: ready-to-drink.

FLUID INTAKE ACCORDING TO LOCATION

In figure III, the volume and contribution of fluid types according to locations are shown, whereas median intakes (P25-P75) are shown in table VI. In both children and adolescents, the largest consumption of TFI was at home (representing 70 % and 79 % of TFI, respectively). For children, water was the most common beverage consumed at home (47 %), followed by milk and derivatives, and SSB with no relevant differences between males and females. In school, water contributed to half of TFI, followed by SSB and milk and derivatives. No sex differences were observed.

These observations at school were similar to those at other out-of-home locations. These trends were also found for adolescents at every location with some exceptions: adolescent girls at school drank more SSB (41 %) than water (34 %), and adolescent boys at other locations, who reported a higher contribution of SSB (51 %) than water (29 %) or milk and derivatives (10 %).

In terms of absolute volumes consumed, outside of the home (i.e., at school or in other locations), children and adolescents barely consumed water. Children in other locations (except school) drank at least 1 glass of water (94 (19-163) mL/day).

DISCUSSION

There is increasing interest in the fluid consumption patterns of mainly young populations due to its impact on physical (23) and cognitive performance (24,25) and on body weight-related disorders and their consequences (26). In this study performed in Spanish children and adolescents, we observed that more than 70 % of children and adolescents do not meet the TFI AIs derived from the EFSA reference values (8). For both children and adolescents, water was the most consumed beverage by males and females, contributing to half of TFI, followed by milk and derivatives and by SSBs. Collectively, these three beverage categories reached up to 95 % of TFI and consistently represented the top 3 categories of beverage consumption across age, sex, occasion (meals, snacks, out of meals), and location (home, school, other) categories. The mean SSB intake observed in this survey pointed at almost half of the population consuming SSB on a daily basis. Additionally, some youths drink less than 1 serving (250 mL) of water per day, especially at school. Most of fluid consumption occurred at home (70 % and 79 % for children and adolescents, respectively) and during the main meals, with around half of consumption mainly driven by water across gender and age groups; the rest of intakes were quite equally distributed between snacks and out-of-meal moments. Water consumed during snack times was low, with SSB intake being higher than water consumption.

Compared to the same survey methodology as performed in 2012 (10), mean TFI was strikingly lower than what was previously reported in any of the sex/age categories (more than 500 mL lower than previously reported in male children or adolescents, and approximately 400 mL lower in female children or adolescents). Consequently, the percentage of non-adherence to EFSA-derived adequate intakes is substantially higher than previously reported.

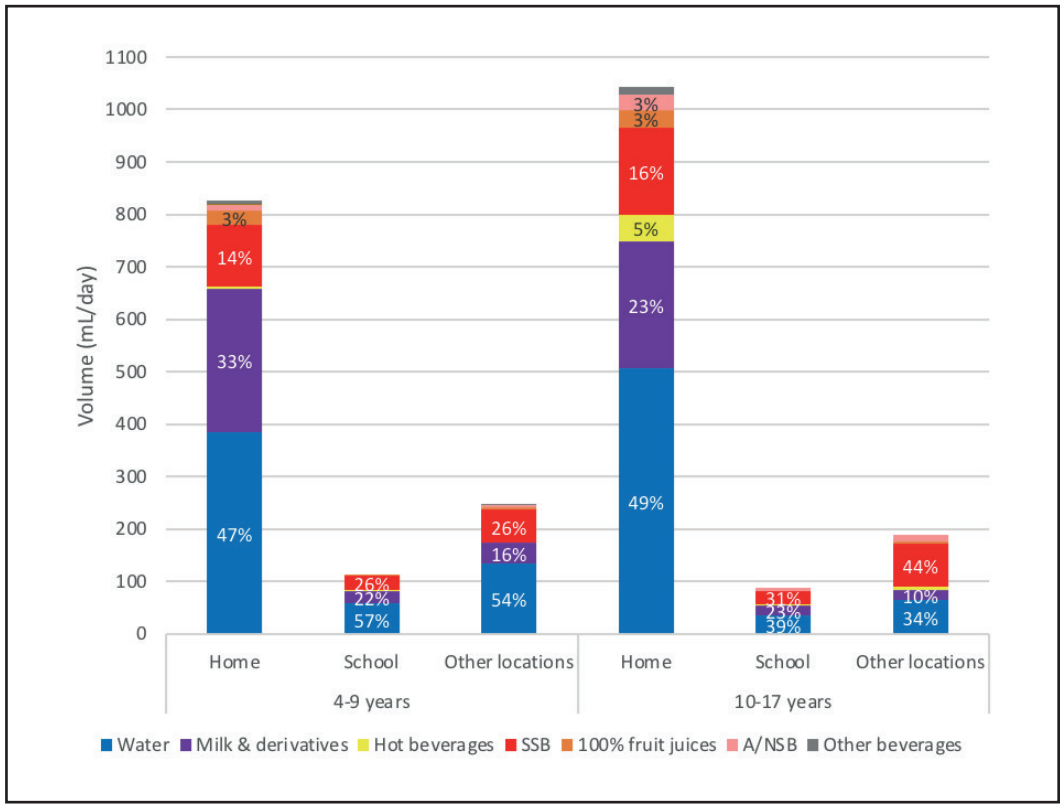

Figure 3.

Volume (mL/day) and contribution (%TFI) of each beverage group to total fluid intake per drinking location in children (4-9 years) and adolescents (10-17 years). SSB: sugar-sweetened beverages; A/NSB: artificial/non-nutritive sweetened beverages.

While children aged 4-9 showed a higher level of compliance with EFSA-derived AIs (8) compared to adolescents in a 2015 publication, the current study shows this is no longer the case.

Moreover, female children aged 4 to 9 years adhered less to EFSA-derived AI values than males, while in adolescents the opposite was observed, with females being more likely to consume adequate fluids than males. Similar findings were observed in a Spanish survey performed in 2012, as well as in other countries such as in Indonesia, Turkey, and Mexico (10). A potential explanation, could be that boys of younger age are more likely to perform activities that require more energy expenditure than girls of the same age (27), whereas adolescent girls are normally more worried about their health and might try to be well hydrated (28). The very low differences in fluid consumption between age groups are striking. For instance, specifically, TFI both at snack times and outside meals did not differ between children (314 and 278 mL, respectively) and adolescents (310 and 294 mL, respectively). Despite having a larger body size and presumably higher water needs, and despite higher EFSA AIs for water intake, male adolescents did not consume more water than their younger counterparts, so this might be of concern from a physiological point of view since their hydration needs are presumably higher. The difference observed between male adolescents and male children is slightly supported by other European studies showing a decrease in milk intake between childhood and adolescence (29,30). Both children and adolescents have lower intakes of water and of milk and dairy products when compared to a survey published in 2015 (11). This observation is supported by some other surveys showing that milk consumption by children is decreasing over time (30-32). Contrary to what has been shown in other surveys (33,34), this decrease in milk consumption is accompanied by a very slight increase in the consumption of sugar-sweetened beverages. In Europe, adolescents consume more SSBs than older adults and younger children, and there is also some grey literature suggesting children as young as one year old are already consuming SSBs (35).

The intake according to drinking occasions was also observed in a 2014 publication, with 54 % of fluid consumption occurring during main meals, mainly driven by water (17).

SSB consumption raises concerns given their negative effects on children's health (7,20,36), and this applied to the Spanish population, where an increment in soft drink consumption by 100 mL has previously been associated with a 0.21 kg/m² increase in BMI (37). In addition, the WHO Childhood Obesity Surveillance Initiative (COSI) observed that the prevalence of obesity among the Spanish population is in the highest level of child obesity with

Table VI. Median (P25-P75) intake (mL/day) of different fluid types according to different locations among children (4-9 years) and adolescents (10-17 years)

	4-9 years							10-17 years						
	Home			School		Other locations		Home			School		Other locations	
	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75
Water	330	160	486	0	0	65	94	19	163	436	221	702	0	0	42	18	0	94
Tap water	76	0	327	0	0	16	0	0	49	94	0	448	0	0	0	0	0	0
Bottled water	71	0	306	0	0	29	36	0	116	90	0	333	0	0	0	0	0	94
Milk & derivatives	249	129	354	0	0	36	0	0	63	204	106	369	0	0	0	0	0	0
SSB	61	0	201	0	0	36	47	0	94	141	55	236	0	0	0	47	0	108
CSD	0	0	9	0	0	0	0	0	0	0	0	47	0	0	0	0	0	47
Juice-based drinks	36	0	141	0	0	6	29	0	49	71	0	154	0	0	0	0	0	47
Flavored water	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Functional beverages	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RTD tea & coffee	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hot beverages	0	0	0	0	0	0	0	0	0	0	0	77	0	0	0	0	0	0
Other fluid types	7	0	89	0	0	0	0	0	0	47	0	100	0	0	0	0	0	5

SSB: sugar-sweetened beverages; CSD: carbonated, sweetened beverages; RTD: ready-to-drink.

approximately 1 in 5 boys, as is also the case in other southern European countries (38). Therefore, more public health policies are needed to slow down and, hopefully, reverse this obesity rate. Of particular concern is the apparently continued rise in SSB consumption among the Spanish and other European populations (increase by 1.2 % in soft drink sales in the EU between 2017 and 2018) (39), whereas we observe a tendency towards a decrease in SSB consumption in other countries such as the USA (40,41). Recent results regarding the effects of SSB taxation in Catalonia, which was introduced on May 1, 2017, have shown a reduction in the consumption of such products (42-44). For now, taxes have been implemented in several countries but the effects on the population's health status have not been examined yet. A recent meta-analysis observed that taxes on SSB reduced also sales and consumption (45). Moreover, some health economic modelling studies suggests promising results of SSB taxes' effect on overweight and obesity (46-49).

In Spain, the average sugar content of SSBs is 10 g per 100 mL, representing 100 kcal (50). Knowing that the estimated, recommended daily energy intake of children and adolescents is about 1800 and 2500 kcal, respectively (51), the consumption of SSBs on a daily basis represents 5.5 % and 4 % of the total energy intake. This observation shows that with only one serving of SSB per day, youths already complete half of the 10 % individual's daily calorie intake coming from added sugars (any sources of sugar, not only from beverages) recommended by the WHO (52).

In addition to SSB-related concerns, the very low water intake seen both in children and adolescents, especially at school, is particularly of concern knowing the importance of good hydration on cognition, especially when these subjects spend most of their day at school (24). Therefore, school-based interventions can play a key role in creating a water-friendly environment for children and adolescents (53). In a certain way, parenting role modelling and controlling home beverage availability may have an impact on the beverage intake behaviors of children (54) when some studies showed that when there were more SSBs available in the home or school environment, children also consume more (55-57). These specific drinking occasions and snack times, because of their low contribution to TFI, might suppose a window of opportunity for substituting water for SSBs and for adding water as a target for future nutritional interventions in young populations.

The most important strength of this study is that the method used to evaluate fluid intake was previously validated for accuracy and reliability (19), even if this validation was performed in an American adult population. Besides, the collection of 7-day records of fluid consumption, providing a representation of a full week and capturing all drinking occasions, may also be considered an important strength (19). A similar survey published in 2015 was also performed under similar conditions and during a similar period of the year, so both may be comparable (11).

However, there are also a number of limitations, mainly related to the data collection performed at school and the sampling method. For the majority of children, a parent was the person responsible for filling in the questionnaire, and thus it is likely that fluid intake at school was underestimated since children would need

to be able to accurately report to their parents what they drank at school upon returning home. The questionnaire for measuring total daily fluid intake has been validated as accurate against a gold standard for water turnover (19), but this validation did not assess the accuracy of the questionnaire at specific locations. Inaccuracies between child recall and parent reporting may be one reason for the very low fluid intake reported at school; however, this low fluid intake is also consistent with other reports in several countries (58,59). The participants were recruited as being part of a database; only individuals having a telephone number were included. Therefore, very low socioeconomic groups could be underrepresented, which may be deducted from the distribution of educational levels among participating parents. Due to the methodology used, with parents/caregivers reporting intakes for children under 16 years of age, consumption may be under- or over-estimated. It should also be acknowledged that no biomarkers of hydration were measured, therefore no conclusions related to the hydration status of children are possible. Furthermore, the fact that the sample was not very large may also represent a limitation**.**

CONCLUSION

This study provides valuable information on fluid intake in a selected sample of Spanish children and adolescents. In combination with previously published data, this most recent survey reiterates the fact that a very low percentage of children and adolescents are drinking liquids adequately. This situation is especially relevant for adolescent boys whose consumption is similar to the one of their younger counterparts while their hydration needs are different. In parallel, the message of the importance of increasing water intake is a necessity as results showed children and adolescents drinking less water than previously with no change in SSB consumption. This behavior, at a time in life when consumption habits are defined that will persist into adulthood, may lead to an increased risk of developing overweight and obesity. It seems that there is a window of opportunity mainly at snack times and outside the meals for changing the pattern of drinking beverages by substituting water for SSBs or by just helping children and adolescents to drink more water at this specific occasions, as well as in other locations other than home. Future research should focus on longitudinal tracking of well-defined populations and study the influence of parental and peers modelling to determine those at higher risk and to provide adequate tools for prevention and intervention in order to slow down the current tendencies in drinking fluids among young population groups.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Pediatría

Percepción de soledad, felicidad y salud, y calidad de la dieta. El rol moderador del estado ponderal

Perception of loneliness, happiness, and health, and quality of diet. The moderator role of weight status

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Resumen

Objetivo: determinar la relación existente entre la percepción de soledad, felicidad y salud, y la calidad de la dieta, observando el rol moderador del estado ponderal en escolares de primaria durante el estado de alarma decretado por la COVID-19.

Métodos: estudio descriptivo transversal de una muestra de 116 escolares españoles. Las percepciones de soledad, felicidad y salud se valoraron mediante tres ítems del cuestionario *Health Behavior in School-aged Children*. La calidad de la dieta mediterránea se valoró a través del cuestionario *Índice de calidad de la dieta mediterránea en niños y adolescentes*. Las variables antropométricas se recogieron a través de un cuestionario autoinformado y para el cálculo del índice de masa corporal se empleó el índice de Quetelet (kg/m^2).

Resultados: el análisis descriptivo no mostró diferencias en la percepción de soledad, felicidad y salud, la calidad de la dieta, y las variables antropométricas ($p > 0,005$), a excepción del peso ($p < 0,005$), según el sexo. El análisis inferencial mostró que los valores más elevados en la calidad de la dieta se correlacionan con valores más altos en la percepción de felicidad y de salud ($p < 0,005$). Por su parte, la prueba de la regresión lineal mostró asociación entre la calidad de la dieta y la percepción de felicidad tras ajustarse el modelo al normopeso ($R^2 = 0,382$; $p < 0,005$). Asimismo, mostró una asociación significativa entre la calidad de la dieta y la percepción de salud tras ajustarse el modelo a los escolares con sobrepeso ($R^2 = 0,455$; $p < 0,005$).

Conclusión: la asociación entre la percepción de salud y de felicidad con la calidad de la dieta parece estar moderada por el estado del peso.

Palabras clave:

Estilo de vida. Cognición. Salud. Nutrición. Dieta. Infancia.

Abstract

Aim: to determine the relationship between perceived loneliness, happiness, and health, and quality of diet, observing the moderator role of weight status in elementary school children during the state of alarm decreed for COVID-19.

Methods: a descriptive, cross-sectional study in a sample of 116 Spanish schoolchildren. The perception of loneliness, happiness, and health was assessed using three items of the Health Behavior in School-aged Children questionnaire. The quality of their Mediterranean diet was assessed using the Mediterranean Diet Quality Index quetsionnaire for children and adolescents. Anthropometric variables were collected through a self-reported questionnaire, and for the calculation of body mass index the Quetelet index (kg/m^2) was used.

Results: the descriptive analysis showed no differences in the perception of loneliness, happiness, or health, quality of diet, or anthropometric variables ($p > 0.005$), except for weight ($p < 0.005$), according to sex. The inferential analysis showed that higher values in quality of diet are correlated with higher scores in perceived happiness and health ($p < 0.005$). In turn, the linear regression test showed an association between quality of diet and perception of happiness after the model was adjusted for normal weight ($R^2 = 0.382$; $p < 0.005$). Likewise, it showed a significant association between quality of diet and perception of health after the model was adjusted for overweight schoolchildren ($R^2 = 0.455$; $p < 0.005$).

Conclusion: the association between perceived health and happiness with quality of diet seems to be moderated by weight status.

Keywords:

Lifestyle. Cognition. Health. Nutrition. Diet. Childhood.

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INTRODUCCIÓN

La pandemia de COVID-19, hecho inesperado, se ha constituido en un factor estresante que impacta en todos los niveles de la vida, incluyendo la salud mental, especialmente por las medidas de emergencia sanitaria de cuarentena, confinamiento y distanciamiento social (1,2).

La investigación en epidemiología social muestra que, dado que somos seres sociales, la comorbilidad de las enfermedades físicas y los trastornos mentales es más alta especialmente en aquellos que tienen una mayor percepción de soledad, debido a la falta o ausencia de relaciones sociales positivas (3). No obstante, algunos escolares pueden sentirse solos a pesar de tener contacto social frecuente, mientras que otros con contacto infrecuente no se sienten solos. Por ello, la soledad es la experiencia subjetiva de estar solo, relacionada con la discrepancia entre la frecuencia deseada y la real del contacto social (4).

Ante esta situación es importante subrayar el importante papel que juega la cognición de un escolar como mediador, ya que un escolar puede preferir estar solo y sentirse feliz y conectado, mientras que otro puede estar rodeado de amigos y seguir sintiéndose solo (5). Ante esta coyuntura, una medida cognitiva subjetiva de las percepciones y prioridades internas es la percepción de salud, que se considera un indicador de salud en las encuestas nacionales e internacionales (6). Diversos estudios han determinado, tanto en la población infantojuvenil (7-10) como en la adulta (11,12), que la percepción de salud puede actuar como predictor del bienestar psicosocial.

A su vez, en una revisión sistemática se ha sugerido que la ingesta dietética puede tener el potencial de influir en el bienestar psicológico (13). En este sentido, la dieta mediterránea es uno de los patrones dietéticos más ampliamente descritos y evaluados en la literatura científica, donde una mayor calidad de la dieta se asocia a un menor riesgo de mortalidad, enfermedades cardiovasculares, enfermedades metabólicas y cáncer (14). Su consumo se caracteriza por una ingesta elevada de verduras, legumbres, frutas, frutos secos, cereales, pescado, marisco y aceite de oliva virgen extra (15). Cada vez hay más pruebas de que una nutrición de calidad es uno de los varios factores clave que dan forma a la composición microbiana durante la infancia y durante toda la vida, lo que afecta a una mejor estructura y función del cerebro (16), ya que la composición de las bacterias residentes en el tracto gastrointestinal puede influir en la función cognitiva (17,18). No obstante, en tres revisiones sistemáticas de ensayos controlados aleatorios donde se analizó la asociación entre la dieta mediterránea y la cognición justifican la necesidad de una investigación adicional (19-21).

Además, cabe mencionar que el tiempo fuera de la escuela durante la pandemia es una situación que condiciona un mayor riesgo de aumento de peso en los escolares, tal como está documentado durante los períodos de receso escolar (22). En este caso, el aislamiento social se asocia a dietas poco saludables (23). Por el temor al contagio, las familias tienden a consumir más comidas procesadas, de alta densidad calórica, que tengan mayor duración en las alacenas y que sean más económicas, por lo que se prevé en esta coyuntura que los escolares estarán realizando ingestas de mayor valor calórico y menor valor nutricional (24).

Sobre la base de estos precedentes, el objetivo de este estudio fue determinar la relación existente entre la percepción de soledad, felicidad y salud y la calidad de la dieta, observando el rol moderador del estado ponderal, en escolares de primaria durante el estado de alarma decretado a causa de la COVID-19.

MATERIAL Y MÉTODO

TIPO DE ESTUDIO Y PARTICIPANTES

Se diseñó un estudio de corte transversal-descriptivo con una muestra de 116 escolares de educación primaria (62 varones y 54 mujeres), con un rango de edad comprendido entre los 8 y los 12 años (M ± DE: 10,22 ± 1,20). Los participantes pertenecían a tres centros educativos públicos, de nivel socioeconómico medio, de Canarias, Málaga y Murcia (España). Estos participantes se seleccionaron mediante muestreo no probabilístico intencional. En primer lugar se contactó con los directores de los centros educativos, informándoles de la investigación y pidiéndoles su consentimiento informado. Una vez recibido este consentimiento, se contactó con los padres o tutores legales de los escolares el 23 de marzo de 2020, informándoles de la investigación y solicitándoles el consentimiento informado. Se excluyeron del estudio aquellos escolares que no entregaron el consentimiento informado. Todos los escolares participaron de manera voluntaria, respetándose el acuerdo de ética de la investigación de la Declaración de Helsinki (2013).

PROCEDIMIENTO

Debido al estado de alarma generado por la COVID-19 (Real Decreto 463/2020, de 14 de marzo), los participantes cumplimentaron el cuestionario a través de la aplicación Google Forms. Antes de la cumplimentación se les explicó detalladamente el cuestionario y se resolvieron todas las dudas a través de la aplicación Webex. En esta sesión "online", los participantes fueron rellenando los cuestionarios de manera anónima, siempre con la supervisión de los investigadores. Cabe destacar que no se detectaron casos perdidos. La recogida de datos se realizó durante los meses de abril y mayo de 2020.

VARIABLES E INSTRUMENTOS

Se utilizó un cuestionario sociodemográfico con preguntas relativas al sexo y la edad de los participantes. Asimismo, los participantes informaron ellos mismos de su peso y talla. El cálculo del índice de masa corporal se realizó a través del índice de Quetelet (kg/m^2). Los participantes se categorizaron en distintos grupos de estado nutricional atendiendo a diferentes criterios. En el estudio se utilizaron los puntos de corte del IOTF (25) según el sexo y la edad.

La percepción de soledad, felicidad y salud se valoró a través de tres ítems extraídos del cuestionario Health Behavior in School-aged Children (HBSC) para escolares de educación primaria (26), tal y como se ha realizado en otro estudio previamente (7). Todas las preguntas utilizadas en el cuestionario HBSC han demostrado una buena fiabilidad y validez en los escolares (27). Los escolares informaron en este trabajo acerca de su estado de salud actual (*En general, usted diría que su estado de salud actual es*) y su percepción de felicidad *(¿Cómo te sientes en tu vida actual?*) a través de una escala tipo Likert con cinco opciones de respuesta, siendo 1 = muy baja y 5 = muy alta. Por su parte, el grado de soledad *(¿Te sientes solo alguna vez?*) se valoró a través de una escala de tipo Likert con cinco opciones de respuesta, siendo 1 = nunca y 5 = siempre.

La calidad de la dieta mediterránea se valoró a través del cuestionario "Índice de calidad de la dieta mediterránea en niños y adolescentes" (KIDMED) (28). Este cuestionario se compone de 16 preguntas dicotómicas que se deben responder con un sí o un no. Estas preguntas versan sobre el consumo de ciertos alimentos asociados al modelo típico mediterráneo. Las respuestas afirmativas a las preguntas que representan un aspecto positivo suman un punto, mientras que las respuestas afirmativas en las preguntas que representan una connotación negativa restan un punto. La puntuación de los participantes en cada ítem debe generar una puntuación global que oscile entre -4 y 12 puntos. Esta valoración de la dieta mediterránea categoriza al alumnado como con una calidad de la dieta alta (≥ 8 puntos), media (4-7 puntos) o baja (≤ 3 puntos).

ANÁLISIS ESTADÍSTICO

La normalidad y la homogeneidad de las varianzas se obtuvieron a través de los estadísticos de Kolmogorov-Smirnov ($p = 0,299$) y Levene ($p = 0,816$), respectivamente. Al observar una distribución normal de los valores registrados, en este estudio se ha optado por un análisis paramétrico. Se realizó la prueba de la "t" de Student para comparar grupos independientes (mujeres *vs*. varones) y un análisis de correlaciones bivariadas y parciales entre las variables del estudio (prueba de Pearson). Asimismo, se realizó un análisis de regresión lineal para estudiar la relación entre la percepción de salud, de felicidad y de soledad y la calidad de la dieta, observando el rol moderador del estado de peso (normopeso = 1, sobrepeso = 2 y obesidad = 3). El análisis de los datos se realizó mediante el programa estadístico IBM SPSS 25.0, fijándose el nivel de significación en el 5 % ($p \leq 0,05$).

RESULTADOS

En la tabla I se presentan los resultados del análisis descriptivo de la muestra del estudio. La prueba de la "t" de Student no arrojó diferencias en términos de percepción de soledad, felicidad o salud, calidad de la dieta y variables antropométricas ($p > 0,005$), a excepción del peso ($p < 0,005$), según el sexo.

Tabla I. Datos descriptivos básicos de la muestra del estudio según el sexo

Sexo	Mujeres (n = 54) M ± DE	Varones (n = 62) M ± DE	P
Edad (años)	10,15 ± 1,22	10,30 ± 1,19	0,504
Peso (kg)	39,26 ± 8,82	43,70 ± 14,23	0,043*
Talla (cm)	143,31 ± 11,06	145,83 ± 12,31	0,247
IMC (kg/m^2)†	19,12 ± 3,67	20,03 ± 4,64	0,242
Percepción de soledad	1,74 ± 0,86	1,85 ± 0,93	0,514
Percepción de felicidad	3,46 ± 0,61	3,51 ± 0,60	0,657
Percepción de salud	3,50 ± 0,50	3,53 ± 0,50	0,694
Calidad de la dieta	7,53 ± 0,43	7,48 ± 2,51	0,912

**Valor $p < 0,05$; calculado con la prueba de la "t" de Student. †Índice de masa corporal (IMC).*

Para el análisis inferencial se aplicó la prueba de Pearson con el fin de analizar la posible correlación entre las variables del estudio. El análisis de las correlaciones bivariadas arrojó que los valores más elevados de calidad de la dieta se correlacionaron con valores superiores en la percepción de salud y de felicidad ($p < 0,005$, para ambas). Asimismo, los valores más elevados en la percepción de soledad se correlacionaron con valores inferiores en la percepción de salud y felicidad ($p < 0,005$, para ambas). De igual modo, se observó una relación positiva entre la percepción de salud y de felicidad ($p < 0,005$). Estas correlaciones se mantuvieron tras realizar pruebas parciales ajustadas al sexo y la edad.

Por último, y con el fin de llevar a cabo un análisis predictivo del efecto de la calidad de la dieta sobre la percepción de soledad, felicidad y salud, observando el rol moderador del estado de peso, se realizó la prueba del análisis de regresión lineal (Tabla III). El modelo I (en crudo) no arrojó diferencias significativas ($R^2 = 0,222$; $F = 4,318$, $p = 0,068$). Sin embargo, el modelo II (ajustado al estado ponderal de normopeso) mostró una dependencia de la percepción de felicidad sobre la calidad de la dieta ($R^2 = 0,382$; $F = 3,643$, $p = 0,017$). El modelo III (ajustado al estado ponderal de sobrepeso) mostró una dependencia entre la calidad de la dieta y la percepción de salud ($R^2 = 0,455$; $F = 2,611$, $p = 0,049$).

DISCUSIÓN

El objetivo de este estudio fue determinar la relación existente entre la percepción de soledad, felicidad y salud y la calidad de la dieta, observando el rol moderador del estado de peso. Uno de los principales hallazgos del estudio muestra que una mayor percepción de felicidad y salud se correlaciona con valores más elevados de calidad de la dieta (Tabla II). Estos hallazgos no se asemejan a lo hallado en otro estudio (29) pero se sitúan en la

Tabla II. Correlaciones bivariadas entre las variables del estudio

Variables	Percepción de felicidad R (valor p)	Percepción de soledad R (valor p)	Calidad de la dieta R (valor p)	Índice de masa corporal R (valor p)
Percepción de salud	0,383 (0,001)	-0,223 (0,016)	0,264 (0,004)	-0,146 (0,117)
Percepción de felicidad	-	-0,383 (0,001)	0,272 (0,03)	-0,180 (0,530)
Percepción de soledad	-	-	-0,117 (0,211)	0,158 (0,090)
Calidad de la dietas	-	-	-	-0,121 (0,195)

línea de otros estudios que muestran la asociación entre una mayor adherencia a la dieta mediterránea y una mayor percepción de felicidad y salud (30-32).

A nivel fisiológico, estos resultados pueden deberse a la ingesta de antioxidantes como son las vitaminas (A, C y E), de fitoquímicos como la cisteína (tanto en proteínas como en huevos), de latón (verduras como el brócoli), de flavonas (frutas cítricas), de polifenoles (tés verdes) o de oleuropeína (aceite de oliva), todos ellos parte de la dieta mediterránea (33). Es decir, en este metaanálisis se concluyó que los antioxidantes son una serie de compuestos capaces de proteger contra el daño oxidativo de las células, tienen efectos antiinflamatorios en el cerebro y favorecen la salud y el estado de ánimo, induciendo una menor cantidad de problemas psicológicos. A su vez, a nivel anatómico, un estudio longitudinal indicó que las ingestas más bajas de alimentos ricos en nutrientes y las ingestas más altas de alimentos no saludables se asocian con una reducción del volumen del hipocampo izquierdo. Este aspecto supone un deterioro de la cognición, que se hace menos, y del comportamiento social, lo cual puede afectar, sin duda, a la percepción de salud y felicidad del escolar (34). De igual modo, a nivel neurobiológico, una dieta rica en grasas puede causar múltiples complicaciones en el cerebro mediante conductas anhedónicas, es decir, alterando la homeostasis energética, la ketamina (un antidepresivo de acción rápida) y las vías de señalización de la insulina, las cuales regulan la plasticidad sináptica y la producción de citocinas proinflamatorias, condicionando la percepción de salud y felicidad (35).

En concreto, en este estudio se analizó el efecto moderador del estado ponderal en estas relaciones, hallándose que una mayor calidad de la dieta se asocia con una mayor probabilidad de tener una mayor percepción de felicidad en aquellos escolares con estado ponderal de normopeso. Por su parte, en aquellos con sobrepeso, tener una mayor calidad de la dieta se asocia a una mayor probabilidad de tener una mejor percepción de salud (Tabla III).

Estos hallazgos podrían deberse a que los escolares con sobrepeso suelen padecer con mayor frecuencia dolor de cabeza, dolor de estómago, dolor de espalda, estado emocional bajo, irritabilidad o mal humor, nerviosismo, dificultad para dormir y mareos, condicionantes que, sin duda, interfieren en la percepción de salud (36). En este sentido, una mayor calidad de la dieta puede mitigar estos efectos negativos y aumentar

Tabla III. Relación de la percepción de la soledad, la felicidad y la salud con la calidad de la dieta: el rol moderador del estado ponderal

		Calidad de la dieta			
		β	EE	t	Valor de p
Modelo I	Percepción de soledad	1,002	0,266	1,016	0,988
	Percepción de felicidad	1,200	0,413	1,953	0,053
	Percepción de salud	1,187	0,477	1,927	0,056
Modelo II	Percepción de soledad	-0,032	0,395	-0,182	0,935
	Percepción de felicidad	1,555	0,630	2,468	0,016
	Percepción de salud	0,305	0,649	0,470	0,640
Modelo III	Percepción de soledad	0,259	0,479	1,520	0,139
	Percepción de felicidad	0,201	0,732	1,189	0,244
	Percepción de salud	0,375	0,871	2,254	0,032
Modelo IV	Percepción de soledad	-0,587	0,500	-1,878	0,090
	Percepción de felicidad	-0,351	0,781	-1,097	0,298
	Percepción de salud	0,141	1,278	0,488	0,636

la percepción de salud (37). Asimismo, la relación entre la percepción de felicidad y la calidad de la dieta puede deberse a que los niveles superiores de triptófano propios de las dietas ricas en nutrientes, como la dieta mediterránea, se relacionan con niveles más elevados de serotonina en el cerebro, jugando el sistema serotoninérgico un papel importante en la regulación del estado de ánimo (38). Por otro lado, las poblaciones mediterráneas (Grecia, España, Italia, Francia, etc.) disfrutan de una mayor expectativa de vida, por lo que estas diferencias, que no pueden explicarse únicamente por factores genéticos, pueden depender de factores ambientales, entre los que la dieta puede jugar un importante papel (12).

A su vez, a nivel psicológico, estos resultados pueden deberse a los mecanismos neurobiológicos comunes que vinculan el sobrepeso y los trastornos del estado de ánimo (39). Cabe destacar que los períodos del desarrollo preadolescentes pueden ser ventanas de vulnerabilidad en la vida temprana para desarrollar inestabilidad emocional, especialmente con los efectos aumentados de las dietas hipercalóricas sobre los sistemas de estrés neuroendocrino y la maduración de los circuitos neuronales que sirven de sustrato a la regulación de las emociones (13). Por ello, los hallazgos de este estudio deben interpretarse con cautela. Asimismo, este estudio presenta unas limitaciones metodológicas derivadas de su carácter transversal, del tamaño de la muestra y de la aplicación de cuestionarios autoinformados, pudiendo generar ciertos sesgos en la evaluación. Otra limitación del cuestionario Kidmed puede ser que en los criterios de alimentación saludable solo se han tenido en cuenta los alimentos de consumo diario, excluyéndose los de consumo ocasional.

En este sentido, estos resultados, fruto de la validez externa, no son generalizables pero pueden utilizarse como indicaciones a tener en cuenta en los programas de intervención, especialmente en la etapa escolar obligatoria, ya que se considera un periodo idóneo de intervención para lograr conductas saludables permanentes, por lo que, tal vez, estos resultados podrían ser un punto de referencia para posteriores estudios con diseños de carácter analítico y longitudinal. El seguimiento de sujetos con diferentes hábitos de alimentación permitirá comprobar el impacto de la dieta en las diferentes dimensiones de la salud.

Con la cautela sugerida, es relevante señalar que las pautas asociadas al desarrollo óptimo del estado de peso y la nutrición deben incidir en la consecución de un estado cognitivo saludable y el mantenimiento de un ritmo de crecimiento adecuado, y asegurar una serie de recomendaciones que permitan prevenir las enfermedades condicionadas por los hábitos inadecuados de alimentación. Como principal fortaleza del estudio cabe destacar la edad de la muestra, ya que la adquisición y el fomento de hábitos adecuados de nutrición puede redundar en la salud de los escolares, fomentando unos ajustes psicosociales adecuados en la edad adulta (33,39). Asimismo, aunque los instrumentos utilizados son subjetivos, sí son instrumentos válidos, confiables y que han demostrado buenas propiedades psicométricas, habiendo sido utilizados en investigaciones previas (7,27,28).

CONCLUSIÓN

Los resultados de este estudio ponen de manifiesto una asociación positiva de la percepción de salud y de felicidad con la calidad de la dieta, aunque esta asociación puede estar moderada por el estado ponderal. Estos resultados adquieren importancia ya que una mejor comprensión de estas asociaciones puede ayudar a desarrollar programas de intervención de salud pública más eficaces en las primeras fases etarias. Asimismo, estos resultados son de interés para ampliar el conocimiento científico disponible respecto al efecto de la crisis sanitaria actual.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Nutrición en el anciano

Detection of nutritional risk and hospital stay in the hospitalized elderly adult

Detección del riesgo nutricional y estancia hospitalaria en el anciano hospitalizado

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Abstract

Background and aims: a high nutritional risk can independently be associated with a longer hospital stay in elderly patients. This study aims to establish the prevalence of the risk of malnutrition and its associated factors in a high-complexity level hospital in Bogotá, Colombia, during 2018.

Methods: a cross-sectional study. The prevalence of the risk of malnutrition was measured using a malnutrition-screening tool (MST), and the association with hospital stage, age, and patient diagnoses was assessed.

Results: a total of 7,192 patients comprised the cohort. Age range was 61 to 108 years, with an average of 77.1 ± 9.2 years, and subjects were mostly female (55.5 %). We identified as main conditions urinary tract infections (8.4 %), congestive heart failure (5.4 %), and chronic obstructive pulmonary disease with an acute exacerbation (4.6 %). The prevalence of the risk of malnutrition was 41.4 %, significantly associated with longer hospital stays ($p < 0.001$), older age ($p < 0.001$), and a diagnosis of delirium (OR = 5.98, 95 % CI: 2.78 to 12.86), diarrhea and gastroenteritis (OR = 5.01, 95 % CI: 2.44 to 10.32), gastrointestinal hemorrhage (OR = 4.44, 95 % CI: 2.38 to 8.28), specified pneumonia (OR = 4.43, 95% CI: 2.11 to 9.30), and high blood pressure (3.94, 95 % CI: 2.07 to 7.50). Other diagnoses included abdominal pain (other) (OR = 3.80, 95 % CI: 1.81 to 7.99), urinary tract infections (OR = 3.64, 95 % CI: 2.07 to 6.24), acute bronchitis (OR = 3.22, 95 % CI: 1.56 to 6.65), and bacterial pneumonia (OR = 3.02, 95 % CI: 1.65 to 5.55).

Conclusion: the prevalence of the risk of malnutrition in our institution is approximately one in two patients, with a significant association to increased hospital stay ≥ 8 days, patient age ≥ 80 years, and mainly diagnoses of delirium, diarrhea, and gastroenteritis of suspected infectious etiology.

Keywords:

Malnutrition. Screening tool. Elderly. Health services.

Resumen

Antecedentes y objetivos: el alto riesgo nutricional puede asociarse independientemente a una estancia hospitalaria más prolongada en los pacientes ancianos. Este estudio tiene por objetivo establecer la prevalencia del riesgo de malnutrición y sus factores asociados en un hospital de alta complejidad de Bogotá (Colombia) durante 2018.

Métodos: este fue un estudio transversal. Se determinó la prevalencia del riesgo de malnutrición mediante la herramienta de detección MST y se evaluó la asociación con la estancia hospitalaria, la edad y el diagnóstico del paciente.

Resultados: en total, 7192 pacientes conformaron la cohorte. El rango de edad era de 61 a 108 años, con un promedio de 77,1 ± 9,2 años, siendo los sujetos en su mayoría de sexo femenino (55,5 %). Se identificaron como condiciones principales las infecciones del tracto urinario (8,4 %), la insuficiencia cardiaca congestiva (5,4 %) y la enfermedad pulmonar obstructiva crónica (4,6 %). La prevalencia del riesgo de desnutrición fue del 41,4 %, asociada a las estancias hospitalarias prolongadas ($p < 0,001$), la edad avanzada ($p < 0,001$) y los diagnósticos de delirium (OR = 5,98, IC 95 %: 2,78 a 12,86), diarrea y gastroenteritis (OR = 5.01, IC 95 %: 2.44 a 10.32), hemorragia gastrointestinal (OR = 4.44, IC 95 %: 2.38 a 8.28), neumonía específica (OR = 4.43, IC 95 %: 2.11 a 9.30) e hipertensión arterial (3.94, IC 95 %: 2.07 a 7.50). Otros diagnósticos asociados fueron: dolor abdominal (otros) (OR = 3.80, IC 95 %: 1.81 a 7.99), infecciones del tracto urinario (OR = 3.64, IC 95 %: 2.07 a 6.24), bronquitis aguda (OR = 3.22, IC 95 %: 1.56 a 6.65) y neumonía bacteriana (OR = 3.02, IC 95 %: 1.65 a 5.55).

Conclusión: la prevalencia del riesgo de desnutrición en la institución es aproximadamente de uno de cada dos pacientes, con una asociación significativa al aumento de la estancia hospitalaria superior a 8 días, a la edad del paciente mayor de 80 años y, principalmente, a los diagnósticos de delirium, diarrea y gastroenteritis.

Palabras clave:

Desnutrición. Herramienta de detección. Ancianos. Servicios de salud.

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Conflicts of interest: Olga Lucía Pinzón Espitia, Juan Mauricio Pardo Oviedo, and Milcíades Ibañez-Pinilla have no conflicts of interest to declare.

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INTRODUCTION

The identification of nutritional risk in elder patients is becoming more and more important, considering that a high nutritional risk may independently be associated with a longer hospital stay (1).

Since 1999, Ferguson et al. (2) developed a Malnutrition Screening Tool – MST – in acute hospitalized adult patients in order to identify patients at high nutritional risk and requiring nutritional therapy. The assessment of such tool included 408 patients admitted to an Australian hospital, excluding pediatric, maternity, and psychiatric patients. The study's target population was asked two questions related to appetite and recent, involuntary weight loss, showing a reliability between 93 % and 97 % for the high malnutrition-screening tool amongst evaluators.

After the application of nutritional screening tools in hospitalized populations of older adults, a prevalence between 15 % and 60 % (3-5) has been reported in the literature. In a study carried out by Stratton et al. (6), 150 patients of advanced age who were consecutively admitted to a health institution were prospectively evaluated. These patients underwent nutritional screening using the MUST tool, and 58 % of the study's target population was found to be at risk for malnutrition; these individuals showed a greater rate of in-hospital mortality, as well as longer hospital stays when compared to those other patients who were identified as at low risk. A similar finding was reported by Matins et al. (1), whose investigation in older adult patients classified as malnourished using the NRS-2002 screening tool found that their subjects had a greater risk of a longer stay (> 8 days).

Recently, nutritional screening tools have been articulated and added to electronic medical records, showing evidence that implementation of an electronic-format tool for detecting malnutrition improves the knowledge, approachability, and practice of the healthcare staff in hospitals. This creates interactions in multidisciplinary nutritional care and, therefore, results in timely referral to specialized nutritional management (7).

As a result, the use of a nutritional risk detection tool has a short-term, positive effect on the quality of a hospital's nutritional care process, since detection of the risk of malnutrition represents a crucial starting point for the successful management of malnourished patients. Eglseer et al. (8) suggest the importance of joining efforts in order to sustainably maintain the performance of nutritional screening, reinforcing a positive standpoint, designating motivated "key opinion leaders", and ensuring the consented support from the management within the framework of comprehensive healthcare.

Given the importance of the topic and the implications for clinical practice and the health of older adult patients, the objective of our research was to establish the prevalence of the risk of malnutrition in the patient population of a high-complexity level hospital, together with its associated factors.

MATERIALS AND METHODS

STUDY DESIGN AND PARTICIPANTS

This was a cross-sectional study where the prevalence of nutritional risk and associated factors was determined. Patients were included of both sexes, aged ≥ 60 years, hospitalized during the first 24 hours of being admitted to the emergency observation area of a high-complexity level healthcare services provider institution in Colombia from January 1 to December 31, 2018. Patients without a nutritional risk measurement were excluded.

DATA COLLECTION

The nutritional risk calculation tool applied in this investigation was developed by Fergusson et al., and is known by the acronym MST (Table I). For this tool, the authors reported a high reliability (between 93 % and 97 %), this also being a fast, simple-to-apply tool with an application time at the institution averaging five minutes per patient (2).

Nutritional screening was carried out in patients who complied with the inclusion criteria. Two registered dietitians/nutritionists carried out a structured interview and a nutritional risk evaluation.

The information was plotted in an Excel (version 2013) database. Data filtering was carried out using simple frequencies and crossing variables. Information was processed by the SPSS statistical package, version 25.0.

Table I. Malnutrition Screening Tool

Malnutrition Screening Tool (MST)*	
Have you recently lost weight without trying?	
No	0
Yes	1
Unsure	2
If the answer is yes, how much weight (kilograms) have you lost?	
1-5	1
6-10	2
11-15	3
> 15	4
Unsure	2
Have you been eating poorly due to loss of appetite?	
No	0
Yes	1
Total	

**Score ≥ 2 = patients at risk of malnutrition.*

Source: Ferguson M, Capra S, Bauer J, Banks M. Development of a valid and reliable malnutrition screening tool for adult acute hospital patients. Nutrition 1999;15(6):458-64.

STATISTICAL ANALYSIS

The descriptive analysis of qualitative variables used absolute and relative frequencies expressed as percentages. For the quantitative variables, measures of central tendency (mean and median) and dispersion (range and standard deviation) were applied.

The prevalence of nutritional risk was measured as a probability expressed as percentage. The association between risk of malnutrition and different factors (sex, age group, pooled stay, and diagnosis) was assessed using Pearson's chi-squared independence test. Odds ratios (OR) and their respective 95 % confidence intervals were also used. For numerical variables (age and hospital stay), the Kolmogorov-Smirnov and Shapiro-Wilk tests were used for the previous testing of normality. In case of normality, Student's t-test was used for the mean differences between two independent groups, with a prior evaluation of the homogeneity of variances (Levene's test), and for distributions other than normal a non-parametrical Mann Whitney-Wilcoxon (M-W) test was used.

A multivariate analysis was performed by means of unconditional logistic regression for risk of malnutrition, estimating the ORs and 95 % confidence intervals. The statistical testing was evaluated at a 5 % significance level ($p < 0.05$).

ETHICAL DISCLAIMER

This study was approved by the Méderi Technical Research Committee (CIMED, for its acronym in Spanish) and the Universidad del Rosario Research Ethics Committee, ensuring respect for patient confidentiality guidelines, and complying with the Declaration of Helsinki and the national regulations intended to guarantee the ethical principles for medical research in humans.

RESULTS

The agreement measurement for the malnutrition risk scale was evaluated by two nutritionists, who found a high level of concordance (kappa = 0.85, $p < 0.001$).

A total of 7192 patients, predominately female, with a minimum age of 61 years and a maximum age of 108 years, comprised the total cohort. Average age was 77.1 ± 9.2 years, and median age was 77 years. The predominant age group was that of 70-79 years (Table II). The five most frequent pathologies for hospital admission were urinary tract infections, congestive heart failure, chronic obstructive pulmonary disease with an acute exacerbation, bacterial pneumonia, and gastrointestinal hemorrhage (Table II). The pathology groups, according to the 10th revision of the International Classification of Diseases and Related Health Problems (ICD-10), reported with the highest frequency were circulatory system diseases (1594; 22.2 %), respiratory system diseases (1105; 15.4 %), and genitourinary tract diseases (794; 11 %).

The prevalence of the risk of malnutrition was 41.4 % (n = 2955), and was significantly higher in women (42.5 % vs 39.9 % in men, p = 0.0028). A significant linear tendency was evidenced in the study population: risk of malnutrition increased with older age ($p < 0.001$, tendency by chi-square test) and with extended hospital stay ($p < 0.001$, tendency by chi-square test) (Table III). The average hospital stay was 7.78 ± 7.36 days

Table II. Demographic and main diagnostic characteristics of the patient cohort screened (n = 7142)

Characteristics	n (%)
Sex	
Female	3,963 (55.5)
Male	3,179 (44.5)
Age (years)	
< 70	1757 (24.6)
70-79.9	2429 (34.0)
80-89.9	2257 (31.6)
≥ 90	699 (9.8)
Main diagnoses	
Unspecified site urinary tract infection	598 (8.4)
Congestive heart failure	380 (5.4)
Chronic obstructive pulmonary disease with exacerbations	326 (4.6)
Non-specified bacterial pneumonia	218 (3.1)
Non-specified gastrointestinal hemorrhage	166 (2.3)
Non-specified chronic obstructive pulmonary disease	143 (2.0)
Acute heart attack, with no other explanation	138 (1.9)
Essential (primary) high blood pressure	133 (1.9)
Non-specified acute bronchitis	107 (1.5)
Syncope and collapse	102 (1.4)

Table III. Relationship between age and length of stay (pooled) with risk of malnutrition, measured with MST

	Malnutrition risk			
	n	%	OR	95 % CI for OR
Age (years)				
< 70	668	38.0	1.000	
70-79.9	979	40.3	1.101	0.970-1.248
80-89.9	993	44.0	1.281	1.128-1.454
≥ 90	315	45.1	1.337	1.120-1.597
Stay (days)				
< 3	512	34.5	1.000	
3-5.9	859	38.1	1.169	1.020-1.340
6- 8.9	618	42.9	1.432	1.233-1.663
≥ 9	964	49.2	1.845	1.606-2.120

(median = 5.79), and was significantly longer in patients at higher nutritional risk (8.64 ± 8.05 days, median = 6.47) than in those classified at low nutritional risk (7.17 ± 6.76 days; median = 6.47; $p < 0.001$, M-W).

A significant association between diagnosis (ICD-10) and risk of malnutrition was found ($p < 0.001$, Pearson's chi-square test), with the highest prevalence for the risk of malnutrition being found in the diagnoses of non-specified delirium (56.4 %), specified pneumonia (50.8 %), diarrhea and gastroenteritis of suspected infectious etiology (47.8 %), non-specified gastrointestinal hemorrhage (47.6 %), high blood pressure (44.4 %), non-specified urinary tract infection (43.6 %), non-specified bacterial pneumonia (42.7 %), and other abdominal pain (41.9 %).

MULTIVARIATE ANALYSIS

The factors that together were significantly linked to high risk of malnutrition were increased hospital stay, and increased age (ICD-10). The diagnoses with a stronger association with risk of malnutrition were: non-specified delirium (OR = 5.98, 95 % CI: 2.78 to 12.86), diarrhea and gastroenteritis of suspected infectious etiology (OR = 5.01, 95 % CI: 2.44 to 10.32), non-specified gastrointestinal hemorrhage (OR = 4.44, 95 % CI: 2.38 to 8.28), specified pneumonia (OR = 4.43, 95 % CI: 2.11 to 9.30), high blood pressure (3.94, 95 % CI: 2.07 to 7.50), other abdominal pain (OR = 3.80, 95 % CI: 1.81 to 7.99), non-specified urinary tract infections (OR = 3.64, 95 % CI: 2.07 to 6.24), non-specified acute bronchitis (OR = 3.22, 95 % CI: 1.56 to 6.65), and non-specified bacterial pneumonia (OR = 3.02, 95 % CI: 1.65 to 5.55) (Table IV).

DISCUSSION

Out of the 7192 patients receiving nutritional screening, 2955 cases at risk of malnutrition were detected, i.e., a prevalence of 41.4 % was found, similar to that reported in previous studies carried out in Venezuela (48.4 %) (9), Mexico (40.8 %) (10), Ecuador (37.1 %) (11), and Colombia (60.1 %) (12). The prevalence of malnutrition in studies using the MST tool was equivalent to that reported in this study. For example, a university hospital in southern Brazil reported malnutrition in 33.1 % of the population (13), while in two primary care university hospitals in Porto the estimated prevalence was 55.1 % (1).

According to a systematic review by Correia et al. (14), which included 66 studies involving 29,474 patients from 12 Latin American countries, a prevalence of malnutrition was noted in 40 %-60 % of patients at the time of admission; a prevalence greater than 45 % was specifically reported for Colombia (15,16).

Regarding hospital stay, it is considered that the longer patient stay is, the higher the risk of malnutrition becomes. Martins et al. (1) reported that patients classified as malnourished were at greater risk, regardless of longer stay (8 days). These values were also reported by prevalence studies suggesting that the prevalence of malnutrition increases with stay duration (11,17,18).

The average hospital stay in this study was 7.78 days, with a stay significantly higher in patients at high nutritional risk lasting 8.64 days. Peniche-Herrera et al. (19) evaluated 138 medical files seeking to determine whether the risk of preoperative malnutrition was a causative factor for prolonged hospital stay after gastrointestinal surgery, with evidence that the presence of the risk of preoperative malnutrition is linked to prolonged hospital stay (OR = 1.33, 95 % CI: 1.07-1.64, $p = 0.008$).

A population study in patients admitted to hospital in two European countries reported that in patients at high risk of malnutrition stay was longer than 11 days (20). A similar report was made by Sorensen et al. (21) in the EuroOOPS study, which affirmed that patients at risk of malnutrition had more complications, greater mortality, and longer stays than patients at no risk. Therefore, hospital stay is a key factor in the administrative management of healthcare institutions, considering that malnutrition is common at hospital admittance and tends to worsen during hospitalization.

Out of the ten pathologies with the largest number of patients based on the ICD-10 diagnosis, there was evidence that circulatory and respiratory system diseases had a prevalence of risk of malnutrition higher than 30 %. Patients with congestive heart failure had a risk of malnutrition of 33.9 %, a value close to that reported by Gomes et al. (22), with high nutritional risk in 44 % of patients with heart failure. A prevalence of 36.5 % and 23.2 % for the risk of malnutrition was reported for pathologies such as chronic obstructive pulmonary disease (COPD) with or without exacerbation, respectively. These figures are similar to those reported in the literature, ranging between 10 % and 60 % (23,24), with the development of nutritional intervention strategies being of paramount importance in clinical practice because malnutrition is common amongst COPD patients (25).

Other relevant pathology in this study was the diagnosis of high blood pressure, where 32.5 % were at risk of malnutrition. This value is lower than that reported in the research carried out in Colombia by Giraldo et al. (26), who found that 62.5 % of older adult patients with high blood pressure presented risk of malnutrition. The differences in cohort conformation, the different screening tools used to establish the risk of malnutrition, and the particularities of each hospital institution may explain the differences found in the studies discussed in this publication.

The present study has various strengths. The size of the sample stands out with a large volume for the study population, an adequate representation of both sexes and age groups, and the inclusion of different health insurers. In addition, information was recorded by nutritionists, thus creating acceptable confidence at the collection of the data defined by the MST tool, established in the electronic medical records.

Finally, with regard to the implications for research and clinical practice, the present research suggests there is a need to carry out additional studies evaluating nutritional risk at different hospitals in the country, given the population's variability. Likewise, the importance of identifying and characterizing the clinical outcomes linked to the risk and cost of malnutrition is highlighted. This is in pursuit of the development of nutritional

Table IV. Multivariate analysis model of unconditional logistic regression for risk of malnutrition

	ß	OR	95 % CI for OR	Sig.
Sex (ref: male)	0.106	1.111	1.009-1.225	0.033
Age (ref: < 70 years)				
70-79.9	0.093	1.097	0.965-1.248	0.159
80-89.9	0.278	1.321	1.157-1.507	0.000
≥ 90	0.328	1.389	1.155-1.67	0.000
Stay (ref: < 3 days)				
3-5.9	0.2	1.221	1.063-1.403	0.005
6-8.9	0.419	1.52	1.304-1.771	0.000
≥ 9	0.687	1.988	1.723-2.293	0.000
Diagnosis (ref: L031)				
Cystitis, unspecified	1.293	3.644	2.066-6.424	0.000
Congestive heart failure	0.793	2.209	1.233-3.959	0.008
Chronic obstructive pulmonary disease with acute exacerbation, unspecified	0.887	2.427	1.346-4.376	0.003
Bacterial pneumonia, unspecified	1.107	3.024	1.648-5.55	0.000
Gastrointestinal haemorrhage, unspecified	1.49	4.436	2.376-8.282	0.000
Chronic obstructive pulmonary disease, unspecified	0.95	2.587	1.361-4.918	0.004
Acute myocardial infarction, unspecified	0.242	1.274	0.65-2.497	0.481
Essential (primary) hypertension	1.371	3.941	2.071-7.501	0.000
Acute bronchitis, unspecified	0.806	2.239	1.136-4.412	0.020
Syncope and collapse	1.041	2.832	1.438-5.577	0.003
Atrial fibrillation and flutter	0.63	1.878	0.929-3.797	0.079
Cerebrovascular disease, unspecified	1.17	3.221	1.56-6.65	0.002
Other gastroenteritis and colitis of infectious and unspecified origin	1.612	5.014	2.435-10.324	0.000
Chronic kidney disease, unspecified	0.743	2.101	0.985-4.482	0.055
Other and unspecified abdominal pain	1.334	3.798	1.805-7.993	0.000
Pneumonia, unspecified	1.488	4.426	2.107-9.298	0.000
Chest pain, unspecified	0.838	2.311	1.063-5.026	0.034
Diabetes mellitus without complications	0.744	2.104	0.957-4.623	0.064
Delirium, unspecified	1.788	5.978	2.779-12.86	0.000
Angina pectoris, unspecified	1.141	3.13	1.418-6.908	0.005
Pulmonary embolism without mention of acute cor pulmonale	0.685	1.985	0.884-4.456	0.097
Heart failure, unspecified	0.963	2.62	1.181-5.813	0.018
Bile duct stone with cholecystitis	1.02	2.773	1.238-6.214	0.013
Embolism and thrombosis of other specified veins	0.661	1.937	0.835-4.495	0.124
Dyspnea	0.49	1.633	0.691-3.857	0.264
Other diagnoses	1.31	3.705	2.145-6.397	0.000
Constant	-2.08	0.125		0.000

Ref: reference category.

care programs by hospital institutions, taking into account the factors that increase the risk and supported by the available evidence.

One in every two patients admitted to a hospital institution had a high risk of malnutrition linked to hospital stays longer than 8 days, age ≥ 80 years, and the specific diagnoses of delirium, diarrhea and gastroenteritis of suspected infectious etiology, gastrointestinal hemorrhage, specified pneumonia, high blood pressure, other abdominal pain, non-specified urinary tract infections, acute bronchitis, and bacterial pneumonia.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Nutrición en el anciano

Cost, microbiological, and nutritional properties of pureed food production in nursing homes. The ABADIA Study

Propiedades nutricionales, microbiológicas y costes de producción de las dietas de textura modificada en las residencias de ancianos. El estudio ABADÍA

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Abstract

Introduction: although nutritional differences between different types of texture-modified diet (TMD) have been evaluated, the resources and costs associated with their preparation have been less studied.

Objective: to describe the nutritional, microbiological properties and costs of: 1) in-home produced pureed food (hTMD); 2) concentrated nutrient-dense commercial food products, hand-blended (cTMD); 3) food prepared using the MixxPro® automatic food mixer (cTMD-Mix).

Methods: an observational, prospective study carried out in three geriatric nursing-homes. Patients ≥ 65 years, receiving TMD, with a stable clinical condition, estimated survival/expected internment > 1 month, and sufficient cognitive capacity were included. The following data were recorded: 1) patient socio-demographic and clinical variables; 2) TMD compliance and symptoms related to dysphagia during the meal; 3) patient appetite; and 4) kitchen information and resources used to prepare a TMD.

Results: sixty-two residents were included (65.0 % women, 88.3 years (SD: 9.3); 43.5 % malnourished, 79.0 % with good appetite). The proportion of food eaten/median kcal served/portion/mean kcal consumed were: hTMD: 95.5 % (SD: 10.7)/92.4 kcal (IQR: 75.6-128.1)/88.2 kcal (IQR: 72.2-122.3); cTMD: 89.2 % (SD: 15.9)/323.4 kcal (IQR: 284.2-454.1)/288.5 kcal (IQR: 253.5-325.1); and cTMD-Mix: 80.3 % (SD: 21.4)/358.0 kcal (IQR: 344.0-372.1)/287.5 kcal (IQR: 276.5-298.8). No microorganisms were detected. The average time spent in preparing each portion and its costs were: hTMD: 11.2 min (SD: 3.89)/€2.33 (SD: 0.63); cTMD: 1.7 min (SD: 0.28)/€2.01 (SD: 0.39); and cTMD-Mix: 1.6 min (SD: 0.00)/€2.00 (SD: 0.33).

Conclusions: in patients with dysphagia and/or chewing difficulties, concentrated nutrient-dense food products, particularly those produced using the MixxPro® automatic food mixer, ensure a high caloric intake and allow quick and safe food preparation.

Keywords:

Nursing home.
Dysphagia.
Swallowing problems.
Malnutrition.
Texture-modified diets.
Pureed.

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Conflicts of interest: this research was supported by Nestlé Health Science. NB is an employee of Nestlé Health Science. MC and HDP work for an independent research entity that received Nestlé Health Science funding to coordinate and conduct the study, and write up the manuscript. MDBP has received fees as a speaker at teaching and training activities for Nestlé Healthcare, Fresenius Kabi, Nutricia, Vegenat Healthcare, Persan Farma, Lilly, Novo Nordisk, and Adventia Farma. AMC has nothing to disclose. All authors declare their independence from the sponsor regarding the analysis of results and compilation of the conclusions.

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Resumen

Introducción: aunque existe evidencia acerca de las diferencias nutricionales entre los distintos tipos de dieta de textura modificada (DTM), los recursos y los costos asociados a su preparación se han estudiado menos.

Objetivo: describir las propiedades nutricionales, las microbiológicas y los costes de: 1) una dieta triturada de manera artesanal (hDTM); 2) una dieta preparada con alimentación básica adaptada (ABA) (cDTM); y 3) una ABA preparada con el mezclador automático de alimentos MixxPro® (cDTM-Mix).

Métodos: estudio observacional prospectivo realizado en tres residencias. Se incluyeron pacientes ≥ de 65 años que recibían DTM, con estado clínico estable, con supervivencia/internamiento estimado > 1 mes y capacidad cognitiva suficiente. Se registraron: 1) las variables sociodemográficas y clínicas del paciente; 2) el cumplimiento y los síntomas relacionados con la disfagia durante la comida; 3) el apetito del paciente, y 4) la información de la cocina y los recursos utilizados para preparar la DTM.

Resultados: se incluyeron 62 residentes (65,0 % mujeres, 88,3 años (SD: 9,3), 43,5 % desnutridos, 79,0 % con buen apetito). La proporción de alimentos consumidos/mediana de kcal servidas/porción/media de kcal media consumidas fueron: hDTM 95,5 % (SD: 10,7)/92,4 kcal (IQR: 75,6-128,1)/88,2 kcal (IQR: 72,2-122,3); cDTM: 89.2 % (SD: 15.9)/323,4 kcal (IQR: 284.2-454.1)/288,5 kcal (IQR: 253.5-325.1), y cDTM-Mix: 80,3 % (SD: 21.4)/358,0 kcal (IQR: 344.0-372.1)/287,5 kcal (IQR: 276.5-298.8). No se detectaron microorganismos. El tiempo medio empleado en la preparación y el coste por porción fueron: hDTM: 11,2 min (SD: 3,89)/2,33 € (SD: 0,63); cDTM: 1,7 min (SD: 0,28)/2,01 € (SD: 0,39), y cDTM-Mix: 1,6 min (SD: 0,00)/2,00 € (SD: 0,33).

Conclusiones: en los pacientes con disfagia y/o dificultades para masticar, los productos de ABA comerciales, en particular los que se producen con el mezclador automático de alimentos MixxPro®, aseguran una elevada ingesta calórica y permiten una preparación rápida y segura.

Palabras clave:

Residencias. Disfagia. Problemas de deglución. Dietas de textura modificada. Purés.

INTRODUCTION

Swallowing difficulties are common in the elderly, especially among institutionalized people. Half of institutionalized individuals are estimated to suffer from oropharyngeal dysphagia (OD) (1,2). Malnutrition is one of the main consequences associated with OD. Although prevalence rates vary depending on the method used, over half of the institutionalized elderly are malnourished or at risk of suffering malnourishment (3,4). Besides, approximately 80 % of pneumonia cases in elderly people with swallowing disorders correspond to cases of aspiration pneumonia, one of the leading causes of death in this cohort (5).

Between 26 % and 67 % of the meals served in geriatric nursing homes are texture-modified diets (TMD) (6,7). The in-home production of TMD (hTMD) requires blending the food and then diluting it with water or broth, thus reducing its nutritional intake (8-11), and increasing variability between prepared meals (11). Up to 83 % of patients receiving hTMD do not meet the necessary nutritional requirements, leading to nutritional deficiency (12,13). Recently, the European Society for Clinical Nutrition and Metabolism (ESPEN) recommends providing enriched TMD to support adequate dietary intake in elderly with malnutrition or at risk of malnutrition and with signs of OD (14). Concentrated nutrient-dense commercial food products (cTMD) for adults with OD provide a suitable alternative to hTMD. Caloric and protein intake is significantly increased by cTMD, which improves the nutritional status of the patient (12,15,16).

It should be borne in mind that the high amount of handling required to prepare hTMD meals increases the risk of food poisoning (17-19), and is also labor-intensive, requiring significant investment in resources and time spent by the kitchen staff.

There are currently automatic food mixers that can automatically prepare cTMD (cTMD-Mix), with the potential to significantly increase time and resource savings, and to minimize microbiological risks.

Although there are studies that describe the nutritional differences between hTMD and cTMD, as far as we know this is the first study to evaluate the resources and costs associated with TMD preparation. This observational study aims to describe the nutritional, microbiological properties, and the cost of three types of TMD: hTMD, cTMD, and cTMD-Mix.

METHODOLOGY

STUDY DESIGN

A proof-of-concept study with a descriptive, observational design was carried out in three geriatric nursing homes. The nursing homes were selected based on: 1) availability of own kitchen (not an external catering service); 2) cook with experience in the preparation of TMD ≥ 6 months; 3) experience of the specialist prescribing the diet ≥ two years.

In each of the nursing homes TMD was prepared using a method according to its routine practice: 1) in-home TMD (hTMD); 2) concentrated nutrient-dense commercial food products (cTMD); 3) cTMD-Mix prepared using the MixxPro® automatic food mixer to produce blended meals (cTMD-Mix).

The study was led by a committee of four experts (an endocrinologist, a catering manager, a bromatologist, and a food technologist) who participated in preparing the Case Report Form (CRF) and in the correct interpretation of study results.

PATIENTS

The study included patients ≥ 65 years of age, who were receiving TMD at the start of the study, with a stable clinical condition and an estimated survival > 1 month, with an expected internment ≥ 30 days, with sufficient cognitive capacity to complete the questionnaires (as assessed by the specialist prescribing the diet) either alone or with the help of a caregiver, and who were not participating in any other clinical trial. The study excluded those patients who required a change in diet (oral, enteral, or parenteral) for more than two days.

The participants were identified by the healthcare professional who prescribed the TMD following a consecutive, non-random recruitment. Patients were followed up for 15 days.

The following tests were conducted for each participant: nutritional screening using the Mini Nutritional Assessment Short Form (MNA®-SF) (at baseline), risk of dysphagia assessment using the Eating Assessment Tool (EAT-10) (at baseline), and appetite determination using the Short Nutrition Assessment Questionnaire (SNAQ) (before the main course). Data of symptoms associated with swallowing during feeding (choking, fractional swallowing, throat clearing, coughing during and after ingestion) were also collected at each meal.

PREPARATION OF TEXTURE-MODIFIED DIETS (TMD)

For all three TMD types, the preparation methods of the meal's main course were evaluated for five different varieties: chicken, veal, fish, egg, or lentils.

The hTMD was prepared using traditional processing methods and further blending. The cTMD was based on Meritene® (Nestlé Health Science) commercial products in the instant puree range (chicken with rice and carrots, veal with vegetables, fish with rice, puréed eggs Provenzal style, and lentils with vegetables). This range of dehydrated products was reconstituted with water, either manually (cTMD) or mechanically using a MixxPro® automatic food mixer (cTMD-Mix).

STUDY VARIABLES

Four independent CRFs were designed to collect the study variables: 1) to be filled in by the specialist prescribing the diet, recording the patient's main socio-demographic and clinical variables; 2) to be filled in by nurses or healthcare assistants, collecting data on compliance and symptoms related to dysphagia occurring during the meal; 3) to be filled in by the patient, including data on appetite; and 4) to be filled in by the catering manager, including information on the kitchen and the resources used to prepare each diet variety (Table I).

The staff responsible for data collection received appropriate training in person. Additionally, if the staff required it, online training was available during the study.

An external laboratory conducted the microbiological and nutritional (estimation of kcal per portion) analysis.

STATISTICAL ANALYSIS

Data were analyzed with the STATA statistical package, version 14. The absolute and relative frequencies of qualitative variables were calculated. The mean, standard deviation (SD), and interquartile ranges were calculated for the quantitative variables.

The compliance of each patient was calculated based on: 1) the amount of TMD served during the 15 days: mean amount served (according to the five cooking records) x 15 days; and 2) the average compliance of the patient during the 15 days of follow-up data recorded in the nursing questionnaire.

The average calorie count per portion was obtained based on the average number of calories per portion, and the average amount served per portion. The mean number of calories consumed per portion was calculated from the mean calories served per portion, and the mean compliance.

The costs related to food preparation were calculated on the following basis: 1) the cost of each of the ingredients used (€/kg, €/volume, or €/unit) according to the reference prices on the wholesale markets (20-23) or to the prices of origin; 2) the cost of human resources required for each of the processes — pre-processing, processing, blending (if applicable), homogenization (if applicable), and cleaning) — based on the time spent on each process, number of employees and wages (according to professional category (24,25) and updated to €/2019 in line with the CPI (26)); and 3) the number of portions prepared.

The time spent cooking, baking, frying, grilling, and blending/homogenizing was considered to calculate energy costs. For each process, the cost/hour was applied based on electricity or gas energy consumption, estimating the average cost of the corresponding energy supply at the time of the data analysis (27,28). Given the variability extant in the energy used by different types of blenders, a conservative 200 W value was applied. For instance, for the MixxPro® automatic food mixer, a maximum consumption of 2000 W was assumed, and a working time of 1 min per portion. Gas consumption was calculated by means of a direct extrapolation of the minutes recorded and energy consumption. The same energy tariffs were applied to all three centers, and similar appliances were assumed to have the same energy consumption.

The amount served per portion in each center was different, so the standardized cost per 100 g was calculated as follows: cost/100 g = 100 g x cost per portion [€/portion / amount served per portion (g). Based on this result, the average cost per 100 g was obtained for each menu.

The average cost per 100 kcal portion was obtained from the average calories served per portion, and the cost per portion.

ETHICAL CONCERNS

The study was approved by the Clinical Research Ethics Committee at the *Complejo Asistencial Universitario de León* (E. OBS1676), and was conducted according to the principles of the Helsinki Declaration and good clinical practice (GCP). Patients were informed about the study and signed an informed consent. The data were duly anonymized.

RESULTS

PATIENT CHARACTERISTICS

Of the total number of patients starting the study (n = 64), two were excluded: one did not adjust to the diet, and one died.

Table I. Variables collected during the study; source and time of collection

Variable	Source	(No.) time of collection
Questionnaire completed by the prescriber		
Patient age	Medical record	(1) Baseline
Sex	Medical record	(1) Baseline
Body mass index (BMI)	Medical record	(1) Baseline
Diagnosis for which TMD is prescribed	Medical record	(1) Baseline
Chronic comorbidities	Medical record	(1) Baseline
Nutritional supplementation requirements	Medical record	(1) Baseline
Swallowing/gastrointestinal complications	Medical record	(1) Baseline
Risk of dysphagia [Risk of dysphagia ≥ 3]	EAT-10	(1) Baseline
Malnutrition [Malnutrition, < 7; risk of malnutrition, 8-11; good nutritional status, ≥ 12]	MNA® -SF	(1) Baseline
Questionnaire completed by nurses		
Symptoms related to dysphagia during eating (main course) [coughing during and after ingestion, throat-clearing, fractional swallowing and choking]	Reported by nursing staff	(15) Days 1 to 15
Compliance with the main course of the meal [0 %, 25 %, 50 %, 75 % or 100 %].	Reported by nursing staff	(15) Days 1 to 15
Questionnaire completed by the patient		
Appetite [good appetite, ≥ 14 points]	SNAQ	(3) Days 1, 7 and 15
Questionnaire completed by the cook		
Kitchen features [number of employees, professional category, number of daily regular meals and number of daily blended meals]	Catering staff	(1) Baseline
Data for preparation of each meal variety [number of meals prepared and ration weight, raw materials used (weight or volume or units of all ingredients required), human resources required (number of employees involved in the process*, professional category and time required). Energy consumption (time spent using kettles/pots, ovens, grills, fryers, pans, mixers, etc.)]	Catering staff	(5) During the preparation of each variety (chicken, veal, fish, egg, or lentils)
Temperature of the prepared meal [temperature after homogenisation and before serving]	Catering staff	(15) Three independent records per diet variety
Microbiological analysis [presence of coagulase-positive *Staphylococcus, Salmonella* spp*, Escherichia coli* ß-glucuronidase+, and *Listeria monocytogenes*] and *energy content* (kcal/100 g)]	Accredited external laboratory (UNE-EN ISO/ IEC 17025:2005)	(15) Three independent records per diet variety

**The time required for cleaning was estimated based on the time required to clean each utensil (by hand or machine) and the number of utensils used during the preparation of each diet variety.*

Finally, 62 patients, 65 % women, with a mean age of 88.3 (SD: 9.3) years completed the follow-up and were included in the analysis (hTMD, n = 20; cTMD, n = 20; and cTMD-Mix, n = 22). Only 3.2 % of participants were well nourished (MNA®-SF ≥ 12). Baseline patient characteristics are shown in table II.

A total of 79.0 % of patients had a good appetite (SNAQ ≥ 14 points) during follow-up [hTMD: 100.0 %; cTMD: 75.0 %; cTMD-Mix: 63.6 %].

Overall, compliance with the diet was good. On average, the proportion of food eaten was above 80 %: hTMD: 95.5 % (SD: 10.7); cTMD: 89.2 % (SD: 15.9); cTMD-Mix: 80.3 % (SD: 21.4). Regarding compliance and the mean amount served per portion, patients receiving hTMD, cTMD, and cTMD-Mix ingested a daily mean of 197.7 g (SD: 21.6), 284.6 g (SD: 49.6), and 281.9 g (SD: 73.4), respectively. Similarly, considering the calories served, the calories consumed per portion were 88.2 (IQR: 72.2-122.3)

Table II. Baseline characteristics of study patients

	Total (n = 62)	hTMD (n = 20)	cTMD (n = 20)	cTMD-Mix (n = 22)
Age, years [mean (SD)]	*88.3 (9.3)*	89.9 (6.5)	94.2 (6)	81.6 (9.9)
Women [% (n)]	*65.0 (39)*	80.0 (16)	47.4 (9)	66.7 (14)
BMI, kg/m^2 [mean (SD)]	*23.9 (4.3)*	22.7 (2.9)	22.8 (3.4)	25.9 (5.5)
MNA®, [% (n)]				
Malnourished	*43.5 (27)*	60.0 (12)	50.0 (10)	22.7 (5)
At risk of malnutrition	*53.2 (33)*	40.0 (8)	50.0 (10)	68.2 (15)
Normal nutritional status	3.2 (2)	0.0 (0)	0.0 (0)	9.1 (2)
Risk of dysphagia (EAT-10 ≥ 3), [% (n)]	*91.9 (57)*	100.0 (20)	75.0 (15)	100.0 (22)
With nutritional supplements, [% (n)]	*30.6 (19)*	20.0 (4)	40.0 (8)	31.8 (7)
Number of comorbidities, [% (n)]				
0	1.6 (1)	0.0 (0)	0.0 (0)	4.5 (1)
1	32.3 (20)	85.0 (17)	10.0 (2)	4.5 (1)
≥ 2	*66.1 (41)*	15.0 (3)	90.0 (18)	90.9 (20)
Previous swallowing and intestinal complications, [% (n)]				
Aspiration pneumonia	*33.9 (21)*	80.0 (16)	25.0 (5)	0.0 (0)
Constipation	19.4 (12)	0.0 (0)	0.0 (0)	54.5 (12)
Nausea or vomiting	9.7 (6)	0.0 (0)	30.0 (6)	0.0 (0)
Diarrhea	3.2 (2)	0.0 (0)	10.0 (2)	0.0 (0)
Abdominal pain	1.6 (1)	0.0 (0)	0.0 (0)	4.5 (1)

hTMD: in-home TMD; cTMD: commercial TMD, hand blended; cTMD-Mix: commercial TMD, automatically blended; SD: standard deviation; BMI: body mass index; MNA: mini nutritional assessment; EAT-10: eating assessment tool.

for hTMD; 288.5 (IQR: 253.5-325.1) for cTMD; and 287.5 (IQR: 276.2-298.8) for cTMD-Mix.

The mean number of symptoms associated with swallowing during feeding (choking, fractional swallowing, throat clearing, coughing during and after ingestion) was 68 (hTMD), 46 (cTMD), and 10 (cTMD-Mix) for every 100 meals served, respectively.

CHARACTERISTICS OF PROCESSED MEALS

The average number of TMD served per portion, as well as the energy intake, differed in the three nursing homes: 207.0 g (SD: 9.0) and 92.4 kcal (IQR: 75.6-128.1) for hTMD; 319.2 g (SD: 35.4) and 323.4 kcal (IQR: 284.2-375.3) for cTMD; and 351.0 g (SD: 0.0) and 358.0 kcal (IQR: 344.0-372.1) for cTMD-Mix (Fig. 1). Greater variability was observed for those meals requiring higher levels of food handling for their processing: 56.1 % (hTMD), 26.1 % (cTMD), and 7.8 % (cTMD-Mix).

The mean temperature of meals after blending was 80.6 °C (SD: 1.6) for hTMD, 88.2 °C (SD: 1.02) for cTMD, and 85.0 °C (SD: 0.0) for cTMD-Mix; while at the time of serving to patients, it was 54.3 °C (SD: 1.22) for hTMD, 58.7 °C (SD: 0.31) for hTMD, and 75.0 °C (SD: 0.0) for cTMD-Mix.

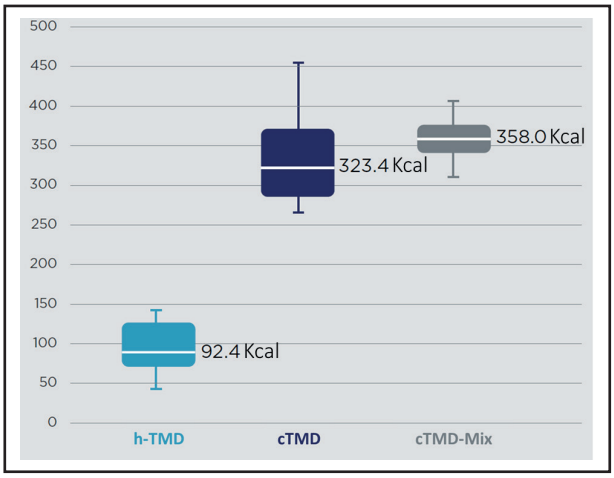

Figure 1.

Kilocalories served per ration: interquartile ranges (hTMD: in-home TMD; cTMD: commercial TMD, hand blended; cTMD-Mix: commercial TMD, automatically blended).

No microorganisms were detected in any of the analyzed samples.

USE OF RESOURCES AND COSTS ASSOCIATED WITH FOOD PREPARATION

The number and type of kitchen employees involved in food preparation varied between nursing homes (Table III).

In each kitchen, 69 % (hTMD), 81.8 % (cTMD), and 53.8 % (cTMD-Mix) of the total number of prepared meals (including non-blended types) were TMD. The mean number of portions prepared during the study period was 28.8 (SD: 2.9) for hTMD, 26.0 (SD: 1.4) for cTMD, and 70.0 (SD: 0.0) for cTMD-Mix. The average time spent in preparing each portion was 11.2 min (SD: 3.89) for hTMD, 1.7 min (SD: 0.28) for cTMD, and 1.6 min (SD: 0.00) for cTMD-Mix (Table III).

The total cost per portion (human resources, ingredients, and energy consumption) amounted to €2.33 (SD: 0.63), €2.01 (SD: 0.39), and €2.00 (SD: 0.33) for hTMD, cTMD, and cTMD-Mix, respectively. In the nursing home employing hTMD the main cost component was associated with human resources, whereas in the centers using cTMD and cTMD-Mix the main cost was related to raw materials (Fig. 2).

Table III. Use of resources and time spent in meal preparation

Type of diet	No. of portions prepared	Process	Resource	Total time (SD) min	Time/portion (SD) min
hTMD	28.8	Pre-processing	1 cook	77.0 (45.3)	2.7 (1.7)
		Processing	1 cook	112.0 (24.0)	3.9 (0.9)
		Blending/homogenization	1 cook	12.8 (1.9)	0.4 (0.1)
		Serving up	1-2 cooks	8.8 (2.8)	0.3 (0.1)
		Cleaning	1 cook	110.8 (24.3)	4.0 (1.0)
		Total	-	321.4 (96.1)	11.2 (3.9)
cTMD	26.0	Pre-processing	1 assistant	4.4 (5.4)	0.2 (0.2)
		Processing	1 assistant	15.0 (0.7)	0.6 (0.0)
		Blending/homogenization	1 assistant	5.2 (0.4)	0.2 (0.0)
		Serving up	2 healthcare assistants	10.4 (0.9)	0.4 (0.0)
		Cleaning	1 catering assistant	7.00 (0.0)	0.3 (0.0)
		Total	-	42.0 (6.2)	1.7 (0.3)
cTMD-Mix	70.0	Pre-processing	1 cook	15.0 (0.0)	0.2 (0.0)
		Processing	2 cooks 1 assistant	90.0 (0.0)	1.3 (0.0)
		Blending/homogenizing	-	-	-
		Serving up	-	-	-
		Cleaning	1 catering assistant	10.0 (0.0)	0.1 (0.0)
		Total	-	115 (0.0)	1.6 (0.0)

hTMD: in-home TMD; cTMD: commercial TMD, hand blended; cTMD-Mix: commercial TMD, automatically blended; SD: standard deviation; Min: minutes.

Figure 2.

Breakdown of cost per ration (hTMD: in-home TMD; cTMD: commercial TMD, hand blended; cTMD-Mix: commercial TMD, automatically blended).

The average cost per 100 g was €1.12 (SD: 0.29) for hTMD, €0.65 (SD: 0.18) for cTMD, and €0.57 (SD: 0.09) for cTMD-Mix. Finally, the average cost per 100 kcal was €2.80 (SD: 1.32) for hTMD, €0.62 (SD: 0.18) for cTMD, and €0.58 (SD: 0.13) for cTMD-Mix.

DISCUSSION

TMD is recommended for patients who have difficulty swallowing. To facilitate its intake, the texture of the original food is modified by blending, and very often water or broth is added, which can lead to nutritional deficiency in the prepared meal and greater variability between portions (15). In line with previous studies (11), our work has demonstrated a lower energy intake and a higher variability associated with hTMD meals.

The need to blend food to adapt it to a patient's swallowing requirements can also modify its organoleptic qualities and be associated with suboptimal intake (8,29). In our study, the percentage of food eaten, as compared to food served, was high (> 80 %), and it was higher in patients receiving hTMD than in those receiving cTMD or cTMD-Mix. However, this difference may be accounted for because the portions served in the nursing homes serving hTMD (approximately 200 g) were smaller than those served in the centers offering commercial diets (approximately 350 g). In fact, the total amount of ingested foor per portion was about 30 % higher in the homes serving commercial meals. This fact, together with the lower caloric intake of hTMD, could diminish the feeling of fullness, and explain the greater appetite observed in patients with hTMD. Similarly to our study, Rubio et al. compared the intake of an hTMD with a hyperproteic and hypercaloric powdered preparation (cTMD), observing that the total amount ingested by the patient was lower in the cTMD group, with a higher energy and protein intake (30). Other studies have described that in both institutionalized elderly patients and elderly outpatients with swallowing difficulties, a higher energy and protein intake was achieved with cTMD as compared with hTMD (31,32). Similarly, our results show that, although compliance was higher in the nursing home with hTMD, the final kilocalories ingested were much higher in the patients receiving cTMD or cTMD-Mix than in the patients receiving hTMD.

Another reason for prescribing TMD is to reduce the risk of choking and prevent aspiration pneumonia. Up to 70 % of institutionalized people may suffer from choking during meals (33). Evidence of symptoms related to swallowing (such as choking) associated with hTMD vs. cTMD is minimal; moreover, results on the effectiveness of TMD to prevent aspiration pneumonia are inconclusive (34,35). In the present study, the number of swallowing-related symptoms observed was higher in patients receiving hTMD, decreasing with the diets requiring lower levels of manipulation during preparation, as was the case of cTMD-Mix. These results would be consistent with the fact that patients with hTMD reported more aspiration pneumonia (before study initiation) than patients receiving cTMD and cTMD-Mix. However, due to the study's nature, these results are neither representative nor conclusive enough to establish a cause-effect relationship.

During diet elaboration, food needs to reach a temperature above 65 °C, and should not be exposed to temperatures between 15 °C and 45 °C to guarantee microbiological safety (12). The three types of diet studied showed a good safety profile. In all cases, microbiological safety temperatures (> 65 °C) were reached during preparation, and the presence of microorganisms was not detected in the analysis. It should be noted that only cTMD-Mix remained above 65 °C until the time of serving.

As far as we know, this is the first study conducted in geriatric nursing homes to evaluate the use of resources and costs of TMD production for patients with dysphagia or mastication difficulties using natural and commercial foods, and three different processing methods ((hTMD, cTMD, cTMD-Mix).

Raw material costs were lower for hTMD when compared to cTMD and cTMD-Mix. However, the time required to prepare each portion was much lower in the latter. Approximately, 1.5 minutes for commercial diets and 11 minutes for hTMD were required. Considering the resources needed to prepare the diets, the cost per portion and the cost per 100 g served were lower for the commercial diets than for the home-made ones.

Previous studies suggest that patients who switch from hTMD to fortified TMD (13,31) or cTMD (32) experience significant weight gain improvements. Additionally, two observational studies showed that cTMD-Mix was a simple and effective way to improve nutritional status in elderly institutionalized residents with swallowing disorders (36,37). The scope of our study was not to assess the nutritional status of patients. Considering that most of our participants were already receiving TMD before the study started, our results appear to be in line with the above studies. In this respect, the percentage of patients with malnutrition was higher in the nursing home serving hTMD and lower in the nursing home serving hTMD-Mix.

Our study presents some limitations. The first one relates to the study population, as patient recruitment was made according to convenience, and the number of participants was relatively low, preventing a robust statistical analysis. Despite the small sample size, since study participants include elderly residents with a high level of dependence, we can assume that the study population is representative of nursing home residents. Similarly, the study involved a reduced number of kitchens, each one with specific characteristics and peculiarities, so their practices may not be representative. However, it is important to keep in mind that the study objective was descriptive rather than comparative. Some participants might have required help to eat; however, since such data were not collected, it cannot be established whether having support influenced the amount of food consumed. Finally, since the nursing home staff collected the data, there may be inter-staff variability in measurements. In order to reduce this possible bias, the staff responsible for data collection received appropriate training, both in person and online; a graduated scale widely used in observational studies was used to assess the amount ingested; only objective symptoms related to dysphagia disorders

such as choking, fractional swallowing, throat clearing, coughing during and after ingestion were reported. Despite these limitations, the study provides useful information for future analyses of the potential benefits and costs of TMD as prepared using different processes.

In conclusion, in patients with dysphagia and/or chewing difficulties, concentrated, nutrient-dense food products (Meritene®, Nestlé Health Science), particularly those produced using the MixxPro® automatic food mixer, ensure a high caloric intake, even in subjects with lower compliance rates. Moreover, they allow quick and safe food preparation, reducing both kitchen workload and production costs. Further studies with a larger sample of patients and centers are needed to obtain representative results and establish whether there is any cause-effect of such diets on patient nutritional status.

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ARÁN

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Trabajo Original

Obesidad y síndrome metabólico

Nutritional guidance, monitoring, and supplementation before and after bariatric surgery — Are we doing this correctly?

Orientación, seguimiento y suplementación nutricional antes y después de la cirugía bariátrica: ¿lo estamos haciendo correctamente?

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Abstract

Background and aims: minimizing nutritional depletions after a Roux-en-Y gastric bypass (RYGB) may improve clinical results in the treatment of obesity. We evaluated nutritional aspects of obese women undergoing RYGB at a reference university hospital with a department specialized in bariatric surgery.

Method: based on the Dietary Reference Intakes developed by the Food and Nutrition Council, Institute of Medicine, and the guidelines issued by the American Society for Metabolic and Bariatric Surgery, we assessed the quantitative and qualitative adequacy of nutritional intake, supplementation, and biochemical monitoring of 20 women both before and 3 and 12 months after a RYGB. Data on nutritional intake was obtained by applying different food surveys, quantitatively interpreted by the Virtual Nutri Plus® software and using reference nutritional databases.

Results: nutritional intake deficits were already found before the RYGB ($p \leq 0.05$). These worsened postoperatively ($p \leq 0.05$), a period also marked by a qualitatively poor diet. The nutritional supplementation prescribed did not fully achieve the reference recommendations, and was poorly complied with by patients. Furthermore, nutritional monitoring was not carried out in all patients, recommended biochemical markers were not screened, and vitamin D depletions occurred.

Conclusion: our data suggest that institutions specialized in bariatric patient care may not be adequately adhering to well known guidelines, or applying efficient strategies to improve compliance.

Keywords:

Nutrition surveys. Nutritional status. Nutritional requirements. Nutrition assessment. Bariatric surgery. Gastric bypass.

Resumen

Antecedentes y objetivos: minimizar el deterioro nutricional después del baipás gástrico en Y de Roux (BGYR) puede mejorar los resultados clínicos en el tratamiento de la obesidad. Se evaluaron aspectos nutricionales de mujeres obesas sometidas a BGYR en un hospital universitario de referencia con servicio especializado de cirugía bariátrica.

Método: con base en la Ingesta Dietética de Referencia desarrollada por el Consejo de Alimentos y Nutrición del Instituto de Medicina, y las directrices de la Sociedad Estadounidense de Cirugía Bariátrica y Metabólica, evaluamos la adecuación cuantitativa y cualitativa de la ingesta nutricional, la suplementación y el seguimiento bioquímico de 20 mujeres tanto antes como 3 y 12 meses después de un BGYR. Los datos de la ingesta nutricional se obtuvieron mediante la aplicación de diferentes encuestas alimentarias, interpretadas cuantitativamente por el software Virtual Nutri Plus® y utilizando bases de datos nutricionales de referencia.

Resultados: se encontraron déficits de ingesta nutricional antes del BGYR ($p < 0,05$). Estos empeoraron en el postoperatorio ($p < 0,05$), período también marcado por una mala alimentación cualitativa. La suplementación nutricional prescrita no cumplió plenamente con las recomendaciones de referencia y no fue bien cumplida por los pacientes. Además, la monitorización nutricional no se aplicó en todos los pacientes y no se examinaron todos los marcadores bioquímicos recomendados, hallándose depleciones de vitamina D.

Conclusión: nuestros datos sugieren que las instituciones especializadas en la atención de pacientes bariátricos podrían no estar siguiendo adecuadamente las pautas recomendadas, ni aplicando estrategias eficientes para mejorar su cumplimiento.

Palabras clave:

Encuestas de nutrición. Estados nutricionales. Requerimientos nutricionales. Evaluación nutricional. Cirugía bariátrica. Baipás gástrico.

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INTRODUCTION

A high consumption of foods rich in energy density (mainly processed) and poor in protein, whole grains, and micronutrients may favor protein and micronutrient depletion in obese subjects (1,2). As part of the treatment of obesity, the Roux-en-Y gastric bypass (RYGB) is efficient in promoting significant and sustained weight loss along with metabolic benefits (i.e., diabetes remission), but being a restrictive and malabsorptive procedure it may worsen previous nutritional deficits and induce new ones (3,4). These deficits may range from 33 % to 40 % in the first year after surgery, and may contribute to the development of some debilitating organic disorders such as osteoporosis, Wernicke's encephalopathy, anemia, and peripheral neuropathy (5,6).

In this scenario, nutritional guidance and monitoring through multiple nutritional indicators are required for patients submitted to RYGB both before and after the procedure. Particularly, quantitative and qualitative data on food intake offer the main parameters on which to design dietary interventions, while reference guidelines can be applied for adequate nutritional supplementation and monitoring (7,8). When properly followed, these practices may help to achieve better clinical results in maintaining nutritional status and weight control after surgery (9,10).

The Bariatric and Metabolic Surgery Unit at the Digestive Surgery Department of a reference university hospital in the public health care system employs nutritional guidance and follow-up before and after RYGB. We assessed some dietetic and nutritional indicators in obese women treated at this institution in order to evaluate whether the dietary guiding and nutritional supplementation/monitoring offered were adequate in terms of adherence, sufficiency/insufficiency, and intervention period (pre- and post-operative). In parallel, by comparison with the reference tool "7-day food record" (7dR) we tested whether a 24-hour food recall (24hR) could adequately identify depletions in nutritional intake in this population, to allow an early design of proper dietary interventions.

MATERIALS AND METHODS

ETHICAL ISSUES AND SUBJECTS

The present investigation is part of the SURMetaGIT study (11), registered at www.clinicalTrials.gov (NCT01251016). Its specific protocol was approved by the local Ethics Committee (protocol nº 1011/19). After signing an informed consent form, 20 alphabetized adult women (18-60 years)who were obese (35-50 kg/m^2 of body mass index [BMI]) and candidates to RYGB were selected from February 2011 to December 2014. Exclusion criteria included refusal to participate in the study and participation in another interventional study protocol. All patients were submitted to a standardized RYGB without silicone ring and with standard biliopancreatic (50-60 cm) and feeding (100-120 cm) loop size, while routinely receiving dietary counseling along with the prescription of nutritional supplementation and monitoring before and after surgery. All the patients were assessed during the preoperative period and at 3 and 12 months after the RYGB for different nutritional indicators.

ANALYSIS OF THE QUANTITATIVE AND QUALITATIVE ADEQUACY OF FOOD INTAKE

A quantitative food intake analysis was performed by using the reference method 7dR. In order to fill out the 7dR questionnaire each patient took home a Food Consumption Book - Visualizing Portions (12) after being properly instructed on how to select the photo number corresponding to the size of the portion ingested. During the recording week each patient received a telephone call to remind her to fulfill the food consumption book and to solve any possible doubts. In parallel, quantitative analyses of food intake were also carried out by applying a 24hR questionnaire. This was done to evaluate whether this simple tool, which offers immediate data on food intake, could perform similarly to the 7dR in the studied population. To answer the 24hR form the amount of food consumed was recorded in terms of units, home measurements, or through photos, during face-to-face interviews. The Virtual Nutri Plus® software (VNP) (13) was used to calculate total calories, macro and micronutrient intake, from the data obtained from both the 7dR and 24hR tools. The following data sources were used to estimate the nutritional composition of the ingested meals: Table of Chemical Composition of Food, developed by Sonia Tucunduva Philippi (14), and a local Table of Food Composition (TACO) (15). For the qualitative food intake assessment, a food frequency query (FFQ) including the most usual diets of our patients was applied. This included type, origin (i.e., natural or processed) and method used for cooking, milk and dairy products, animal proteins, oils, appetizers, cereals/legumes, fruits and vegetables, candy and desserts, drinks, and diet and light products (Table IV).

To verify the adequacy of the amount of nutrient intake in the pre- and post-operative periods from 7dR data we assessed compliance with the reference tables of the Dietary Reference Intake (DRIs) issued by the Food and Nutrition Council, Institute of Medicine(16) rather than prescribed energy and individual nutrient intakes. As protein intake, accordingly to the DRIs, is recommended in relation to body weight, this was calculated considering the mean weight of our patients for each period studied. To assess the adequacy of nutrient quality from FFQ data at the postoperative period, we verified compliance with the groups of foods recommended by the Nutritional Pyramid for Post-gastric Bypass Patients (17). Intake values up to 25 % above or below the recommended levels were considered adequate.

ANALYSIS OF NUTRITIONAL SUPPLEMENTATION ADEQUACY AND ADHERENCE

The nutritional supplementation offered to the patients was analyzed in terms of: 1) Adequacy: we verified whether the sup-

plements prescribed by the Nutrition Service matched those recommended for bariatric patients by the American Society for Metabolic and Bariatric Surgery (ASBMS)(18). 2) Adhesion: we verified whether bariatric outpatients had taken the recommended supplementation by asking them about it from their first consultation — when the answer was yes, we recommended continuation; when the answer was not, we recommended to start taking the supplementation.

ANALYSIS OF THE PERFORMANCE AND MONITORING OF NUTRITIONAL COUNSELING

To assess the performance of nutritional counseling whether the systemic levels of biochemical markers for protein and micronutrients were within the normal range was assessed. This evaluation was limited to the biochemical exams performed only by medical indication, which allowed us to identify the frequency of the nutritional and blood chemistry monitoring applied.

SAMPLE SIZE AND STATISTICAL ANALYSIS

A sample of 20 participants was considered adequate to obtain representative data and a comparison of two food consumption assessment tools (24hR and 7dR), with a power of 80 % calculated based on the number of nutrient measurements and the number of instruments through a non-parametric ANOVA test, under a 0.05 alpha value. Descriptive data and continuous variables were expressed in terms of mean and standard deviation or median and minimum-maximum values. For the comparative analysis of data we used Student's t-test and paired Mann-Whitney test when appropriate, with a confidence level of 95 %. All analyses and graphs were carried out using the R program (version 3.4.1).

RESULTS

DESCRIPTIVE PATIENT DATA

Patients had a mean age of 48.7 ± 7.0 years, and their descriptive characterization is shown in table I. All patients experienced a decrease in body measurements and weight loss after their RYGB.

PRE- AND POST-OPERATIVE QUANTITATIVE ASSESSMENT OF NUTRITIONAL INTAKE

The quantitative data on food intake obtained with the 7dR are described in table V (calories and macronutrients) and table VI (vitamins and minerals). There was a significant reduction in the consumption of calories, macronutrients, and micronutrients (except vitamins B12, C and D, and calcium) per day at 3 and 12 months after RYGB, as compared to the preoperative period. A lower intake of polyunsaturated fat and a higher intake of carbohydrates were observed at the 12-month postoperative cutoff, in comparison to the 3-month postoperative cutoff. No significant differences were observed in the data between the 24hR and 7DR tools regarding the intake of energy, macronutrients, and micronutrients indicated for supplementation in RYGB patients (vitamin B12, folate, iron, zinc, and calcium) ($p > 0.05$) (Fig. 1). Nevertheless, at the 12-month postoperative cutoff the 24hR tool did not identify the increase in carbohydrate intake identified by the 7dR (versus at 3 months postoperative), and highlighted a deficit in vitamin D and calcium intake (versus at 3 months postoperative) not identified by the reference tool 7dR.

Table I. Descriptive characteristics of the obese patients submitted to Roux-en-Y gastric bypass

Variable	Factor	Value
Ethnicity (%)	Brown	25.0
	Black	15.0
	White	60.0
Scholarity (%)	Incomplete elementary school	15.0
	Elementary school	25.0
	High school	35.0
	Incomplete graduation	5.0
	Graduation	20.0
Weight (kg)	Preoperative	114.5 ± 15.9
	Postoperative, 3 months	94.2 ± 13.8
	Postoperative, 12 months	80.1 ± 11.5
Body mass index (kg/m^2)	Preoperative	46.4 ± 5.4
	Postoperative, 3 months	37.9 ± 4.2
	Postoperative, 12 months	32.5 ± 3.7
Waist/Hip ratio (cm)	Preoperative	138.5 ± 12.3
	Postoperative, 3 months	123.1 ± 11.6
	Postoperative, 12 months	112.2 ± 9.9

As shown in table II, according to the DRI recommendations, excessive carbohydrate and deficient protein and fiber intakes were observed preoperatively. The consumption of carbohydrates and proteins was slightly below and above these recommendations at 3 and 12 months after surgery, respectively, whereas the deficiency in total fiber consumption was aggravated by surgery in both the short (3 months) and long term (12 months). Inadequate preoperative consumption of micronutrients included a mild insufficiency of vitamins B2 and B6, phosphorus, selenium, and zinc; a relevant deficiency in the ingestion of vitamins B5, D and E, folate, calcium, magnesium, and potassium; and an elevated consumption of sodium. All inadequacies in micronutrient consumption worsened postoperatively, except for vitamin D and iodine (whose intakes showed a slight increase in the postoperative period at 3 months) and sodium (whose intake decreased slightly in the two post-operative time points evaluated);

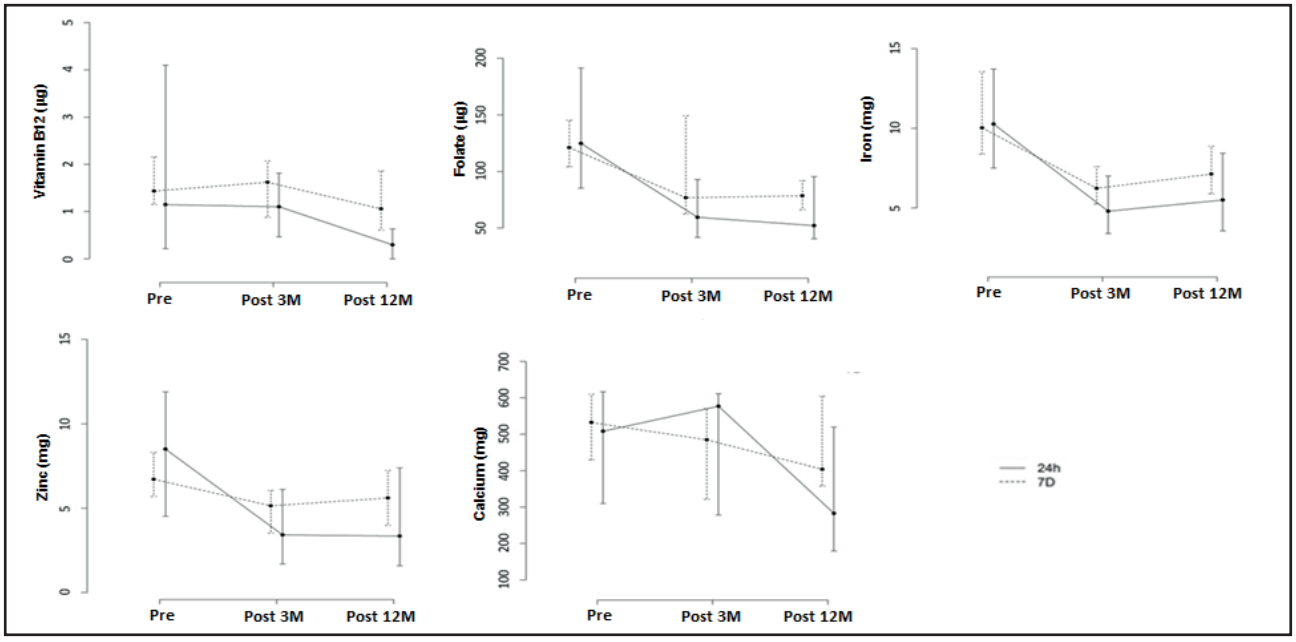

Figure 1.

Ingestion of micronutrients by obese patients before and at 3 and 12 months after a Roux-en-Y gastric bypass, according to a 7-day food registry and 24-hour food recall. Data are expressed as median ingestion per period (pre- and 3 and 12 post-operative months). Pre: preoperative; Post 3M: at 3 months postoperative; Post 12M: at 12 months postoperative; 24h: 24-hour food recall; 7D: 7-day food record.

Table II. Adequacy of nutrient intake by obese patients before and 3 and 12 months after a Roux-en-Y gastric bypass, according to the Dietary Reference Intakes (DRIs)

Nutrient	DRIs	Preoperative	Postoperative	
			3 months	12 months
Protein (g/kg)	0.8	**0.6 ± 0.9**	**0.5 ± 1.1**	**0.7 ± 1.6**
Carbohydrates (g)	130.0	*208.8 ± 47.3*	*112.8 ± 34.0*	*140.2 ± 49.7*
Total fiber (g)	25.0	**15.0 ± 5.6**	**9.7 ± 3.9**	**10.0 ± 3.3**
Vitamin A (µg)	700.0	*737.8 ± 693.6*	*700.9 ± 637.1*	*772.8 ± 874.4*
Vitamin B1 (mg)	1.1	*1.6 ± 1.2*	**1.0 ± 0.6**	**0.9 ± 0.3**
Vitamin B2 (mg)	1.1	**0.9 ± 0.3**	**0.7 ± 0.4**	**0.6 ± 0.4**
Vitamin B3 (mg)	14.0	*16.8 ± 5.5*	**10.4 ± 4.1**	**11.6 ± 5.5**
Vitamin B5 (mg)	5.0	**2.0 ± 0.5**	**1.5 ± 0.6**	**1.4 ± 0.6**
Vitamin B6 (mg)	1.3	**1.0 ± 0.3**	**0.7 ± 0.2**	**0.8 ± 0.23**
Vitamin B12 (µg)	2.4	*3.3 ± 4.7*	**1.45 ± 0.8**	**1.3 ± 0.8**
Vitamin C (mg)	75.0	*359.3 ± 799.2*	*136.4 ± 113.57*	*107.1 ± 71.5*
Vitamin D (µg)	5.0	**1.6 ± 4.1**	**3.4 ± 12.7**	**0.3 ± 0.2**
Vitamin E (mg)	15.0	**9.6 ± 3.0**	**6.4 ± 1.8**	**6.4 ± 1.6**
Calcium (mg)	1000.0	**517.9 ± 135.7**	**477.2 ± 204.9**	**460.7 ± 215.9**
Copper (mg)	0.9	*3.8 ± 13.3*	**0.7 ± 0.3**	**0.7 ± 0.5**
Folate (µg)	400.0	**127.8 ± 32.6**	**95.0 ± 52.0**	**88.5 ± 47.0**
Iron (mg)	18.0	*38.6 ± 81.8*	**9.1 ± 12.5**	**8.7 ± 5.0**
Phosphorus (mg)	700.0	**658.9 ± 184.7**	**461.2 ± 156.2**	**488.0 ± 142.6**
Magnesium (mg)	320.0	**150.4 ± 33.2**	**104.7 ± 27.6**	**112.4 ± 33.3**
Manganese (mg)	1.8	*2.1 ± 3.5*	*2.06 ± 5.21*	**1.0 ± 0.3**
Potassium (mg)	4700.0	**1719.1 ± 375.8**	**1341.1 ± 411.2**	**1313.8 ± 432.1**
Selenium (µg)	55.0	**47.5 ± 10.5**	**26.5 ± 12.7**	**27.9 ± 17.6**
Sodium (mg)	*1300.0*	*3534.2 ± 804.2*	*2731.4 ± 556.4*	*2444.2 ± 422.7*
Zinc (mg)	8.0	**7.1 ± 2.3**	**4.8 ± 1.9**	**5.6 ± 2.2**

Data on consumption expressed as mean ± standard deviation. Values highlighted in bold and italics indicate intake below and above DRI recommendations, respectively.

Table III. Adequacy of daily micronutrient supplementation prescribed for obese patients submitted to Roux-en-Y gastric bypass, according to the recommendations of the American Society for Metabolic and Bariatric Surgery (ASMBS)

Micronutrient	ASMBS Recommendation	Service supplementation
Vitamin A	5,000-10,000 IU/day	16,000 IU/day
Vitamin B1	**≥ 12 mg/day**	**3 mg/day**
Vitamin B12	350-500 µg/day	500-1,000 µg/month
Vitamin D	3,000 IU/day	4,400 IU/day
Vitamin E	**15 mg/day**	**0**
Vitamin K	**90-120 µg/day**	**0**
Calcium	1,200-1,500 mg/day	1,200 mg/day
Copper	**2 mg/day**	**0**
Iron	45-60 mg/day	40-80 mg/day
Folate	**400-800 µg/day**	**0**
Zinc	**8-22 mg/day**	**0**

Values highlighted in bold indicate intake below ASMBS recommendations.

however, these micronutrients continued to be consumed in inadequate amounts as compared to DRIs. Some inadequacies in micronutrient consumption were exclusive to the postoperative period, including those of vitamins B3 and B12, iron, and copper in both postoperative time points, and of manganese at 12 months after surgery.

POSTOPERATIVE QUALITATIVE ASSESSMENT OF NUTRITIONAL INTAKE

There was a decrease in the consumption frequency of the most important protein sources reported by our patients at 12 months after RYGB, including chicken meat, solid fresh cheese, skimmed or semi-skimmed milk, and legumes, in relation to the postoperative 3-month cutoff. The exception in this food group occurred for beef, whose intake remained similar at 3 and 12 months postoperatively. There was also an increase in the consumption of tubers, white rice, pasta, bread, and biscuits at 12 months after surgery as compared to the 3-month postoperative cutoff. In parallel, no changes were observed in the intake of raw and cooked vegetables and fruit with low sugar content.

According to the food pyramid recommended by the ASMBS, the intake of protein-rich foods, and of raw and cooked vegetables and fruits with low sugar contents was deficient at the post-operative time points studied. Tubers were not consumed or were below the recommended amount, regardless of the small increase in the amount ingested at 12 months after surgery.

The specific analysis of the food groups whose ingestion the ASMBS advised against showed that at the 3-month postoperative cutoff half of the patients consumed sausages (sausage, salami, ham, and mortadella) and 40 % consumed sandwiches, pizza, sfiha, snacks, cheetos, and fasts-foods at least once a week, whereas at the 12-month postoperative time point the consumption frequency of these foods had not changed but the number of patients consuming them increased. The consumption frequencies of margarine and diet soft drinks were high in the postoperative period after 3 months (2-4 times per week). In the 12-month postoperative cutoff only the frequency of diet soft drink consumption decreased, but the number of patients consuming both these foods increased.

ADEQUACY OF NUTRITIONAL SUPPLEMENTATION

In addition to the recommendation for supplementary protein ingestion, the patients who underwent RYGB in the present study had prescriptions for a multivitamin supplement (in drops) provided by the institution (116,667 IU of vitamin A; 0.1 mg of vitamin B1; 0.067 mg of vitamin B2; 0.467 mg of vitamin B3; 1,667 mg of vitamin C; 30 IU of vitamin D), as well as for supplementation with vitamin D and vitamin A (3,000 IU/day and 16,000 IU/day, respectively, in drops), vitamin D (4,400 in tablets), vitamin B12 (500-1,000 µg/month in injections), iron (40-80 mg/day in tablets), and calcium (1,200 mg/day in tablets) to be purchased by the patients themselves with their own resources. The total sum of these supplements provided adequate amounts of calcium and iron, higher amounts of vitamins A, D, and B12, and insufficient vitamin B1, according to the ASMBS recommendations (Table III). These supplements did not include vitamins E and K, copper, folate, and zinc (also recommended by the ASMBS), whose supplementation was prescribed only occasionally, and at the discretion of the physician in charge. Of the study patients, in the postoperative period one received a specific prescription of zinc (tablets), two of folic acid (tablets), and one of protein (albumin or whey protein), whereas no prescriptions were issued for vitamins E and K in any of them.

ADHERENCE TO NUTRITIONAL SUPPLEMENTATION

The supplements prescribed in both postoperative periods were only partially taken by the patients. Supplement compliance at 3 months postoperatively was 100 % for multivitamin HC; 40 % for vitamin D and vitamin A; 75 % for vitamin B12; 10 % for folic acid; 85 % for iron; 40 % for albumin; 0 % for zinc; 20 % for calcium; and 5 % for protein. Supplement compliance at 12 months postoperatively was 90 % for multivitamin HC; 45 % for vitamin D and vitamin A; 20 % forvitamin B12; 75 % for folic acid; 80 % for iron; 10 % for albumin; 5 % for zinc; 25 % for calcium; and 0 % for protein.

Table IV. Food frequency query administered to obese patients 3 and 12 months after a Roux-en-Y gastric bypass

Food	Portion (n°/description)	Frequency							
		1/day	≥ 2/ day	5-6/ week	2-4/ week	1/ week	1-3/ week	R/N	Amount (g/mL)
Skimmed milk									
Semi-skimmed milk									
Whole milk									
Yogurt									
White cheese (mines/frescal)									
Yellow cheese (dish/mozzarella)									
Creamy cheese									
Fried/scrambled egg									
Boiled egg									
Beef meat									
Pork meat									
Chicken									
Fresh fish									
Canned fish (sardines, tuna)									
Sausages (sausage, salami, ham, mortadella)									
Meat preserved in salt (cod, dried meat, feijoada ingredients)									
Viscera (liver, kidney, heart)									
Olive oil									
Salad dressing									
Bacon									
Butter									
Margarine									
Mayonnaise									
Snacks (crisps, cheese, peanuts)									
Sandwiches									
Pizza									
Sfiha									
Canned food (corn, peas, palm hearts, olives)									
Brown rice									
Polished rice									
Whole grain bread									
French bread									
Salty crackers									
Sweet cookies									
Cakes									
Spaghetti									
Beans									
Raw leaf									
Sautéed/cooked									

(Continuation in the next page)

Table IV (Cont.). Food frequency query administered to obese patients 3 and 12 months after a Roux-en-Y gastric bypass

Food	Portion (n°/description)	Frequency							
		1/day	≥ 2/ day	5-6/ week	2-4/ week	1/ week	1-3/ week	R/N	Amount (g/mL)
Raw vegetables									
Cooked vegetables									
Tubers (manioc, potatoes, yams)									
Fruits									
Ice cream									
Pies									
Jelly									
Candy									
Chocolates									
Coffee with sugar									
Coffee without sugar									
Natural juice with sugar									
Natural juice without sugar									
Artificial juice with sugar									
Artificial juice without sugar									
Soda									
Sweeteners									
Margarine									
Cottage cheese/yogurt									
Soft drinks (light)									

PERFORMANCE/MONITORING OF NUTRITIONAL SUPPLEMENTATION

Patients frequently presented normal values for biochemical markers of protein and micronutrients at all study time points. The exception was lower levels of vitamin D in the preoperative period (17 [9-27]) as compared to the reference value (30-100), which almost normalized during the postoperative period at 3 (26 [15-45]) and 12 months (26 [21-32]). Borderline hemoglobin and protein values were found in all of the study cutoff time points but remained within the normal range. However, the monitoring of nutritional blood chemistry markers was poor in frequency and comprehensiveness, only partially meeting ASMBS recommendations. No requests for vitamin A, B1, K, and E testing were found for any of the patients studied at any of the evaluated periods, nor for zinc (at 3 months) and copper (at 3 and 12 months) during the postoperative period. In addition, the evaluated markers were not assessed in the total patient population.

DISCUSSION

A marked decrease in macronutrient intake is largely reported after bariatric procedures, so that food intake may result in a deficiency > 50 % in nutritional needs in some patients (19,20). In particular, protein consumption may fall dramatically and become insufficient, possibly due to intolerance of protein sources, mainly of meat (5,21-23). Accordingly, our sample of patients submitted to RYGB exhibited a deficiency in protein intake (mean, 50 g/day), but this did not worsen in the long term, and they tolerated eating meat. When comparing the 3- and 12-month postoperative cutoffs, we found significant changes only in the consumption of carbohydrates (increased) and polyunsaturated fats (decreased). These changes occurred in parallel to a high intake of industrialized foods and a consequent decrease in the use of polyunsaturated fats for food cooking. An insufficient consumption of total fiber was also observed by us, and is consistent with the higher intake of refined and industrialized carbohydrates. Since the amount and quality of the carbohydrates ingested during the postoperative period of bariatric surgery may result in reduced weight loss (24), our data suggest the relevance of controlling carbohydrate intake in patients having undergone a RYGB, and highlight the difficulties involved in achieving this aim, even under nutritional counseling.

Depletion of micronutrients is also widely reported in bariatric patients even before surgery (7,25,26). Accordingly, deficits in micronutrient intake were largely observed by us before the RYGB, although some of these occurred only postoperatively. Actual-

Table V. Ingestion of calories and macronutrients by obese patients before and 3 and 12 months after a Roux-en-Y gastric bypass, according to a 7-day food registry

Variable	Preoperative	Postoperative, 3 m	Postoperative, 12 m	p-value (1)	p-value (2)	p-value (3)
Calories (kcal)	1677.6 972.3-2625.0	1004.2 514.9-1382.8	985.2 748.7-1864.9	*< 0.001*	*< 0.001*	0.07
Proteins (g)	71.4 43.0-89.8	47.7 22.5-82.7	57.3 24.1-86.2	*< 0.001*	*0.007*	0.128
Carbohydrates (g)	203.3 120.1-348.5	108.5 65.7-193.9	129.8 64.8-264.1	*< 0.001*	*< 0.001*	*0.037*
Total fibers (g)	13.8 6.5-31.1	9.4 4.1-17.7	9.7 4.4-15.4	*0.001*	*0.002*	0.783
Insoluble fibers (g)	3.4 1.4-6.3	2.3 0.9-4.2	2.5 0.7-4.5	*0.02*	*0.004*	0.6
Soluble fibers (g)	1.89 0.6-3.6	1.1 0.6-3.2	1.5 0.2-3.3	*0.019*	*0.012*	0.388
Total fat (g)	62.2 34.8-99.5	38.8 19.1-52.9	37.9 26.5-53.6	*< 0.001*	*< 0.001*	0.886
Saturated fat (g)	15.7 98.1-28.2)	8.9 5.2-17.3	9.7 5.1-16.4	*< 0.001*	*< 0.001*	0.841
Monounsaturated fat (g)	16.52 8.2-26.3	12.0 4.7-17.2	11.4 7.3-17.7	*< 0.001*	*0.002*	0.654
Polyunsaturated fat (g)	12.1 6.5-18.3	8.5 5.7-10.3	6.3 3.8-8.9	*< 0.001*	*< 0.001*	*< 0.001*
Cholesterol (mg)	194.1 62.3-343.7	125.5 52.4-334.2	136.2 59.9-331.4	*0.007*	*0.004*	0.784

p-value (1): at 3 months postoperative vs. *preoperative; p-value (2): at 12 months postoperative* vs. *preoperative; p-value (3): at 12 months postoperative* vs. *3 months postoperative. Results obtained using Student's t-test and Mann-Whitney paired test, expressed as median and minimum-maximum ingestion values for the period. Italic values indicate a significant statistical difference ($p \leq 0.05$).*

ly, we found depletions of all the assessed micronutrients early (3 months) after surgery except for vitamins C and A, and sodium. Deficits in micronutrient intake may negatively impact several physiological functions, and increase the risk of comorbidities, as well as affect the metabolism of leptin and insulin (27).

A qualitative improvement in food ingestion should compensate for the small portion of diet actually eaten, but this goal seems difficult to achieve. A low consumption of food sources of proteins, fruits, vegetables, and vegetable oils, and a high consumption of carbohydrates, sugars, and fats are reported in this population (28). Indeed, the postoperative intake of foods to be avoided, as recommended by the ASMBS, remained high in our study. This finding suggests that, despite receiving nutritional counseling, our patients exhibited quantitative but not qualitative dietary changes, which may result in relevant nutritional deficiencies.

Nutritional guidance seeking to promote the quality of food intake and to include micronutrient supplementation after bariatric surgery is fundamental to avoid the potential nutritional deficiencies to which bariatric patients are most susceptible (29). The patients who took part in this study were advised to prioritize protein-rich foods and to avoid caloric and/or highly processed foods with low nutritional quality for consumption, along with the intake of specific vitamin-mineral supplements. However, adherence to these recommendations was low, and the quality of the nutritional supplementation that was recommended did not fully comply with the ASMBS recommendations (18). In addition, we also found inadequacies in nutritional biochemical monitoring, even considering that not all patients included the study were examined for serum levels of nutritional markers, and some of the markers recommended by the ASMBS (18) were not measured in the patients examined.

There is no specific strategy to correct the inadequacies pointed out in our study concerning the nutritional care of patients submitted to RYGB. Nevertheless, such strategies may include actions to promote patient education regarding the nutritional and clinical consequences of their surgery. Educational actions should start already during the preoperative period, since orientations to promote meal fractioning, increase intake of high nutritional value foods, and decrease high-calorie foods have been shown their ability to modify the dietary patterns of pre-bariatric patients (30). Particularly, in our study, the application of a 24hR questionnaire provided data on nutritional intake quite similar to those provided by the 7dR. Our findings shed some light on the possibility of obtaining representative data on the eating habits of patients submitted to RYGB from the first visit, thus allowing early, personalized nutritional counseling.

Table VI. Ingestion of micronutrients by obese patients before and 3 and 12 months after a Roux-en-Y gastric bypass, according to a 7-day food registry

Variable	Preoperative	Postoperative, 3 m	Postoperative, 12 m	p-value (1)	p-value (2)	p-value (3)
Vitamin A (mg)	461.4 153.7-2655.6	500.8 63.0-2358.1	660.9 28.0-4143.2	0.596	0.756	0.622
Vitamin B1 (mg)	1.4 0.8-6.6	0.8 0.34-2.5	0.8 0.4-1.7	*0.007*	*< 0.001*	0.701
Vitamin B2 (mg)	0.8 0.5-1.6	0.6 0.2-1.6	0.6 0.3-2.0	*0.03*	*< 0.001*	0.784
Vitamin B3 (mg)	15.2 7.4-28.1	10.1 4.5-22.3	10.7 4.7-29.5	*< 0.001*	*0.002*	0.729
Vitamin B5 (mg)	1.97 1.0-2.9	1.5 0.6-2.9	1.3 0.6-3.7	*0.010*	*< 0.001*	0.189
Vitamin B6 (mg)	1.0 0.5-1.6	0.7 0.3-1.2	0.9 0.2-1.3	*0.010*	*0.014*	0.261
Vitamin B9 (mg)	121.0 89.1-200.4	76.9 1.5-195.1	78.5 30.3-237.9	*0.021*	*0.001*	0.571
Vitamin B12 (mg)	1.2 0.6-16.9	1.84 0.2-22.3	1.1 0.5-41.7	0.729	0.070	0.294
Vitamin C (mg)	110.7 25.8-3575.7	105.1 22.1-448.2	94.9 5.4-290.3	0.409	0.097	0.522
Vitamin D (mg)	0.7 0.1-19.1	0.3 0.1-57.5	0.3 0.1-0.7	0.231	*0.001*	0.064
Vitamin E (mg)	9.0 4.7-15.9	6.7 3.2-9.5	6.6 3.7-9.3	*0.001*	*< 0.001*	0.959
Calcium (mg)	532.4 311.9-843.1	484.7 106.6-993.0	403.9 92.9-806.4	0.375	0.177	0.717
Copper (mg)	0.8 0.5-60.5	0.5 0.2-1.3	0.6 0.2-2.5	*< 0.001*	*0.004*	0.312
Iron (mg)	10.0 6.8-344.8	6.2 2.7-60.7	7.1 3.6-24.2	*0.001*	*< 0.001*	0.165
Phosphorus (mg)	584.5 428.5-1001.1	460.0 186.3-834.3	520.6 180.5-763.9	*< 0.001*	*< 0.001*	0.41
Iodine (mg)	7.6 2.3-47.3	17.0 2.5-51.2	5.9 0.9-39.1	*0.021*	0.165	*< 0.001*
Magnesium (mg)	143.8 85.3-209.6	109.6 54.7-165.8	115.4 46.8-164.9	*< 0.001*	*< 0.001*	0.349
Manganese (mg)	1.2 0.7-16.9	0.8 0.5-24.1	0.9 0.5-1.9	*< 0.001*	*0.003*	0.409
Potassium (g)	1733.3 838.6-2276.9	1330.9 630.5-2276.9	1408.7 392.5-1984.2	*< 0.001*	*0.001*	0.956
Selenium (mg)	47.6 28.0-62.5	21.9 7.7-47.3	25.4 2.6-86.0	*< 0.001*	*< 0.001*	0.812
Sodium (g)	3412.4 2300.4-5942.7	2648.4 1795.7-3977.3	2371.0 1733.0-3528.6	*< 0.001*	*< 0.001*	*0.027*
Zinc (mg)	6.7 2.5-12.4	5.1 1.4-7.7	5.6 1.9-9.7	*0.002*	*0.040*	0.202

p-value (1): at 3 months postoperative vs. *preoperative; p-value (2): at 12 months postoperative* vs. *preoperative; p-value (3): at 12 months postoperative* vs. *3 months postoperative. Results obtained using Student's t-test and Mann-Whitney paired test, expressed as median and minimum-maximum ingestion values for the period. Italic values indicate a significant statistical difference (p ≤ 0.05).*

Our study presents some limitations that deserve to be highlighted. We analyzed a small sample made up only of women, but its size had a power of 80 % power to answer the scientific questions investigated, and the inclusion of only women by rigid selection criteria made the population homogeneous for analysis. In addition, the biochemical data analyzed were restricted to specific tests requested by physicians. Consequently, there is a shortage of these analyses, which may account for the fact that we did not find any biochemical changes in nutritional markers that were consistent with the non-conformities identified in quantitative and qualitative nutritional intake. On the other hand, this approach allowed us to identify a quantitative and qualitative deficiency of requests for blood chemistry tests capable of reflecting debilitated nutritional states in the bariatric patients who were cared for in the study's institution.

In summary, despite receiving routine dietary guidance, our patients undergoing RYGB presented quantitative and qualitative deficiencies in nutritional intake, which may compromise clinical results. Furthermore, the nutritional supplementation and monitoring that was put in place exhibited a poor compliance with well known guidelines, and/or was poorly adhered to by patients, suggesting that institutions specialized in bariatric care may be neither adequately updating these procedures, nor applying efficient strategies to improve compliance.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Is level of anxiety associated with overweight and obesity risk in university students? The NUTSAU Study

¿El nivel de ansiedad está asociado al riesgo de sobrepeso y obesidad en los estudiantes universitarios? El estudio NUTSAU

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Abstract

Introduction: effective ways of overcoming overweight may depend, in part, on the ability to identify mood disorders (anxiety is most prevalent) and their association with overeating and weight gain. The use of anthropometric indicators for such purposes can inform individual strategies for intervention before obesity sets in.

Objective: to verify the association between anxiety and anthropometric indicators in university students.

Methods: a cross-sectional study was conducted in 147 undergraduates across all programmes taught by the Federal University of Rio de Janeiro (UFRJ) at Macaé. A self-assessment questionnaire was administered in order to gather socioeconomic, lifestyle, and anxiety data. Anxiety status was estimated based on the State-Trait Anxiety Inventory (STAI), and interpreted based on the median of scores ($p \geq 50$). An anthropometric assessment was conducted to measure the subjects' body mass, body mass index (BMI), and waist circumference (WC). Body fat percentage (%BF) data were obtained using bioelectrical impedance analysis (BIA). The data were then analyzed using the chi-square and logistic regression tests, with a 0.05 significance level. For analysis purposes, anxiety was defined as the exposure variable in the present study, and anthropometric indicators as the outcomes.

Results: the students with an anxiety state $p \geq 50$ presented an odds ratio (OR) of 2.69 for being overweight ($p = 0.02$), as well as an OR of 2.77 for having high BF ($p = 0.02$) in the adjusted models.

Conclusion: a higher level of anxiety is associated with anthropometric indicators among university students, specifically for overweight or obesity and high BF percentages.

Keywords:

Anxiety. Body mass index. Mental health. Obesity. Risk groups. Young adults.

Resumen

Introducción: determinar formas efectivas de combatir el sobrepeso puede depender parcialmente de identificar las alteraciones del estado de ánimo, entre las cuales prevalece la ansiedad, y asociarlas al consumo excesivo de alimentos. Puede ser útil utilizar identificaciones antropométricas en tal investigación para definir estrategias personalizadas antes de que aparezca la obesidad.

Objetivo: verificar la asociación entre síntomas de ansiedad e indicadores antropométricos en estudiantes universitarios.

Metodología: este trabajo es un estudio transversal con 147 estudiantes de graduación de la Universidad Federal de Río de Janeiro en Macaé. Se recopilaron los datos con un cuestionario autocompletado sobre rasgos socioeconómicos, estilo de vida y síntomas de ansiedad. Se estimó el estado de ansiedad considerando el Inventario del Estado de Ansiedad (STAI, por sus siglas en inglés) por encima de la mediana ($p > 50$). La evaluación antropométrica consistió en medir la masa corporal, el índice de masa corporal (IMC), la circunferencia de la cintura (CC) y el porcentaje de grasa corporal (GC), obtenidos por bioimpedancia eléctrica bipolar. El análisis de datos se realizó mediante pruebas de regresión logística y del chi cuadrado, con el nivel de significancia establecido en 0,05. A efectos del análisis, se definieron como exposición el estado de ansiedad y como resultados los indicadores antropométricos.

Resultados: los estudiantes con STAI de $p > 50$ presentaron una razón de momios (RM) de 2,69 para el sobrepeso ($p = 0,02$) y de 2,77 para un nivel alto de GC ($p = 0,02$) en los modelos ajustados.

Conclusión: entre los estudiantes universitarios, un nivel de ansiedad más alto se asocia a los indicadores antropométricos de sobrepeso u obesidad y de nivel alto de GC.

Palabras clave:

Ansiedad. Índice de masa corporal. Salud mental. Obesidad. Grupos de riesgo. Adulto joven.

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INTRODUCTION

Anxiety is an emotion or a negative mood defined by some authors as apprehension and anticipation of the future. In Brazil, 9.3 % of the population suffers from some kind of anxiety disorder. This is three times as much as the world average of 3.6 % (1). On distinct levels, the feelings and symptoms caused by anxiety include increased heart rate, excessive sweating, shaking, impatience, frustration, irritability, lack of concentration, hypervigilance, cognitive distortions, fear, agitation, and difficulty speaking (2-4). When experienced at a moderate level, anxiety can impact learning as well as physical and intellectual performance (5). An anxiety state is categorized as a passing emotional state of the human body characterized by unpleasant feelings of tension and consciously perceived apprehension (6).

In terms of behavior, anxiety is related to a sense of aversion and an urge to run away, avoiding both affection and negative experiences (7). Because of this, many people develop harmful habits such as overeating or illegal drug use for mood regulation. This contributes to the development of addictions (8) that, in addition to decreasing serotonin (the neurotransmitter responsible for good mood), can reduce internal and external stimuli, and induce excessive and inappropriate increases in food intake. That, in turn, changes the composition of the body, which consists of fat and lean mass, as well as water (9,10).

In practice, fat body mass is measured primarily using anthropometric methods with specific equipment and calculations. Body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHR), and body fat percentage (%BF) are the most common indicators used for identifying overweight individuals and high body fat distribution. As an isolated measure, BMI cannot distinguish fat from lean body mass, and does not take into account the amount of water, muscle, and bone mass. Bioimpedance tests can be used to estimate those components by applying electric currents to body compartments (11). In order to diagnose an individual as overweight or as having another disorder, a combination of both indirect methods (anthropometrics and bioimpedance) is recommended due to their practicality, speed, and wide population reach.

In a recent literature review about mood and obesity, anxiety has been considered a risk factor for overweight, regardless of the occurrence of depression. Extreme examples cited include binge eating disorder, with episodes of unusually high food intake over short periods of time observed under elevated levels of anxiety and negative emotional states. In fact, eating disorders had been found in 30 % of obese individuals, according to the study. In another review based on a meta-analysis, an association between anxiety and obesity was found in 16 cross-sectional studies, with an odds ratio of 1.4 (CI: 1.2-1.6), suggesting opportunities for further research on specific obesity severity levels (9,12,13).

While the association between anxiety states and anthropometric indicators does not specifically denote a causal relationship in either direction, the present study aims to verify such association in university students using anxiety as the exposure of interest.

MATERIALS AND METHODS

The target population of the Longitudinal Study on the Nutrition and Health of University Students (NUTSAU) were students attending the second semester of each of the seven undergraduate programmes — Biology, Nursing, Engineering, Pharmacy, Nutrition, Medicine, and Chemistry — on offer at the Federal University of Rio de Janeiro (UFRJ), Macaé Campus. Our focus on second-semester students was based on the fact that the students at this point had had time to become more used to the campus and their study and dietary routines for at least six months (14).

The data were collected during the second semester of 2015 in classrooms and at the laboratory of the Research Centre on Health and Society (NUPESS/UFRJ-Macaé), with the assistance of lecturers and undergraduate research scholars of NUTSAU.

The sample for the study was calculated considering a prevalence of 12 %, a margin of error of 5 %, and a confidence level of 95 %. A sample of 147 students was assessed as part of the project.

The students were trained to assist with questionnaire administration, and the measurements from the anthropometric assessments were standardized to ensure intra- and inter-rater reliability (15). Classrooms were visited three times on average for different modules within each programme in an effort to include as many eligible students as possible.

The questionnaire was designed based on current scientific literature in adult public health (16-19). A draft version was pre-tested on nutrition students, and any terms or words not fully understood were replaced. The final version included questions related to gender, age, housing situation regarding house share, economic class, physical exercise, sedentary lifestyles, smoking habits, drinking habits, and anxiety symptoms.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria: second-semester students aged between 17 and 25 years, determined based on habits and routines observed at least six months into their undergraduate studies (14).

Exclusion criteria: pregnant and nursing women, as well as individuals with physical limitations for whom an anthropometric assessment would be impracticable.

Exposure: anxiety symptoms

Anxiety symptoms were assessed using the State-Trait Anxiety Inventory (STAI) scale (6), a self-reported instrument consisting of 20 items in which respondents used one of four ratings (1 = almost never; 2 = sometimes; 3 = often; 4 = almost always) to describe how they felt generally (6,19). Each of these items comprised two parallel scales, one for assessing trait anxiety (STAI-T) and another for state-anxiety (STAI-S). A score of 1-4 was assigned to each answer for quantification and interpretation purposes. For positive questions, the answers were marked in reverse scale ("almost always" scored 1 and "almost never" scored 4). For STAI-S, questions 1, 2, 5, 8, 10, 11, 15, 16, 19 and 20 were positive (6,19).

The scores for each completed questionnaire ranged between 20 and 80. Anxiety values were interpreted dichotomically based on the median value of the scores returned by the analysis of the student-filled questionnaires, as suggested by the relevant literature for use with the STAI anxiety assessment instrument (20-22). As the median was 43 points for both state anxiety and trait anxiety, any anxiety scores equal or greater than 43 points were considered high for both anxiety types in the present study.

OUTCOME: ANTHROPOMETRIC INDICATORS

Body mass (kg) was measured according to Lohman & Martorell (15), using a 50 g precision Tanita Inner Scan® digital scale with a maximum capacity of 150 kg. Each subject dressed in light clothing stood barefoot on the scale's platform. Height was also measured according to Lohman & Martorell (15) using a 1-cm precision Alturaexata® portable stadiometer. The subjects stood upright with their bare feet together, head facing forward in the Frankfurt plane, knees straight, and heels touching the base of the stadiometer. The BMI values were obtained from a calculation of the body mass divided by the height squared (kg/m²), categorized into the ranges used by the World Health Organization for teenagers (< 20 years) and adults (≥ 20 years) (23,24), and classified as either adequate (< 25 kg/m²) or excessive (25 kg/m²).

Waist circumference (WC) was measured with a stretch-resistant tape at the midpoint between the last palpable rib and the anterior superior iliac crest on exhalation, as described by Lohman and Martorell (15). The values obtained were considered adequate measures if < 94 cm or risk factors if ≥ 94 cm for men. The cut-off point for women was 80 cm (21).

Body fat percentage (%BF) was measured for the lower limbs using a Tanita Inner Scan® device with bioelectric impedance analysis (BIA) capabilities. A protocol, which included fasting, no-caffeine, no-alcohol, hydration, and exercise policies, was adopted as preparation for the physical assessment (25). Body fat percentages were categorized using the Lohman and Martorell procedures (15) for statistical analysis, with values < 15 % in the 'adequate' range, and ≥ 15 % in the 'high' range for males. For females, body fat values < 23 % were considered adequate, and values ≥ 23 % were considered high.

The impedance and anthropometric assessments were conducted in the morning, and the questionnaires were administered in the afternoon.

DATA PROCESSING AND ANALYSIS

The statistical analysis was run on SPSS v. 21 software, and Epi-Info with double data entry was used for processing. Frequency and prevalence data were presented for categorical variables, and a comparison was run between groups using chi-squared tests.

The association between exposure (state anxiety), via the median, and the outcome (anthropometric indicators), whether at adequate or inadequate levels, was determined with a logistic binary regression analysis to estimate crude and adjusted odds ratios (OR) for each indicator.

The state anxiety variable was dichotomized and characterized as < median (43 points) and median (43 points). This value refers to the group median according to the authors who use the instrument and follow this premise (23-25) based on the fact that the STAI instrument cannot diagnose the level of anxiety, but it can identify it. The anthropometric indicators were dichotomized as follows: BMI and %BF were considered either adequate or excessive; WC and WHR were considered either adequate or increased risk. Adequate BMI, WC, %BF, and WHR were used as the reference category for the indicators.

The adjusted model for BMI was composed of the following variables: gender, walking time per day, and alcohol consumption, the confounders that influence the association under study the most. For the remaining indicators, WC, %BF, and WHR were adjusted by age, walking time/day, energy, and alcohol consumption. The significance level used for the test was ≤ 0.05.

ETHICAL ASPECTS

The NUTSAU project was authorized by the campus general director of the Federal University of Rio de Janeiro at Macaé, and meets the criteria outlined in resolution 466 of December 12th, 2012 by the National Health Council, submitted and approved by the Research Ethics Committee of the Federal University of Rio de Janeiro, Macaé Campus (CAAE 51104115.4.0000.5699). All of the students were informed of the purposes of the study as appropriate, and asked to sign a free informed consent form.

RESULTS

A profile analysis of the 147 university students found that 63.3 % of the subjects were female and approximately two-thirds of the total of these undergraduates were studying health-related programs. Self-reported responses established that 53 % of the students self-identified as white, and 91.8 % were not recipients of student financial help or bursaries of any kind (housing, undergraduate research grants, community extension and outreach services, or mentoring scholarships). Screen usage time indicators also showed that 89 % of the students used screens for more than two hours a day, and significantly more women (94.6 %) engaged in high levels of usage than men (74.6 %) ($p = 0.01$) (Table I).

Anthropometric assessments placed nearly one fourth (23.8 %) of the students in weight categories that put them at increased health risk based on their BMI, with 16.3 % of overweight and 7.5 % of obese students. The results for WC measurements showed high and very high risk in 8.2 % of the subjects, with women accounting for a larger portion of this risk group ($p = 0.06$). Increased risk levels of WHR were also found in 10.9 % of the students, and 22.4 % of the %BF content measures found were either bad or critical (Table II).

Table I. Student distribution according to socioeconomic, demographic, and anxiety state characteristics. Rio de Janeiro, 2020

Variables	Total	Males	Females	p-value
Age				
Teen	76 (51.7 %)	27 (50 %)	49 (52.7 %)	*0.86*
Adult	71 (48.3 %)	27 (50 %)	44 (47.3 %)	
Course				
Biomedical	94 (63.9 %)	17 (31.5 %)	77 (82.8 %)	*< 0.001*
Math	53 (36.1 %)	37 (68.5 %)	16 (17.2 %)	
Home				
Alone	19 (12.9 %)	8 (14.8 %)	11 (11.8 %)	
With family	78 (53.1 %)	27 (50 %)	51 (54.8 %)	*0.81*
With friends	50 (34 %)	19 (35.2 %)	31 (33.3 %)	
Scholarship				
Yes	12 (8.2 %)	3 (5.6 %)	9 (9.7 %)	*0.54*
No	135 (91.8 %)	51 (94.4 %)	84 (90.3 %)	
Screen time				
Adequate	16 (10.9 %)	11 (20.4 %)	5 (5.4 %)	*0.01*
Excessive	131 (89.1 %)	43 (79.6 %)	88 (94.6 %)	
State anxiety				
≥ median (43 pts)	73 (49.7 %)	22 (40.7 %)	51 (54.8 %)	*0.14*
< median (43 pts)	74 (50.3 %)	32 (59.3 %)	42 (45.2 %)	
Total	147 (100 %)	54 (100 %)	93 (100 %)	

Chi-squared test.

Table II. Student distribution according to anthropometric variations and gender. Rio de Janeiro, 2020

Variables	Total	Males	Females	p-value
Body mass index				
Underweight	3 (2 %)	2 (3.7 %)	1 (1.1 %)	
Normal weight	109 (74.1 %)	38 (70.4 %)	71 (76.3 %)	*0.47*
Overweight	24 (16.3 %)	11 (20.4 %)	13 (14 %)	
Obese	11 (7.5 %)	3 (5.6 %)	8 (8.6 %)	
Waist circumference				
Adequate	135 (91.8 %)	53 (98.1 %)	82 (88.2 %)	
High risk	11 (7.5 %)	1 (1.9 %)	10 (10.8 %)	*0.06*
Very high risk	1 (0.7 %)	-	1 (1.11 %)	
% body fat				
Excellent/Good	43 (29.3 %)	22 (40.7 %)	21 (22.6 %)	
High/Average/Low	71 (48.3 %)	22 (40.7 %)	49 (52.7 %)	*0.07*
Bad/Very bad	33 (22.4 %)	10 (18.5 %)	23 (24.7 %)	
Waist-to-height ratio				
Adequate	131 (89.1 %)	50 (92.6 %)	81 (87.1 %)	*0.41*
Elevated	16 (10.9 %)	4 (7.4 %)	12 (12.9 %)	
Total	147 (100 %)	54 (100 %)	93 (100 %)	

Chi-squared test.

Table III. Association between anxiety and anthropometric indicators in university students. Rio de Janeiro, 2020

Variables	Crude OR (95 % CI)	p-value	Adjusted OR (95 % CI)	p-value*
High body mass index (≥ 25 kg/m²)				
State anxiety				
< median (43 pts)	1	*0.04*	1	*0.02*
≥ median (43 pts)	2.29 (1.04-5.06)		2.69 (1.16-6.23)	
High waist-to-height ratio (≥ 0.5)				
State anxiety				
< median (43 pts)	1	*0.05*	1	*0.04*
≥ median (43 pts)	3.34 (1.02-10.89)		3.42 (1.02-11.40)	
High risk waist				
State anxiety				
< median (43 pts)	1	*0.09*	1	*0.08*
≥ median (43 pts)	3.23 (0.84-12.46)		3.39 (0.84-13.67)	
High % body fat				
State anxiety				
< median (43 pts)	1	*0.04*	1	*0.02*
≥ median (43 pts)	2.38 (1.05-5.37)		2.77 (1.19-6.44)	

**Adjusted for age, walking time/day, energy, and alcohol consumption.*

Among the students with anxiety states above average, the adjusted analysis models found a 2.69 OR for overweight (p = 0.02) and 2.77 OR for bad or critical %BF (p = 0.02) (Table III).

DISCUSSION

This study was developed with university students who faced numerous challenges and responsibilities after starting their degree programmes. They suffered from the expectations placed on them by their families and society at large, and had to deal with dramatic changes in their daily lives due to exhaustively long hours of lectures and studies. All of these factors, which were directly or indirectly linked to the analyzed individuals, may increase the risk of developing or worsening anxiety symptoms, which has reflections on anthropometric indicators in the short term, and poses a potential risk for chronic non-communicable diseases in the long term.

The sample of students was predominantly made up of female subjects, and a majority attended health-related programs. Scholarly literature has shown that such full-time programs with heavier workloads, compounded by internal and external pressures, affect health, which means these students are more prone to showing signs and symptoms related to anxiety (26).

Approximately half of the students did not live with their families — they either shared accommodation with friends or lived alone. Additionally, the fact that only 8.2 % received some kind of financial support in the form of bursaries or scholarships suggests that 91.8 % of these undergraduates were financially dependent or had to work for a living, which may have significantly impacted their quality of life during their education period (27).

One of the lifestyle indicators assessed in the students was the use of electronic devices, specified as screen time. Prolonged use of screen devices was the prevailing trend in the sample, with a predominance of female students exhibiting this behaviour (p = 0.01). Following controls for potential confounding data (gender, income, body mass, and a variety of behaviours related to diets and physical exercise), two studies (28,29) found that such factors can contribute to a deterioration of anxiety symptoms and, as a result, may adversely affect anthropometric indicators.

A large proportion of the students assessed in the present study were found to be in the overweight category according to BMI indicators. Such findings were in line with the data obtained by the Surveillance System of Risk and Protective Factors for Chronic Diseases by Telephone (VIGITEL) survey, which revealed that one third of the young adult population are overweight (15). International studies have suggested that the increasingly high BMI values found in young adults could be a consequence of their lifestyles (30).

However, as much as the BMI analysis provides an important assessment tool, it cannot alone distinguish between lean and fat mass, nor can it provide insight regarding their distribution (11). For this reason, BMI assessment was used in combination with other important indexes for fat estimation, such as WC and WHR, due to their ability to provide a simple and valid diagnosis of abdominal

adiposity, and major indicators of risk factors for heart diseases, for example (31). The use of WC measurements enabled us to identify that 8.2 % of the sample was at a high or very high health risk, and most of these individuals were female. Campagnoli (32) reports a similar trend, pointing out an association between gender and greater proneness to obesity due to a number of factors including the presence of estrogen (a hormone that predisposes an individual to the formation of fat tissue in the body), a low calorie burn rate, and a greater tendency to consume more palatable food. A high WHR was found in 10.9 % of the students, which is associated with the high values found for WC, and suggests that young adults have unhealthy lifestyle and dietary habits.

The %BF results provided useful insight into fat and lean mass discrepancies, and were fairly simple to determine using a variety of approaches (33). Our study found worrying numbers related to this metric, with 22.4 % of the subjects in the bad or critical range of %BF. Considering that 24.7 % of the women involved were in this range (compared to 18,5 % of the men), the findings seem to confirm that men and women have different body compositions, possibly due to hormonal and physiological differences (32).

Most importantly, our study found a significant association between the highest levels of anxiety and anthropometric indicators for BMI and %BF. Such findings contribute to the results of the systematic reviews followed by meta-analyses (34), and corroborate a recent review (9) that linked the mechanisms of anxiety and obesity with the secretion of hormones such as serotonin. Additionally, individuals with higher levels of anxiety frequently avoided situations that could abruptly change their physiological responses, such as increased heart rate and blood pressure, contributing to a reduction in physical exercise (35). The combination of hormonal and physiological factors can lead to greater consumption of palatable food due to the neuronal stimulation and dependence it can induce. High-fat and high-sugar diets can cause inflammatory and cognitive changes (due to inflammation of the hippocampus, a critical region responsible for memory), leading to obesity (36).

In relation to the present study, it is important to highlight the particularities of the data collection location, which, when compared to other educational institutions, imposes limits on the sample size. The Macaé campus of the Federal University of Rio de Janeiro (UFRJ-Macaé) was inaugurated in July 2008, based on the recognition and evolution of the academic community, with the objective of creating courses, projects, and research in Macaé, a municipality in the state of Rio de Janeiro. In 2011, the campus offered eleven different courses within two different areas: exact sciences (chemistry, engineering, and pharmacy) and biological sciences (nutrition, chemistry, nursing, medicine, and biology). In 2015 the data collection of the NUTSAU group took place on this campus, covering all courses and the whole universe of university students present there.

One of the limitations related to the study, in addition to the number of individuals enrolled, is its cross-sectional design, which defined the scope of the inference. In addition, these characteristics also limit the analysis options with more stratification ranges. Because of this, it was then decided to work with the median, aiming at more homogeneous and comparable groups, in addition to careful work with the use of OR for anxiety symptoms and avoidance of closed diagnoses.

As the main potential for contribution by our study, our findings could be used to inform professional healthcare practice by providing evidence on the importance of intervention models that combine both the psychological and nutritional perspectives in order to promote innovative strategies in the prevention and treatment of anxiety and obesity.

CONCLUSION

Self-reported anxiety information in association with anthropometric assessments has allowed us to identify anthropometric risk for individuals with above-median anxiety states, showing an association between higher anxiety levels and anthropometric indicators for overweight or obesity, and high or very high body fat percentages.

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ARÁN

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Trabajo Original

Obesidad y síndrome metabólico

Light-dark cycle inversion effect on food intake and body weight in rats

Efecto de la inversión del ciclo de luz-oscuridad sobre el consumo de alimentos y el peso corporal en ratas

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Abstract

Background: most organisms inhabiting this planet have rhythmic functions in cycles that approximate 24 hours as a result of evolutionary adaptation. Disruption of these rhythms causes disruption in many bodily functions, including energy expenditure and consumption, and lipid and glucose metabolism, in addition to altering several biochemical parameters.

Objective: the aim of this study was to determine the effect of altering the light-dark cycle on diurnal and nocturnal food consumption and body weight in rats.

Material and methods: three experiments were carried out with an experimental group and a control group in each one. The groups included six males with an age of four months at the beginning of the experiment. Each experiment was 30 days long, starting with a baseline of 10 days and then inverting the light-dark cycle for another 20 days. In the first experiment the inversion took place at the end of the baseline period; in the second, the inversion was performed on days 10 and 20; in the third experiment inversions occurred every five days following the initial 10 days of baseline.

Results: our results show a lower body weight gain in the experimental groups when compared to the control groups.

Conclusions: significant differences in total consumption of food were not found, but were seen in the patterns of day and night consumption, along with a tendency to develop alterations characteristic of metabolic syndrome, which increased with the frequency of light-dark cycle inversion.

Keywords:

Light. Dark. Circadian cycle. Food intake. Body weight.

Resumen

Introducción: la mayoría de los organismos que habitan este planeta tienen funciones rítmicas que siguen ciclos cercanos a las 24 horas, resultado de la adaptación evolutiva. La alteración de estos ritmos provoca disrupción en funciones como el gasto y el consumo de energía, y el metabolismo de los lípidos y la glucosa, además de alterar varios parámetros bioquímicos.

Objetivo: el objetivo de este trabajo fue determinar el efecto de la alteración del ciclo luz-oscuridad sobre el consumo diurno y nocturno de alimento y el peso corporal en ratas.

Material y métodos: se llevaron a cabo tres experimentos con un grupo experimental y uno de control en cada uno de ellos. Los grupos estuvieron compuestos de seis machos de cuatro meses de edad cada uno. Cada experimento tuvo una duración de 30 días, comenzando con una línea base de 10 días y realizando inversiones del ciclo luz-oscuridad durante los otros 20 días. En el primer experimento se realizó una inversión al término de la línea base; en el experimento dos se realizó en los días 10 y 20; en el tercero, las inversiones se realizaron cada cinco días, tras los 10 días de la línea base.

Resultados: los resultados muestran una ganancia de peso corporal menor en los grupos experimentales en relación con los grupos de control.

Conclusión: no se encontró ninguna diferencia significativa en el consumo de alimento total pero sí en los patrones de consumo diurno y nocturno, que se intensificaron con el aumento de la frecuencia de la inversión del ciclo luz-oscuridad.

Palabras clave:

Luz. Oscuridad. Ciclo circadiano. Consumo de alimento. Peso corporal.

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INTRODUCTION

Organisms on earth have developed the ability to predict light-dark cycles of around 24 hours, called circadian cycles, which occur with the rotation of the earth on its axis, and this has allowed them to develop endogenous structures with the ability to synchronize almost all physiological and behavioral aspects to lighting conditions (body temperature, activity of the endocrine system, liver metabolism, wakefulness and sleep cycles, among others), whether they have evolved to be diurnal or nocturnal (1). These endogenous structures have been given the name of circadian clocks, and they are classified into three groups: peripheral, central, and homeostatic (2-4).

Evidence has shown that circadian cycles play an important role in maintaining health (5). In the case of nutrition, the relationship that circadian rhythms have is with the development of obesity, lipid metabolism (6), the development of metabolic syndrome, and feeding schedules (7). Diet, body weight, and circadian cycles are closely related (8). There are experiments that suggest that this relationship is bidirectional, since changes in nutritional status may cause changes in the balance of day and night activities, while alterations in the light-dark cycles can alter both the energy balance and the hours of food consumption (8-12).

Additionally, the results of some research suggest that food consumption and body mass may be influenced by fluctuations or alterations in the presence of light or darkness (8-12).

Experimental evidence indicates that homeostatic mechanisms can regulate the functions and behaviors of an organism to achieve internal balance. However, there are also studies that indicate that an alteration in circadian cycles may have repercussions on the functioning of various systems within an organism, resulting in alteration of food consumption, metabolism, storage, and body weight (8). However, the evidence is controversial, and there are investigations such as those carried out by De Assis et al. (13), who reported that an alteration of circadian cycle did not affect food consumption by subjects. The studies that found that changes in circadian cycles did not affect food consumption (14) indicated that the mechanisms by which they could affect it were uncertain.

However, the effects of frequency of exposure to such changes in the light-dark cycle that may have consequences, or the time limit of an event that allows the organism to return to normal conditions, as well as the exact effects of variations in lighting that are now constant and present in any modern civilization, are issues that remain poorly understood (15-24). Therefore, the aim of this research was to determine the effect of inversion of the light-dark cycle on body weight, and on diurnal and nocturnal food consumption in rats.

METHODS

A total of 3 experiments, lasting 30 days each, were designed utilizing 12 experimentally naïve male albino rats each. It was decided to use male subjects exclusively due to some morphological and hormonal differences that could potentially confound results (25). Rats with an age of four months at the beginning of the experiment, and initial weights between 310 and 360 grams (g) were assigned by convenience to the experimental or the control group, six for the control group and six for the experimental group, for each experiment. They were obtained at the vivarium of the *Instituto de Investigaciones en Comportamiento Alimentario y Nutrición* (IICAN). The subjects of this study were managed according to the criteria established by the Official Mexican Standard NOM-062-ZOO-1999 technical specifications for the production, care, and use of laboratory animals (26). In all experiments 5001 Rodent Chow from Purina was used as diet with unlimited access, and records of food intake and body weight were obtained in 12-hour intervals (6:00-8:00 am and 6:00-8:00 pm). To carry out the control of the light-dark cycles, the rats were placed in a laboratory isolated from sunlight using a model TE-102, IPSA brand timer. In all experiments control groups were exposed to a light-dark (L-D) cycle with light presence from 8:00 am to 8:00 pm. In all 3 experiments, the experimental group shared this condition during the first 10 days. In experiment 1 there was a L-D cycle inversion on day 10, with light from 8:00 pm to 8:00 am for the next 20 days of the experiment. This inversion in lightening conditions was performed at day 10 of experiment 2, going back to the original conditions at day 20. Meanwhile, experiment 3 had the same baseline conditions for the first 10 days, which was followed by lighting cycle inversions every 5 days (on days 10, 15, 20, and 25). The statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS), version 21.

RESULTS

In control groups and over the baseline period of experimental groups food was predominantly eaten during the dark phase, with 67.4 % to 76.4 % of ingestions occurring during this 12-hour period as expected for a nocturnal species. However, in experimental groups, following the L-D cycle inversions, the intake pattern was modified as may be observed in figures 1, 2, and 3, representing the experimental group's intake patterns for the three experiments; in all graphs the color black represents the data obtained in the 12-hour period from 8:00 pm to 8:00 am, independently of illumination conditions, whereas white represents the remaining 12-hour period (8:00 am to 8:00 pm). Figure 1 shows the data obtained for the experimental group in the first experiment as diurnal and nocturnal intake percentages; here, it may be observed that after the L-D cycle inversion, there is a corresponding modification of the intake pattern, that becomes predominantly diurnal, thus keeping the main intake during the dark period. However, as the frequency of L-D inversions increases, the ability to display this behavioral adaptation decreases, as can be observed in figures 2 and 3. In the second experiment we may see an intake inversion around 5 days after the L-D cycle modification; however, during experiment 3 this ability seems to get lost as the frequency increases, until in the last phase an equally distributed intake between the light

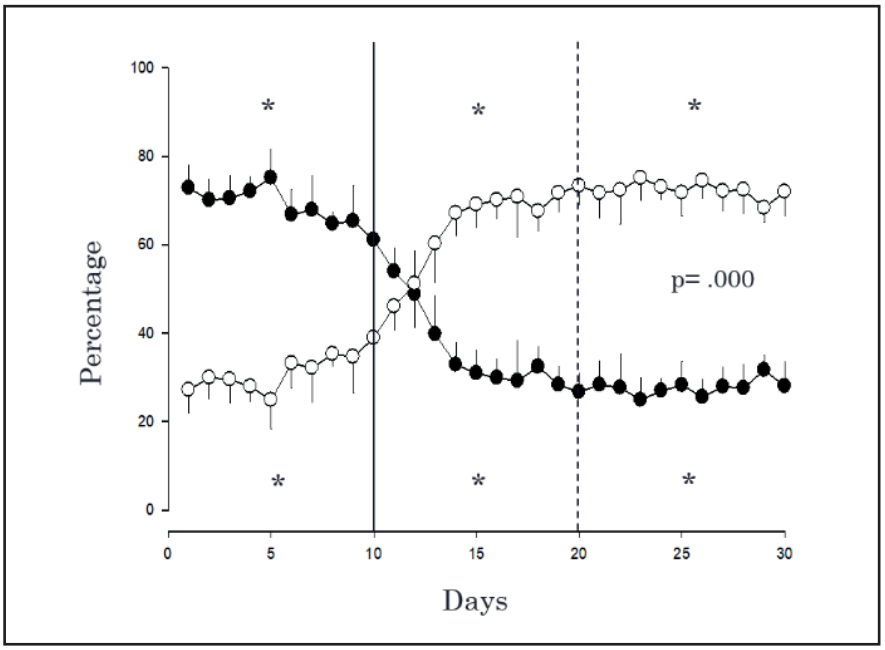

Figure 1.

Experimental group, first experiment. Diurnal and nocturnal food intake percentages.

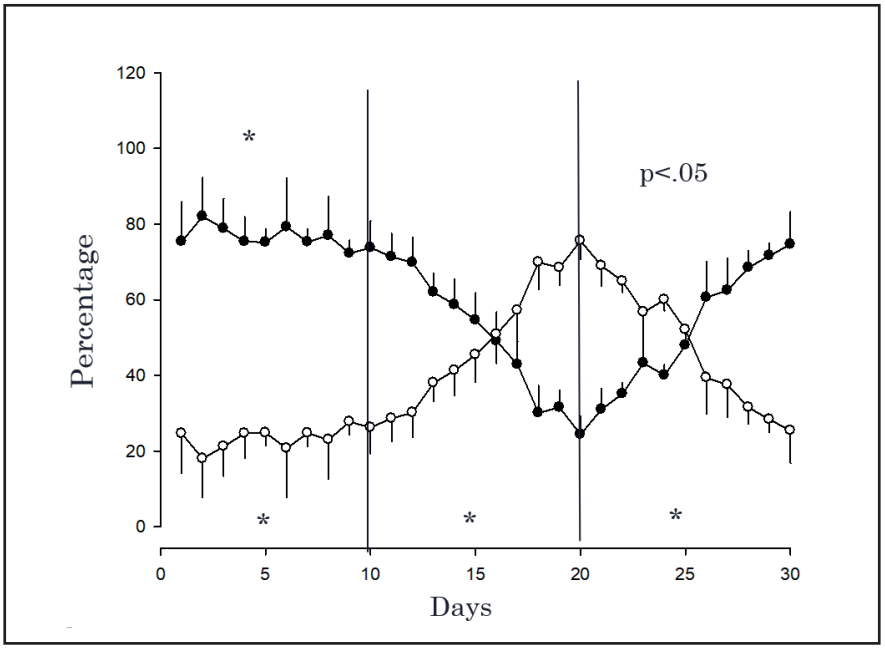

Figure 2.

Experimental group, second experiment. Diurnal and nocturnal food intake percentages.

and dark periods may be observed. An ANOVA and Student's t test were performed to compare groups and phases. Our findings include statistical differences between the experimental and control groups for diurnal intake (control, 6.16 g; experimental, 12.5 g) and nocturnal (control, 16.3 g; experimental, 9.7 g) in the first experiment, as well as in the second experiment (diurnal intake: control, 5.5 g, 6.0 g, and 6.2 g; experimental 4.7 g, 8.7 g, and 10.4 g, $p < 0.05$; nocturnal intake: control, 14.1 g, 14.6 g, and 14.9 g; experimental, 15.1g, 10.2 g, and 10.4 g, $p < 0.05$). Regarding the third experiment, we found statistically significant differences

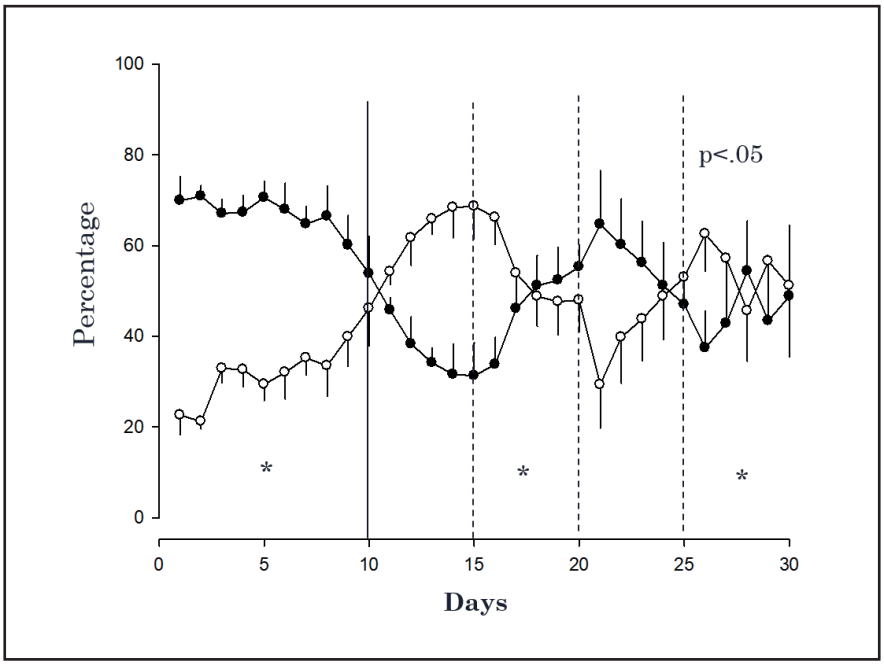

Figure 3.

Experimental group, third experiment. Diurnal and nocturnal food intake percentages.

in diurnal and nocturnal intake between both groups for all experimental phases, and similar diurnal intakes between phases 3 and 5, as well as phases 2 and 5; nocturnal phases 3 and 5 were also similar ($p < 0.05$). Regarding total food ingestion there were no statistical differences between the experimental and control groups or between phases during experiment 1 (control group intake per phase was 21.5 g, 22.3 g, and 22.6 g; experimental group intake was 22.2 g, 22.5 g, and 22.8 g, respectively). In experiment 2 there were no differences between groups or phases in the case of the control subjects; however, there was a statistically significant difference between phases 2 and 3 in the experimental group, as may be observed in figure 2 ($p < 0.05$). No statistically significant differences were found in total food intake between phases or groups in experiment 3. Regarding body weight, however, the average weight gain per day was 1.03 g for the control group and 0.18 g for the experimental group, which resulted in statistically significant differences ($p < 0.05$) between the average body weight seen in the control group (417 g) versus that seen in the experimental group (406 g). This trend was repeated in the third experiment (control, 350.9 g; experimental, 342.1 g, $p = 0.001$) but not in the second one, which presented statistical differences but with higher values for the experimental group (control, 342 g; experimental, 350.9 g, $p = 0.001$).

DISCUSSION

The main findings of this research include: 1) patterns of food consumption that adapted to the lighting conditions to which they were exposed; 2) this adaptation of consumption patterns disappeared when L-D cycle inversion frequency increased; 3) the energy balance of experimental subjects was maintained, exhibiting consumption values similar to those shown by the control group, regardless of inversions in the light-dark cycle and their frequency; 4) there were statistically significant differences in body weight between groups; however, a clear tendency was not found. Most scientific evidence reports an increase in body weight, mass gain, or development of overweight or obesity in subjects undergoing chronobiological alterations. According to Borniger et al. (16), body weight gain occurs, even in the absence of increased food consumption or decreased total caloric expenditure, due to the modification of food intake schedules. Since there is evidence that sleep quality and duration are not affected by the presence of dim light, and this is not interrupted by lighting of these characteristics during the rest period, but has the ability to alter the body weight balance of organisms, it has been concluded that the main oscillator, the suprachiasmatic nucleus (SQN), when synchronized by light signals is altered in the presence of dim light, but not so the peripheral oscillators that respond to the body's food intake signals. This lack of synchrony between the central and peripheral oscillators is the tentative cause of altered body weight control as seen in exposed subjects. Following the above reasoning we may conclude that, possibly, the reason why the subjects in our experiments did not show a clear tendency to increase body weight, to develop overweight or obesity, is the presence of food in free access conditions, and the fact that the behavioral and physiological adaptation to the new lighting conditions in all cases was carried out simultaneously.

The research carried out by Zucker (27) gives us the basis for another possible explanation. In the case of the subjects used in his experiment, which were subjected to constant light while at an early age, and therefore during a growth period, with the natural dislike that nocturnal rodents have for light, there was a loss of body weight. Taking this into account, another logical conclusion would be that the subjects used for these experiments were in the final stages of growth, and that the alteration of the light-dark cycle to which they were exposed had a reducing effect on their growth, causing the rats in the control group to maintain the normal weight gain for the species, whereas the experimental group remained stagnant, keeping the weight they had before the inversion.

Another common characteristic seen in the experiments that report body weight gain in animal models, and in the living conditions of people with night-shift jobs or in those who suffer from jet lag, is the shifting of phases for periods of less or more than 12 hours. However, when researching human phenomena it is important to acknowledge the personal, cultural, and social complexity that may contribute to these results. But whether conditions of continuous light, continuous darkness, advance or delay in the cycle are present, 12:12 behaviors are seldom maintained. The presence of a light-dark cycle lasting 24 hours could be part of the reason that prevented body weight gain from occurring in the subjects of these experiments, as has been reported in other experiments (15,16,22).

The diurnal and nocturnal consumption of food presented by the subjects in the experimental groups was modified according to the frequency of light-dark cycle inversions. During the first experiment an adaptation may be seen in the food consumption pattern that, after a period of about five days, goes from being predominantly nocturnal to diurnal, adjusting itself to the lighting conditions to which the subjects were exposed, similarly to the subjects in the experiment carried out by Humlová and Illnerová (28).

In this case, among the variables analyzed, consumption patterns were not found, but locomotor activity was, the subjects showed behavioral adjustments to the new lighting conditions; considering eating as part of the waking period activities, we could assume that consumption patterns also adjusted to the new lighting conditions. Additionally, the authors reported adaptation rate differences to the new lighting conditions for subjects, depending on their characteristics, when the light-dark cycle progressed for 8 hours, the subjects were able to adapt to the new surrounding conditions two days earlier than when it was delayed.

Despite the clear trend to nocturnal food consumption by rats (24), both in continuous light conditions and when kept in a 12:12 light-dark cycle, there are studies that have experimentally manipulated the duration, continuity, or absence of light periods due to the primary role that the SQN plays in the temporary control of organic functions, and because light has, through photoreception and phototransduction mechanisms, the ability to alter its functioning, the periods of wakefulness and rest of an organism, and with this, their feeding patterns (29,30).

Secondary oscillators can alter the wake-sleep patterns of an organism when the availability of food is limited, leading to the development of activity patterns that anticipate the availability of food (FAA). In the development of these experiments there were no limitations in food availability, therefore these patterns did not appear (8). The consumption patterns over the baseline period of each experiment, as well as those presented by the control groups, follow the consumption trend present in any nocturnal species.

During the first experiment, the control group presented an adaptation in their eating patterns at about 5 days after reversal of the light-dark cycle, moving to a predominantly diurnal food and water consumption pattern, following the lighting conditions to carry out most of their consumption in the dark period. During experiment two, after the first inversion, subjects were able to adapt to the new light-dark conditions to which they were exposed, although without reaching the average consumption presented during the baseline period. After the second exposure, the reversal of the food and water consumption pattern began almost immediately after the reversal of the lighting cycle, without the phase being long enough to reach the average presented in the first phase.

For the third experiment, it is possible to observe that the first inversion of the light-dark cycle is followed by an adaptation trend to the new lighting conditions like that presented in the previous experiments. Subsequent inversions, however, present lower quality in the lighting condition in which food is consumed predominantly; the response to lighting changes on the 20th and 25th, especially, was followed by little variation in the diet pattern, which at this point presented a consumption of food and water independent of the dark-light conditions, with a trend of 50-50 %.

There are studies that report responses like those presented by the above experimental subjects. Adaptation to different lighting conditions has been observed in several experiments, whether subjects were exposed to conditions of continuous light, continuous darkness, lengthening or shortening of light or darkness periods, or simply cycle delay or advance. Rosenwasser (24) used both continuous light conditions, under which the consumption pattern was maintained, with a cycle of around 24 hours, and conditions of 12 hours of light and 12 of darkness, to study the characteristics of food consumption by the subjects.

Cambras et al. (17) used cycle changes, lengthening their duration (25 hours), decreasing it (23 hours), and using conditions of continuous darkness, obtaining experimental evidence of the ability of subjects to adapt their behavior to the extant lighting conditions and their duration. These behavioral variations are present even in diurnal mammals (18). Whether they are subjected to conditions of continuous light, continuous darkness, phase advance or delay, subjects showed their ability to make behavioral adaptations, especially in their activity patterns in relation to new lighting conditions.

This same ability is similarly present in other species such as humans. Subjects exposed to repeated conditions of time zone change present alterations known as jet lag, which include behavioral, physiological, and performance alterations; however, after a few days of exposure to the new conditions, they manage to adapt to the new pattern of lighting, as did the subjects of experiments one and two (24).

This adaptation occurred within a period of time similar to that reported by Nagano et al. (23), of around 6 to 13 days, depending

on the characteristics of the cycle change, although in the case of the present experiments, these characteristics were different. While the period between a light-dark cycle inversion and the next was around 10 days or more, the ability to adapt to new lighting conditions was clear. However, in experiment three, when the frequency of changes increased, taking place every five days, the ability of the subjects to adapt to the new conditions decreased notably.

In this case, the reaction of the subjects to the first inversion of the light-dark cycle clearly presented a trend similar to that presented by the subjects in the experimental group of the first two experiments after the first modification of lighting conditions, with a clear trend to a reversal of the predominantly nocturnal cycle at baseline, eating the greater portion of food during the daytime period but in accordance to the darkness present in that period.

In the second inversion of the cycle, and by not allowing the subjects to make a behavioral adjustment that would allow them to return to conditions similar to those presented at baseline, consuming most of the food during the dark period, a second inversion is made to experimental day 15. After this alteration, the ability of the subjects to adapt to light conditions seems to decrease with each new intervention (those carried out on experimental days 20 and 25), losing their consumption trend when observed in relation to temporality (day or night) or to lighting conditions (absence or presence of light), to end up with a distribution of around 50 % of consumption for each 12-hour period with no apparent trend.

It has been reported that the presence of light during the night period has effects on metabolism, the circadian rhythm of core temperature and body weight, all signals related to food consumption (16). The experiment carried out by Salgado-Delgado et al. (31) reported similar results under different experimental conditions. In this case, the alteration occurred in the activity of the subjects; however, as we have indicated, as long as food is not restricted, changes in consumption patterns can be closely related to those of physical activity. In shift-work animal models, the subjects also experience a dysregulation that leads them to lose their rhythm of food consumption with up to 46 % activity in daytime, suggesting that repeated alteration of the circadian cycle leads to loss of consumption patterns in subjects. All of the above occurs without altering the energy balance of the subjects, unlike in several studies that reported changes in energy balance and body weight, and development of obesity, metabolic syndrome, and high food consumption (1,5,8,32-36).

Total food consumption did not exhibit significant differences in any of the groups, in any of the experiments. Consumption in all phases was also similar, which suggests that the ability to maintain intake balance was not affected by the changes in light-dark conditions to which subjects were exposed. Maintaining the conditions of 12 hours of light and 12 hours of darkness even when reversing the original cycle could be part of the reason why energy balance was not affected, since we are evolutionarily adapted as organisms to inhabit this planet with changes in lighting conditions every 12 hours (1).

The presence of light during the night period has the ability to metabolically alter an organism, affecting its body weight and core temperature; however, in this case it did not disturb total food consumption in these subjects, even when the energy balance was different from that observed in the control group, whose weight gain was greater in the three experiments (16).

One relationship important to consider is that of weight gain and development of obesity as a secondary effect of food consumption during an organism's rest schedule. In the study carried out in rodents by Fonken et al. (37) a possible relationship between exposure to light during the night period and increased body mass is suggested, due to the change in food consumption patterns, with modification of eating times. In this study, in addition, variations were made in the intensity of the light used with three groups of mice (continuous bright light, continuous dim light, and light-dark cycle 12-12), and consumption patterns increased up to 55.5 % during the light phase in the group with the presence of dim light during the dark period. Additionally, a greater gain in body weight was reported both for the group with dim light and for those exposed to bright light during the night period. However, there were no significant differences in total food consumption between the groups, hence they concluded that changes in consumption patterns, as well as in schedules, may be responsible for the variation in body weight among subjects. The results of this research, the increased prevalence of obesity worldwide, and the ever increasing areas with light pollution make the study of the relationship between light-dark conditions and the development of metabolic diseases and obesity an area of opportunity that could provide answers helpful both both to understand this relationship and to develop strategies useful to address both problems, and to develop interventions and treatments that reduce the impact of light pollution both on the health of organisms and in the environment, and on biological diversity.

CONCLUSIONS

Our conclusions are as follows:

- Body weight was maintained in the experimental groups while controls exhibited a species-specific growth curve.
- Experimental groups showed eating patterns that adapted themselves to lighting conditions.
- This adaptation disappeared when the frequency of light-dark cycle inversions was increased.
- Water intake displayed variations closely related to food intake variations.
- Energy balance was maintained in the experimental subjects, showing similar variations, independently of light-dark cycle inversions.

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Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Abdominal obesity and myocardial infarction risk — We demonstrate the anthropometric and mathematical reasons that justify the association bias of the waist-to-hip ratio

Obesidad abdominal y riesgo de infarto de miocardio: demostramos las razones antropométricas y matemáticas que justifican el sesgo de asociación del índice cintura-cadera

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Abstract

Background: the waist-to-hip ratio (WHR) is widely used to evaluate the association of abdominal obesity with myocardial infarction (MI).

Objective: our aim was to determine whether WHR-associated risk provides a bias.

Methods: a case-control study in 252 men. Stratification was used as an approach for removing bias effects. We created a baseline covariate ($WHR_{0.95-0.99}$) from a new matched sample in the stratum between 0.95 and 0.99. This stratum coincides with the overlap area of the distribution, where all subjects have a similar propensity score. We considered other covariate (WHR_S), conditioned on WHR < 1 and waist circumference (WC) being assigned a spurious risk. We hypothesized that subtracting hip circumference from WC (WHD) can be essential to observe the confounding effect provided by WHR.

Results: BMI: AUC: 0.694, 95 % CI (0.628-0.760); OR: 3.8. WC: AUC: 0.743, 95 % CI (0.681-0.805); OR: 5.7. WHR: AUC: 0.798, 95 % CI (0.740-0.855); OR: 8.6. Waist-height ratio (WHtR): AUC: 0.782, 95 % CI (0.724-0.840); OR: 8.5. WHD: AUC: 0.204, 95 % CI (0.146-0.261); OR: 0.36. Prevalence in cases: WHR ≥ 0.95 (84.1 % vs. 38 %; OR: 8.6); WHR < 1 (36.3 % vs. 85.7 %; OR: 2.3); WHR ≥ 1 (63.4 % vs. 14.2 %; OR: 4.4); WC ≥ 94.4 (71.4 % vs. 30.1 %; OR: 5.7); WHD ≥ 2.2 (27.7 % vs. 75.3 %; OR: 7.9); WHRs (50 % vs. 25 %; OR: 2).

Conclusions: WHR provides an association bias in MI cases. This can be extrapolated to other study populations. The bias is explained by a mathematical misconception where the protective effect of HC is overestimated concerning WC and height. The risk associated with WHR as higher than that associated with WC and WHtR entails anthropometric inconsistency and bias, to the extent of becoming epidemiologically false.

Keywords:

Abdominal obesity. Myocardial infarction. Body composition. Anthropometric indicator. Bias.

Resumen

Antecedentes: el índice cintura-cadera (ICC) se utiliza ampliamente para evaluar la asociación de la obesidad abdominal con el infarto de miocardio (IM).

Objetivo: nuestro propósito era determinar si el riesgo asociado a la ICC produce sesgo.

Métodos: estudio de casos y controles en 252 varones. Usamos la estratificación como criterio para eliminar los efectos del sesgo. Creamos una covariable basal ($ICC_{0,95-0,99}$) para una nueva muestra emparejada en el estrato de valores entre 0,95 y 0,99. Este estrato coincide con el área común de solapamiento de la distribución de puntos, donde todos los sujetos tienen un índice de propensión similar. Consideramos otra covariable (ICC_S) condicionada en ICC < 1 y una circunferencia de cintura (CC) donde la asignación de riesgo fuera espúrea. Hipotetizamos que restando CC del valor de la cadera se calculaba otra variable aritmética (DCC) que podría ser esencial para evidenciar el efecto de confusion que genera el ICC.

Resultados: IMC: ABC: 0,694, IC 95 % (0,628-0,760); OR: 3,8. CC: ABC: 0,743, IC 95 % (0,681-0,805); OR: 5,7. ICC: ABC: 0,798, IC 95 % (0,740-0,855); OR: 8,6. Índice cintura-talla (ICT): ABC: 0,782, IC 95 % (0,724-0,840); OR: 8,5. DCC: ABC: 0,204, IC 95 % (0,146-0,261); OR: 0,36. Prevalencia en los casos: ICC ≥ 0,95 (84,1 % *vs.* 38 %; OR: 8,6); ICC < 1 (36,3 % *vs.* 85,7 %; OR: 2,3); ICC ≥ 1 (63,4 % *vs.* 14,2 %; OR: 4,4); CC ≥ 94,4 (71,4 % *vs.* 30,1 %; OR: 5,7); DCC ≥ 2,2 (27,7 % *vs.* 75,3 %; OR: 7,9); ICCs (50 % *vs.* 25 %; OR: 2).

Conclusiones: el ICC produce un sesgo de asociación en los casos de IM. Ello puede extrapolarse a otras poblaciones de estudio. El sesgo se explica por un error de concepto matemático que sobreestima el efecto protector de la cadera con respecto a la CC y la altura. El riesgo asociado al ICC por encima del de la CC o el ICT presenta inconsistencia antropométrica y sesgo, llegando a ser epidemiológicamente falso.

Palabras clave:

Infarto de miocardio. Enfermedad cardiovascular. Obesidad abdominal. Indicador antropométrico. Composición corporal. Sesgo.

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INTRODUCTION

Cardiovascular diseases (CVDs), mainly heart disease and stroke, remain a worldwide leading cause of morbidity and mortality (1). Anthropometrically, important differences have been found in the assessment of the effects of obesity on the risk for coronary disease (2-4). Interestingly, an accurate estimation of body composition (BC) is highly relevant from a public health perspective (5). Hence, metrics associated with abdominal obesity and a nutrition status with excess body fat are essential for establishing the impact of adiposity on the metabolic processes that result in increased myocardial infarction (MI) risk. However, association does not equate to causation on incident MI, and in non-randomized study designs baseline differences in BC between the groups to be compared may introduce a systematic bias in the results.

The INTERHEART study proved waist-to-hip ratio (WHR) was a better indicator for predicting MI risk than body mass index (BMI) and waist circumference (WC) (3). Other more recent studies have also deemed WHR to be an excellent MI risk predictor (6-9). Besides, results from the UK Biobank have conferred to WHR a greater excess risk of MI in women than in men (7). However, evidence is accumulating in support of WC for reflecting MI and cardiometabolic risk (10-17). Additionally, the use of composite metrics such as the waist-height ratio (WHtR) or whole-body fat percentage (%BF) for predicting cardiovascular events and mortality has demonstrated a validity close to that of technological methods (10-17). On the other hand, we have revealed a selection bias for WHR, where this metric explains neither total causation nor the true nature of the risk (13,14). In fact, an important question lies in the discrepancy observed between WHR association and its worst correlations with measures of general and central adiposity (6,7,13,14).

Moreover, since a propensity score was defined, different methods have been used to address selection biases in balancing the distribution of covariates between exposure groups (18,19). Thus, the conditional distribution of risk between groups should be the same when the observed baseline covariates do not present standardized differences. However, a different BC between groups with similar baseline confounding variables may provide a bias in outcomes if the true-risk assignment does not account for the covariates that predict being assigned a true risk. In this sense, as a result of the above, a risk assignment for WHR of < 1 may be systematically the same with respect to different values for WC and hip circumference (HC), and therefore may not be directly comparable. Consequently, the bias for WHR can be substantial if both WC and HC are not controlled in the data analysis to preclude in the stratum of WHR < 1 the same risk assignment between subjects with equal WHR values, but not necessarily referring to the same BC at risk.

The aim of this study was to demonstrate whether the association of WHR and MI provides a bias in the results, and therefore false conclusions may be derived from a mere statistical analysis. We hypothesized that on a number line, each absolute value would represent the distance between the points corresponding to WC and HC as being mathematically the difference between denominator and numerator in WHR. However, subtracting provides an arithmetic variable from a set of numbers that represent an estimate of whole risk, and each value does not depend on the estimate of risk for HC with respect to WC. In contrast, dividing WC by HC will give us a proper abstract fraction with an information bias for whole risk, at least between the lowest point and the 0.99 value. Thus, WHR would be a confounding variable with whole risk conditioned on WC and the estimate of risk for HC concerning WC and height. We review what is known about WHR results worldwide, which will allow us to explain in anthropometric models the reasons that justify our insight when handling whole risk.

METHODS

PARTICIPANTS AND MEASUREMENTS

A case-control study with a sample of 252 European men aged 30-74 years, was evaluated. The minimum sample size for calculations was of 90 cases and at least 1 control per case, with obesity exposure, level of safety, and statistical power at 22 %, 0.99, and 0.99, respectively. The odds ratio (OR) for detection was 3. Study participants were recruited from a 2019 database in a Health Area in Spain**.** Cases were selected from a post-myocardial infarction cardiac rehabilitation program between 2012 and 2019, and data were collected in the first fitting days after hospital diagnosis. Exclusion criteria were nonage or any chronic disease. One age-matched (± 5 years) control was recruited per case in the same Health Area among health center users and State Administration workers. Exclusion criteria were identical for controls and cases, with the additional criterion that controls had no previous diagnosis of coronary disease or history of exertional chest pain. Trained staff used standard protocols to obtain measurements (15,16). All subjects signed an informed consent form according to the Declaration of Helsinki, and the study was approved by the ethics committee at the referral hospital.

Weight (kg) and height (cm) were measured. WC and HC were determined at the umbilicus and at the maximum circumference around the buttocks, respectively (cm). BMI (kg/m^2), WHR, and WHtR were calculated. Waist-hip difference (WHD), obtained by subtracting HC from WC, was calculated to provide an "x" value for each subject, including positive, zero, and negative results (x = HC - WC).

STUDY DESIGN

A receiver operating characteristic (ROC) analysis was carried out. The cutoff points were defined where sensitivity plus specificity was highest. Other standardized cutoffs were also analyzed. We used stratification as an approach for removing bias effects for WHR, as well as to control the effects of confounding factors derived from the density and distribution of their points between groups (18). We created a baseline covariate ($WHR_{0.95\text{-}0.99}$) from a new matched sample in the stratum between 0.95 and 0.99. This stratum coincides with the common area of overlap of the distribution for WHR in both groups, where all subjects had a similar

propensity score. Thus, pairs of cases and controls were formed such that one-to-one matched subjects had the nearest equivalent fraction (caliper distance of ± 0.01 within the same stratum). If, after conditioning, no systematic differences remain between both groups, this will be an indication that the model was correctly specified, balancing the distribution of the measured covariate. Thus, in both homogeneous groups, each subject would have the same probability (nonzero) to be assigned the whole risk, and risk assignment should be strongly ignorable (18). Consequently, in the matched sample we considered other baseline covariate with binary outcomes for spurious risk assignment (WHRs). It was conditioned on a risk assignment that defined spurious risk for $WHR_{0.95\text{-}0.99}$ where WC took a lower value than both its own cut-off and HC. A standard difference that higher than 10 % will be taken to indicate a considerable difference in the prevalence of WHRs between both groups. If, after comparing prevalences, no systematic differences remain, this will be an indication that a true risk in that stratum has been correctly assigned.

STATISTICAL ANALYSIS

Data were computed using IBM's SPSS package, version 22.0. Descriptive statistics including mean, standard deviation, and frequency are provided. Normal distributions were assessed using the Kolmogorov-Smirnov test. Student's t-test and the Chi-squared test were used to establish differences between parametric and non-parametric variables, respectively. The total area under the curve (AUC) was tested with no parametric differences, and values were used for identifying the strength of association for each indicator. ORs according to the defined cut-offs were calculated by using a binary logistic regression analysis. Contingency tables were used in the calculation of OR in other cases. The prevalence between different cut-offs or conditionings for the selected covariate was compared. OR was used to identify the strength of association for each indicator. The confidence interval was set at 95 % in all cases. A p-value < 0.01 was considered significant.

RESULTS

The baseline characteristics of participants and the established cutoffs are summarized in table I. Obesity indicators and WHD showed strongly significant differences ($p < 0.01$). Among single indicators, HC showed no differences ($p = 0.24$). WC and height showed significant differences ($p < 0.01$) in direct and inverse association with MI, respectively. There was no significant difference for $WHR_{0.95\text{-}0.99}$ ($p = 0.11$). A WHR cutoff ≥ 0.95 and

Table I. Baseline characteristics of study participants. Indicators with cut-off points defined by ROC analysis, and standardized for WHR and WHD. Values are means ± standard deviation for continuous variables, and percentages (%) for categorical variables

Variables	MI (n = 126)	95 % CI	Control (n = 126)	95 % CI	P/OR
Age (y)	53.9 ± 9.7	52.2-55.6	51.7 ± 9.3	50.1-53.4	p = 0.07
Height (cm)	169.4 ± 7.2	168.1 ± 170.7	173.5 ± 6.7	172.3-174.7	*p < 0.001
BMI (kg/m^2)	28.6 ± 4.02	27.9-29.3	26.2 ± 3.4	25.6-26.8	*p < 0.001
WC (cm)	101.7 ± 20.3	98.1-105.3	91.4 ± 10.1	89.6-93.2	*p < 0.001
HC (cm)	99.0 ± 12.9	96.8-101.3	97.5 ± 6.4	96.4-98.6	p = 0.24
WHR	1.01 ± 0.06	1-1.02	0.93 ± 0.06	0.92-0.94	*p < 0.001
WHD (cm)	(-1.3) ± 6.8	(-2.5)-(-0.1)	6.1 ± 6.6	4.9-7.3	*p < 0.001
$WHR_{0.95\text{-}0.99}$	0.97 ± 0.1 (n: 24)	0.96-0.98	0.968 ± 0.1 (n: 24)	0.96-0.97	p = 0.11
WHtR	0.60 ± 0.11	0.57-0.62	0.52 ± 0.05	0.50-0.53	*p < 0.001
WHR ≥ 0.95	84.1		38		8.6 (4.7-15.6)
WHRs	50 (n: 24)		25 (n: 24)		2
WHR < 1	36.5		85.7		2.3
WHR ≥ 1	63.4		14.2		4.4
WHD > 0	33.3		84.1		2.5
WHD ≤ 0	66.6		15.8		4.2
WHD ≥ 2.2	27.7		75.3		7.9 (4.5-13.9)
WHtR ≥ 0.54	79.3		30.9		8.5 (4.8-15.2)
WC ≥ 94.4	71.4		30.1		5.7 (3.3-9.9)
BMI ≥ 26.6	65.8		33.3		3.8 (2.2-6.9)

*ROC: receiver operating characteristic; WHR: waist-to-hip ratio; WHD: waist-hip difference; MI: myocardial infarction; CI: confidence interval; OR: odds ratio; BMI: body mass index; WC: waist circumference; HC: hip circumference; WHtR: waist-to-height ratio; WHRs: spurious risk for WHR. *Level of significance.*

WHtR ≥ 0.54 exhibited a higher prevalence in cases (OR: 8.6 and 8.5, respectively). A WC cutoff ≥ 94.4 had a notable prevalence in cases (OR: 5.7). A WHD cutoff ≥ 2.2 presented a notable prevalence in the control group (OR: 7.9). WHR ≥ 1 (OR: 4.4) and WHD ≤ 0 (OR: 4.2) showed a notable prevalence in cases. WHR < 1 and WHD > 0 showed a notable prevalence among controls (OR: 2.3 and 2.5, respectively). The prevalence of WHRs was twice as much in cases than in controls.

Boxplots for the distribution of WHR and WHD are shown in figure 1.

In ROC curves (not shown) WHR ≥ 0.95 presented the strongest association (AUC: 0.798 (0.740; 0.855). WHtR and WC exhibited a strong association (AUC: 0.782 (0.724; 0.840) and 0.743 (0.681; 0.805), respectively. WHD showed no association (AUC: 204 (0.146; 0.261), it being actually a protective factor associated with controls with a reciprocal AUC of 0.796 (0.739; 0.854) and a cutoff ≥ 2.2. Graphs representing the anthropometric models used for understanding biases, and explanations about the results are plotted in figures 2-4.

DISCUSSION

In the present study the association for the metrics of abdominal obesity was comparable to that of larger samples worldwide (3,7-10,16). On the other hand, to date, WHD, $WHR_{0.95\text{-}0.99}$ and WHRs were never referenced, whereas they are key indicators in our study. In spite of using the same two measurements, the results for WHR and WHD indicate differences in association. The selected risk cutoffs are mathematically key for understanding bias in WHR results. In previous studies (3,6-9,16) WHR showed a high magnitude of association, even consistently in studies where WHR-associated risk presented an information bias (13,14). In our current analysis, WHR also showed a high discriminatory power, even above that of WC and WHtR; however, our purpose was to demonstrate a selection bias.

It is noteworthy, firstly, that neither at-risk BC or raised %BF is affected by HC (14). Secondly, WC and HC represent absolute values without expressing equality for whole risk as a mathematical object. In addition, WC is the strongest simple indicator linked to visceral adiposity and unhealthy BC (14,16). Besides, numbers for WHR < 1 are abstract fractions with an equivalence relation = 1 / >1 representing a whole or unit that provides an information bias per se. In mathematics, WHR < 1 indicates the equal parts of WC that we have in HC without demonstrating anthropometric consistency or risk plausibility beyond that of WC.

Discrepancy between strong association for WHR and a lower anthropometric coherence for biological risk gave birth to our idea that something was wrong on the true-risk association (13,14). Geometrically, WC and HC represent parallel lengths from different bodily components accounting for cardiometabolic risk, while WHR is simply a way of representing size (part/whole) that is not a whole number of whole risk but a decimal value. However, WHD is a concrete number in the measuring of baseline anthropometric characteristics, but not BC *per se.*

From an anthropometric perspective, the standard human body has a HC larger than WC (WHR < 1) without posing any putative risk or protective effect. By deduction, HC > WC is a natural inequality satisfying a true premise, which responds to a linear equation: HC = WC + x, where x = HC - WC, the standard value being higher in women than in men. We have deliberately drawn horizontal rays where values for WC and WHD may lie (Figs. 2 and 3). Thus, only when "x" is mathematically zero there is equality (WC = HC; WHR = 1; WHD = 0) for a risk conclusion to be certain.

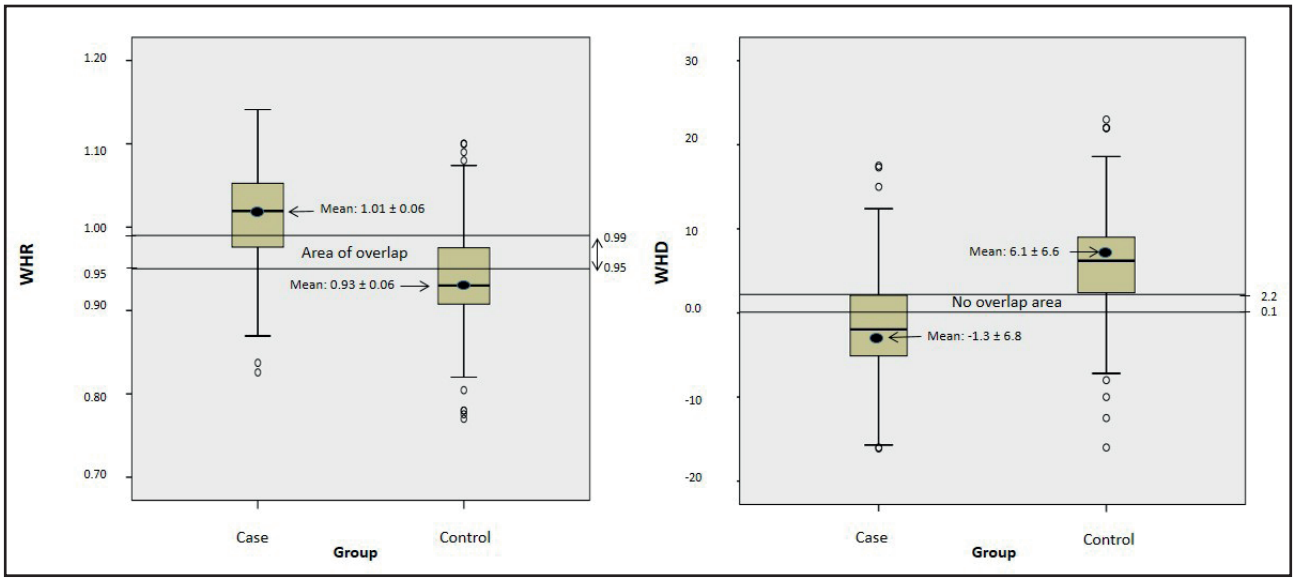

Figure 1.

Boxplots for the distribution of WHR and WHD between both groups (WHR: waist-to-hip ratio; WHD: waist-hip difference).

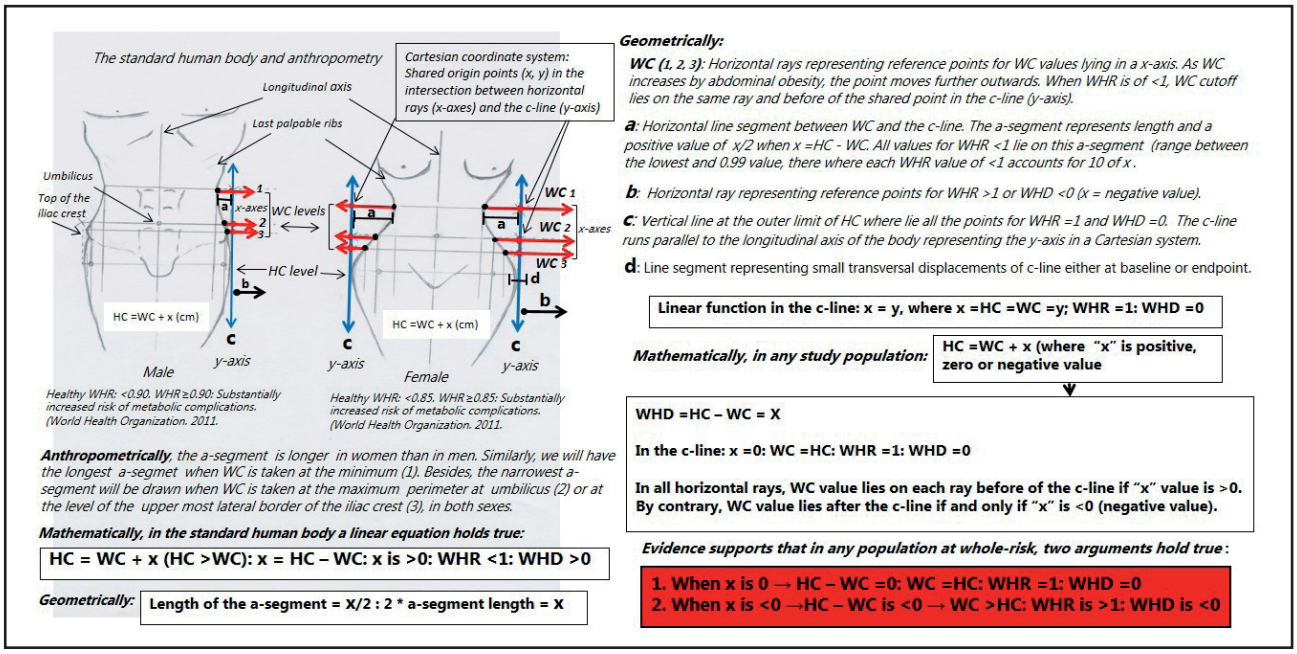

Figure 2.

Original creative assembly taken from anthropometric models and geometric lines on the standard human body. Geometrical and mathematical demonstrations for a correct anthropometric assessment of abdominal obesity and CVD risk. Drawings represent the human body (both sexes) where metrics are sample mean values per standard deviation for WC, HC, WHR, and WHD, these being actually valid for any anthropometrically healthy population and ethnicity. Within the respective lines would lie points of increased abdominal obesity representing mean values for thousands of cases of CVD, as well as biological changes pointing towards greater excess risk of CVD as WC increases. Similarly, the corresponding cut-off points associated per standard deviation, or quintiles, quartiles/tertiles, or receiver operating characteristic (ROC) analysis for WC, WHR, and WHD will always lie ahead of the c-line. These anthropometric models and schemes are valid for both case-control and cohort studies, and any type of cardiovascular event (CVD: cardiovascular disease; HC: hip circumference; WC: waist circumference; WHD: waist-hip difference; WHR: waist-to-hip ratio).

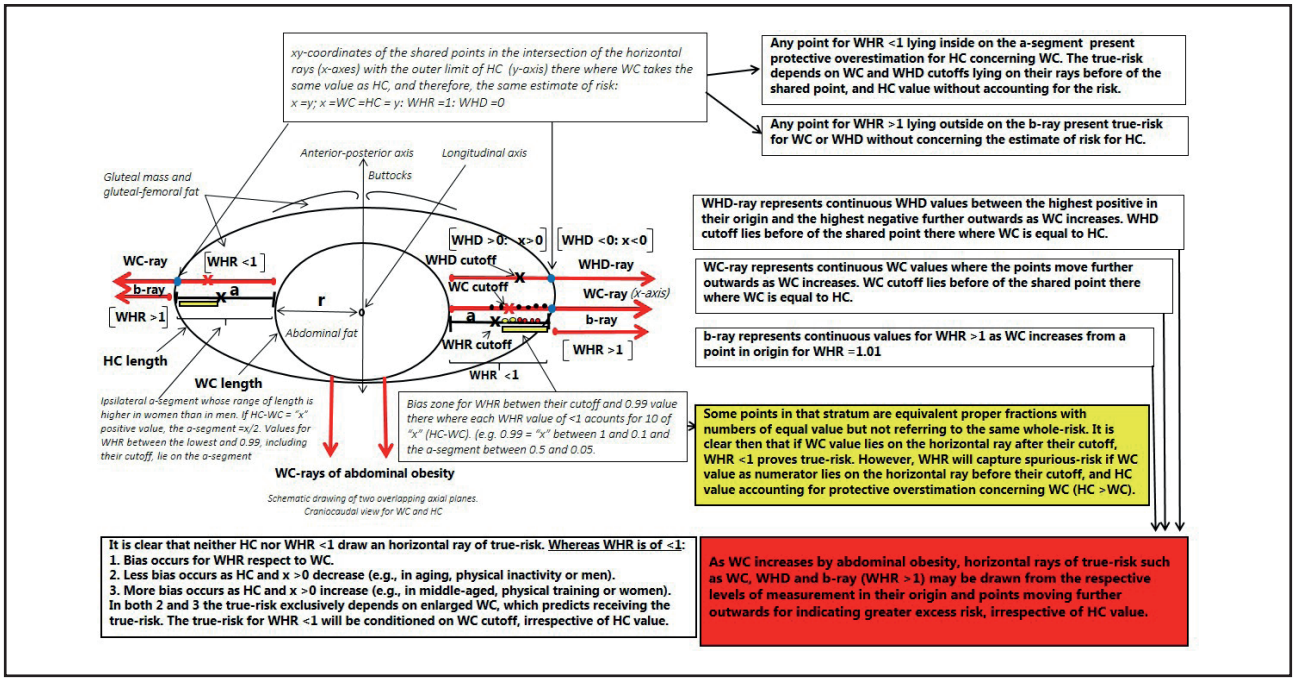

Figure 3.

Craniocaudal view for WC and HC from a schematic neutral model of the human body. Overlapping axial planes. Explanations for understanding are given in the main text. Names of lines and rays, where appropriate. The origin of the horizontal rays represent the same level of measurement for WC (HC: hip circumference; r: radius; WC: waist circumference; WHD: waist-hip difference; WHR: waist-to-hip ratio).

In fact, a narrow hip lower than or equal to WC appears unlikely in any anthropometrically healthy person. Obviously, only when WHR is ≥ 1 or WHD ≤ 0 (x = zero or a negative value) may true-risk indicators be used in order to draw a valid conclusion. In our results, these arguments are taxatives because within these limits there was no overlap in the distribution of points for cases and controls (Fig. 1), and whole risk was associated to cases. On this basis, accepting a WHR cutoff < 1 as a marker of whole risk would be wrong because HC > WC and WHD > 0 were associated with the control group. Besides, WC and HC may only coincide in one estimate of risk when WC takes the same value as HC (shared origin point (x, y) in a Cartesian coordinates system where the horizontal x-axis intersect with the vertical y-axis, and x = y (WHR = 1; WHD = 0) (Fig. 2 and 3).

Mathematically, equal numbers for WHR < 1 would mark different individuals and an infinite number of proper fractions where HC = WC + x is fulfilled for receiving the same WHR value, but not referring to the same whole risk (e.g., 93/98 vs. 94/99 vs. 95/100, etc., = 0.95: x = 5; 93/95.9 vs. 94/96.9 vs. 98/100.9, etc., = 0.97: x = 2.9; 93.8/93.9 vs. 94.2/94.3 vs. 96/96.1, etc., = 0.99: x = 0.1; HC > WC in all). However, from a biological standpoint there would be true risk when WC (≥ 94.4) predicts a whole-risk assignment, and a spurious risk when WC (< 94.4) predicts a spurious-risk assignment, and therefore a bias would occur for WHR by selecting spurious-risk points as true-risk ones when they merely represent a protective overestimation for HC concerning WC. In fact, we have checked that $WHR_{0.95\text{-}0.99}$ presented no significant inter-group difference for indicating a similar baseline covariate (18). However, after conditioning, WHRs presented a higher prevalence in cases, which indicated that risk assignment was incorrect and inconsistent. Accordingly, the selected points for WHR < 1 at the top will yield a misclassification with respect to WC because HC values do not account for the same estimate of risk as WC. In contrast, WHD showed no overlap area between their positive cutoff (2.2) and 0.1 (equivalent to WHR = 0.99). Similarly, WC and WHD cutoffs also lied on their rays ahead of their shared point with HC as anthropometrically expected, but never presenting a selection bias (Fig. 2 and 3). Hence, accepting a risk-code for WHR < 1 without proving whole risk for WC alone would not be a valid selection. In our results, WHR < 1 was associated with controls whereas WHR ≥ 1 showed a higher prevalence in cases, with a scientifically incongruous WHR-associated risk above WC. These findings and the rays of risk preclude a direct risk comparison between WC and WHR given that any WHR cutoff < 1 will always involve a protective overestimation for HC, and therefore, a systematic bias.

Surprisingly, most studies in predicting CVD risk always showed a WHR risk cutoff < 1 while selection biases were never discussed (3,7-11,16,17,20-27). Additionally, evidence supports that WHR is lower in women than in men (3,7-11,16,17,20-29) by involving a relatively larger HC and the longest a-segment, which ranges between the lowest (e.g., 0.76) and 0.99 value (Fig. 2). However, a HC larger than WC when the second predicts a risk code does not involve cardiovascular protection either. This observation may help explain a higher bias for WHR in the prediction of CVD in women due to a higher selection of fractions there where HC does not account for the same estimate of risk as WC. Similarly, a higher bias for WHR would occur when WC is taken at the minimum level due to a longer range between the lowest value and 0.99. In both approaches, the higher the range, the higher the bias that occurs due to the selection of a higher number of spurious-risk points where the protective effect for HC would always be overestimated.

Some previous studies reported a trend towards a higher risk for CVD as HC decreased (3,8,21,22), but there is currently no supporting evidence that HC carries any cardiometabolic risk (15-17), especially because most studies showed high mean values for HC (always HC > WC) (3,7,9,13,14,17,29). Obviously, from any value of HC > WC, WHR moves towards 0.99 as HC decreases, but not necessarily affecting true risk. It is clear then that something does not add up between a high association for WHR and its relationship with whole risk (13,14). Additionally, HC-adjusted WC has shown the strongest association with coronary disease and cardiovascular mortality (21-23); but this association also appears to be wrong due to a selection bias whole risk. By combining WC and HC at the same level of equality (21-23) (HC = WC instead of HC = WC + x), the paired equivalence of two different values would adulterate the WHR-associated risk, and we will find spurious-risk points in the strongest association even when HC = WC + 0.1. On the contrary, with the same baseline characteristics, when WHD = 0.1 there will always be true risk without selection bias or conditioning the covariate. Thus, in all direct quantitative comparisons between tertiles/quantiles, quintiles, ROC analysis and other statistical models, either WHR- or HC-adjusted WC will falsely yield stronger results for predicting risk than WC, since the model cannot distinguish between equal numbers with a different true risk each one of them, as was said above.

In another consideration, we have revealed that WHR and WHtR predict different risks if HC and height do not have a relationship such as height / HC = 2. This ratio would occur if, and only if, WHR / WHtR = 2 (e.g., 0.90/0.45, 0.95/0.475, 0.98/ 0.49, 1/0.5, etc.) (13), which also seems anthropologically unlikely (HC is always higher than height / 2). In fact, when we have compared ROC curves and ORs to identify association strength, the risk cutoff selected for WHR (≥ 0.95) was always lower than that for WHtR (0.54) x 2 (WHR / WHtR < 2), which indicated a different sensitivity and no risk equivalence between both indices. Along this line, the UK Biobank study showed an association of incident MI with WHR and WHtR, and a 1-SD higher WHR was more strongly associated than WC and WHtR in both sexes (7). However, WHR at the top was always < 1 when WHtR at the bottom showed a value of > 0.45-0.5 (WHR / WHtR < 2); so risk comparisons between both indices turned out to be biased (7,13,14). Hence, when a WHR cutoff is lower than WHtR x 2, a selection bias will occur for WHR due to a protective overestimation of HC with regard to height (13).

In our research line, we have warned that risk assessment is a matter of volume in relation to mass and density of bodily components (13,14). Thus, if we consider the human body as a three-dimensional solid, shaped somewhere between a cylinder and two truncated cones, both the areas of the bases and height can be used to calculate its total volume, although without

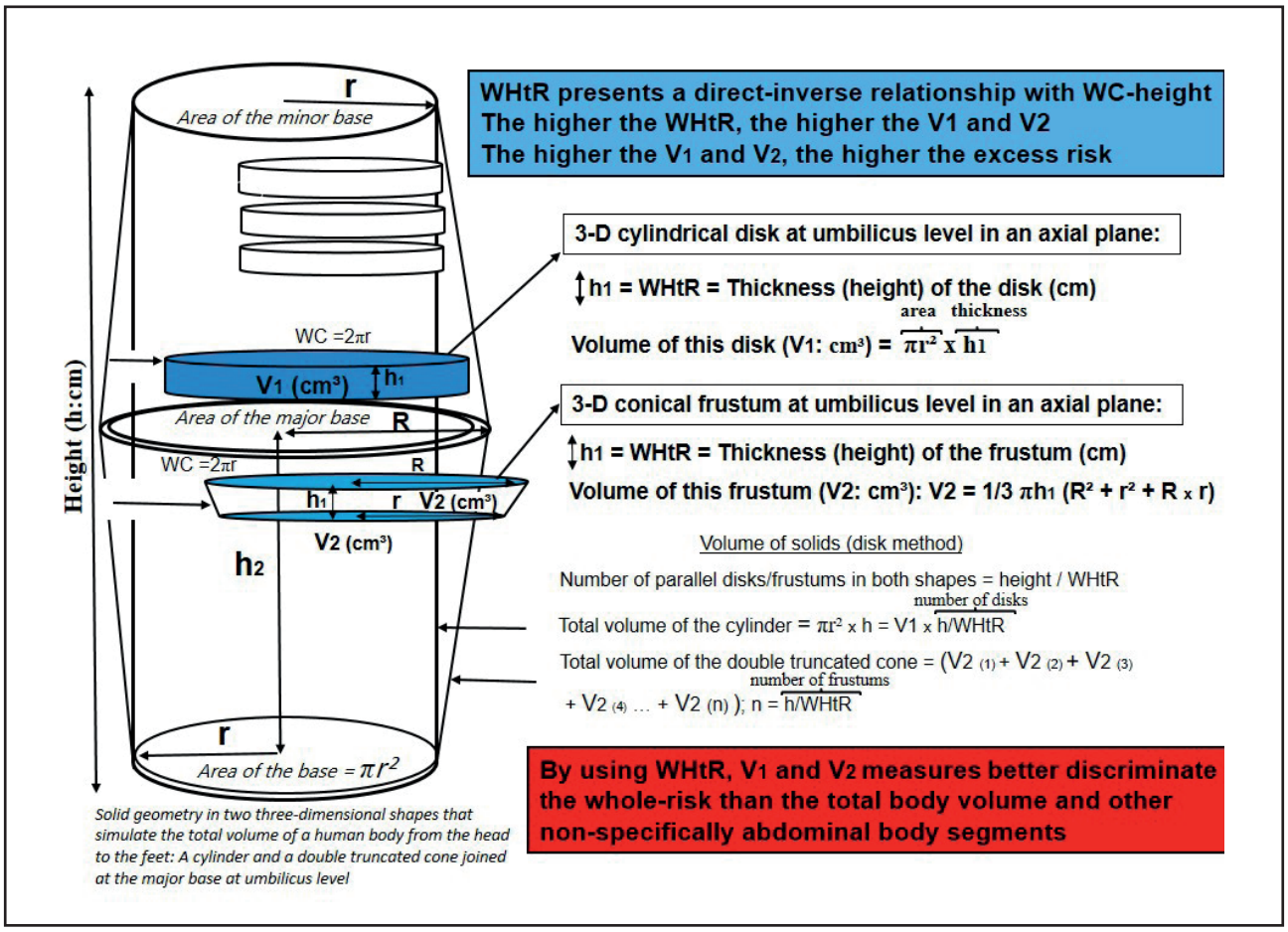

Figure 4.

Geometric model representing the human body as a solid cylinder or two truncated cones joined together at their major bases. "Volume" refers to the amount of three-dimensional space that bodily components occupy in relation to their mass and density (h: height for both shapes; h_1: thickness of the disk and frustum; h_2: height of a single truncated cone (h/2); WC: waist circumference; WHtR: waist-to-height ratio; R: radius of the major base; r: radius of the minor base; V_1: volume of the cylindrical disk; V_2: volume of the conical frustum. The base of the cylinder and the major base of the truncated cone have a length equal to WC as appropriate).

differentiating between biological components. However, the volume of a three-dimensional disk or frustum at the umbilicus level depends on WC and WHtR in a segment whose intra-abdominal components occupy all the space available except for a small peripheral-subcutaneous volume, which is less deleterious than intra-abdominal fat depots. Thereby, WHtR gives us the relative risk volume that we have by unit of height in direct-inverse relationship with WC-height, and the higher the WHtR, the higher the risk (Fig. 4).

Conceptually and anthropometrically, from an abdominal obesity volume, relative adiposity and at-risk BC, WC and height, and skinfolds to a lesser extent, are the basic measurements for predicting cardiometabolic and CVD risk (10,11,13,14,16,17,24-40), and technological methods should find the highest risk correlations here. It is clear that by using HC we will never capture an abdominal risk volume, nor a BC at greater risk of MI as compared to those of WC alone. Epidemiologically, this conceptual premise should be the key issue to guide anthropometric research, and to enable us to understand the differences between association and causality for biological risk when handling physical characteristics linked to different bodily components.

The most important strength of our findings is that WHR presents a high association, but partially capturing a dimension of spurious risk (13,14). Most studies have taken WHR from where HC values were comparatively higher than WC and height / 2 (WHR < 1; WHR / WHtR < 2). That way, researchers accepted a risk assignment for true negative values of WHR, making them as mathematically incorrect by the assumption of HC as protective factor. Thus, WHR has been used in thousands of people to evaluate the association of abdominal obesity and cardiovascular event risk without taking into account our mathematical observation (3,6-9,16,17,20-23,25-29,33,34,37). Accordingly, all WHR-associated risk above WC and WHtR is misleading evidence that has fooled scientists because of the research process itself, which slanted arithmetic data in an artificial direction. While this happened in important studies our disclosures were unknown;

so recommendations made on the issue related to WHR use for determining abdominal obesity and a substantially increased risk of metabolic complications and MI turned out to be false or at least to entail an information bias when pointing to central obesity (3,6-9,16,17,29).

In our graphs (Fig. 2-4) any whole population may be represented, including cases and controls and longitudinal follow-up for abdominal obesity and CVD risk. From any WC level, the horizontal rays keep a direct and inverse-negative relationship with WC and WHD, respectively. As WC increases by abdominal obesity, the points with greater excess risk move further outward. Similarly, as WHtR increases, the higher the relative volume, the higher the whole risk. In contrast, WHR draws neither rays nor greater excess risk, at least up to a 0.99 value, where in any range a higher-lesser bias occurs as HC increases-decreases and WC does not move in their ray. Therefore, in classifying a directly progressive true risk between the WHR risk cutoff and 0.99, it appears that no valid scores may be found. The answer is mathematical: in that stratum of points for WHR we could always find equal numbers, which precludes that true risk and spurious risk may be separated without accounting for WC being assigned the true risk. In summary, in assessing abdominal obesity and MI risk prediction WHR exhibits a systematic bias because of its being a confounding variable. Since the whole risk assigned to WHR < 1 is a false premise (mathematically not correct), the conclusions drawn from the statistical association will be epidemiologically in error. Any WHR cutoff < 1 precludes the same estimate of risk for WC and HC, making anthropometrically impossible the validity of WHR for predicting MI risk beyond that of WC alone. Consequently, WHR neither offers any advantages above WC, nor provides an accurate estimation of volume and at-risk BC. WHR remains attractive at first sight but will never perform better than WC or WHtR, at least regarding the true nature of risk. Our detailed research anthropometrically has no limitations, quite the opposite is the case. Evidence supports that our findings exhibit external validity and may be extrapolated to other ethnically-based or sex-specific study populations. With a WHR cutoff < 1, the association of abdominal obesity and MI is mathematically incorrect and anthropometrically unjustified, and will introduce biases in the results and provide false conclusions. It will easily be checked by transferring metrics and the corresponding risk cutoffs to the equations/formulas and our anthropometric models. Imaging-derived measurements of the real at-risk BC, especially %BF and visceral adiposity volume, should confirm it.

CONCLUSION

This study demonstrates an association bias for WHR in predicting MI risk. WHR-associated risk becomes a misleading evidence derived from a generalized mathematical misconception, which overestimates the protective effect of HC concerning WC and height. True risk exclusively derives from abdominal obesity volume and enlarged WC, which renders HC irrelevant. Any association of MI/CVD risk with WHR above WC and WHtR is mathematically biased and anthropometrically inconsistent; it becomes epidemiologically false and clinically useless. WHtR as pointing to a relative abdominal volume will not entail any bias, and may capture a dimension of risk above WC. This only happens when height shows an inverse association for increasing the discriminative ability of WHtR beyond that of WC, as proven. We offer new insights and anthropometric demonstrations that should be incorporated into clinical understanding when rigorously handling CVD risk as associated with metrics from abdominal obesity and unhealthy nutrition status by excess %BF.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Development and validation of prognostic models to estimate body weight loss in overweight and obese people

Desarrollo y validación de modelos de pronóstico para estimar la pérdida de peso corporal en personas con sobrepeso y obesidad

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Abstract

Background: predicting weight loss outcomes from information collected from subjects before they start a weight management program is an objective strongly pursued by scientists who study energy balance.

Objective: to develop and validate two prognostic models for the estimation of final body weight after a six-month intervention period.

Material and methods: the present work was developed following the TRIPOD standard to report prognostic multivariable prediction models. A multivariable linear regression analysis was applied to 70 % of participants to identify the most relevant variables and develop the best prognostic model for body weight estimation. Then, 30 % of the remaining sample was used to validate the model. The study involved a 6-month intervention based on 25-30 % caloric restriction and exercise. A total of 239 volunteers who had participated in the PRONAF study, aged 18 to 50 years, with overweight or obesity (body mass index: 25-34.9 kg/m^2), were enrolled. Body composition was estimated by dual-energy X-ray absorptiometry (DXA) and by hand-to-foot bioelectrical impedance (BIA) analysis.

Results: prognostic models were developed and validated with a high correlation (0.954 and 0.951 for DXA and BIA, respectively), with the paired t-tests showing no significant differences between estimated and measured body weights. The mean difference, standard error, and 95 % confidence interval of the DXA model were 0.067 ± 0.547 (-1.036-1.170), and those of the BIA model were -0.105 ± 0.511 (-1.134-0.924).

Conclusions: the models developed in this work make it possible to calculate the final BW of any participant engaged in an intervention like the one employed in this study based only on baseline body composition variables.

Keywords:

Body composition.
Exercise intervention.
Dietary intervention.
BIA. DXA.

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Clinical Trial Registry number: this study was registered at www.clinicaltrials.gov (ID: NCT01116856).

Conflicts of interest statement: the authors declare no conflicts of interest.

Authors' contributions: all authors (Rojo-Tirado, M.A., Benito, P.J., and Calderón, F.J.) have made substantial contributions to the present study's conception and design, acquisition of data, and analysis and interpretation of data. In addition, all authors have been involved in drafting the manuscript and revising it critically for important intellectual content. Moreover, all authors have given their final approval for the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Resumen

Antecedentes: predecir los resultados de la pérdida de peso a partir de la información recogida de los sujetos antes de que empiecen los programas de control de peso es un objetivo a largo plazo.

Objetivo: desarrollar y validar un modelo de pronóstico para la estimación del peso corporal final después de un período de intervención de seis meses.

Material y métodos: el presente trabajo se desarrolló siguiendo el estándar TRIPOD para reportar modelos pronósticos de predicción multivariable. El análisis de regresión lineal multivariable se aplicó al 70 % de los participantes para identificar las variables más relevantes y desarrollar el mejor modelo pronóstico para la estimación del peso corporal. Luego, el 30 % restante se utilizó para validar el modelo. Se realizó una intervención de 6 meses basada en la restricción calórica y el ejercicio. Los participantes fueron 239 voluntarios que habían participado en el estudio PRONAF, de 18 a 50 años de edad y con sobrepeso u obesidad (índice de masa corporal: 25-34,9 kg/m^2). La composición corporal se evaluó mediante la absorción de rayos X de energía dual y el análisis de la impedancia bioeléctrica de mano a pie.

Resultados: los modelos desarrollados se calibraron y validaron con una alta correlación (más de 0,94), no mostrando las pruebas t emparejadas diferencias significativas entre los pesos corporales estimados y los medidos.

Conclusiones: los modelos desarrollados en este trabajo permiten calcular el peso corporal final de cualquier participante que participe en una intervención como las empleadas en este estudio, conociendo únicamente sus variables de composición corporal iniciales.

Palabras clave:

Composición corporal. Intervención de ejercicio. Intervención dietética. BIA. DXA.

INTRODUCTION

The prevalence of obesity has dramatically increased worldwide among both children and adults in recent years (1,2). Forty to sixty percent of the adult population in the western world is actively attempting to reduce their body weight (BW). Nevertheless, overweight and obesity remain highly predominant sources of health problems, which suggests that many of those attempts are unsuccessful (3). Decreased caloric intake and increased physical activity remain the first line of treatment for most weight management programs (4,5).

The usual course of weight loss therapy shows that weight is lost quickly at first, and the point of greatest loss occurs 6 months after beginning treatment; then weight is slowly regained until weight returns near the original level (6). Predicting weight loss outcomes from information collected from subjects before they start weight management programs is a long-standing goal (7). In the area of human energy metabolism and body weight regulation, several mathematical models of weight change have been proposed over the past few decades (8-11). Such models provide a theoretical prediction of how body weight will change for a given energy intake and physical activity intervention assuming perfect adherence. These models have been validated under highly controlled conditions when adherence to the intervention can be assured. However, under less controlled conditions of people following an outpatient weight loss program, the ability to estimate the loss of body mass (or weight) at the end of the intervention represents an intellectual gap for health professionals. Therefore, intervention studies are needed that demonstrate the magnitude of the error in their estimates, and suggest more accessible strategies to estimate final weight. In previous literature references it was shown that no differences exist between the types of treatment followed as long as a diet is included (12,13), as has been also demonstrated within this sample (14,15). So, for health professionals it would be interesting to predict the weight that their patients will lose just by assessing easy-to-measure simple variables such as body composition variables at the start of the intervention. Therefore, the aim of this research was to explore several body composition variables in order to develop a comprehensive prognostic model for the estimation of final body weight after a particular six-month intervention period.

METHODS

SOURCE OF DATA

The sample population used for this study was drawn from a clinical trial (ClinicalTrials.gov ID: NCT01116856) conducted from January 2010 through June 2011, and followed the ethical guidelines of the Declaration of Helsinki. The Institutional Review Board at La Paz University Hospital (PI-643) reviewed and approved the study design and research protocol. Details concerning the theoretical background, protocol, and intervention of the clinical trial are described elsewhere (16). Furthermore, the present work was developed following the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) standard for reporting prognostic models of multivariate prediction (17).

PARTICIPANTS

The study participants were recruited through several advertisement campaigns covering a wide variety of media (television, radio, press, and the internet). A total of 2,319 potential participants, recruited from the general population, were informed about the nature of the study, and those who were 18 to 50 years old, had a BMI between 25 and 34.9 kg/m^2, were non-smokers, were sedentary (i.e., two hours or less of structured exercise per week) (18), and had glucose levels < 5.6 mmol/L (< 100 mg/dL) were invited to participate in this study. Women with any disturbances in their menstrual cycle were not eligible to participate in the study. Eligible participants who were willing to participate provided their written informed consent prior to joining the study, and then completed a baseline assessment at the involved medical center,

after which they were randomly assigned to the study groups. Randomization was computer-generated (Fig. 1).

Participants underwent a 6-month diet and exercise-based intervention, focusing on behavioral change, in two different waves: one of overweight participants (from January 2010 to June 2010) and one of obese participants (from January 2011 to June 2011). Each wave was split into four randomly assigned groups, stratified by age and sex: strength group (S), endurance group (E), combined strength and endurance group (SE), and control group, which followed the physical activity recommendations. The measurements took place within the first week (pre-intervention values) for all participants at baseline and after 22 weeks of intervention, in week 24 (post-intervention values).

Before the intervention started all participants were instructed to continue their usual daily activities as performed right before the intervention period, and their physical activity was assessed by a SenseWear Pro3 Armband™ accelerometer (Body Media, Pittsburgh, PA, USA) for a full week every month. Participants were instructed to wear the monitor continuously for 5 days, including weekend days and weekdays, following general recommendations (19). Data were recorded at 1-min intervals. Daily energy expenditure was calculated using the Body Media proprietary algorithm (Interview Research Software Version 6.0). In addition, they were required to report the kind, duration, and intensity of any physical activity undertaken, and the amount of any food ingested during the intervention period by means of a personal diary.

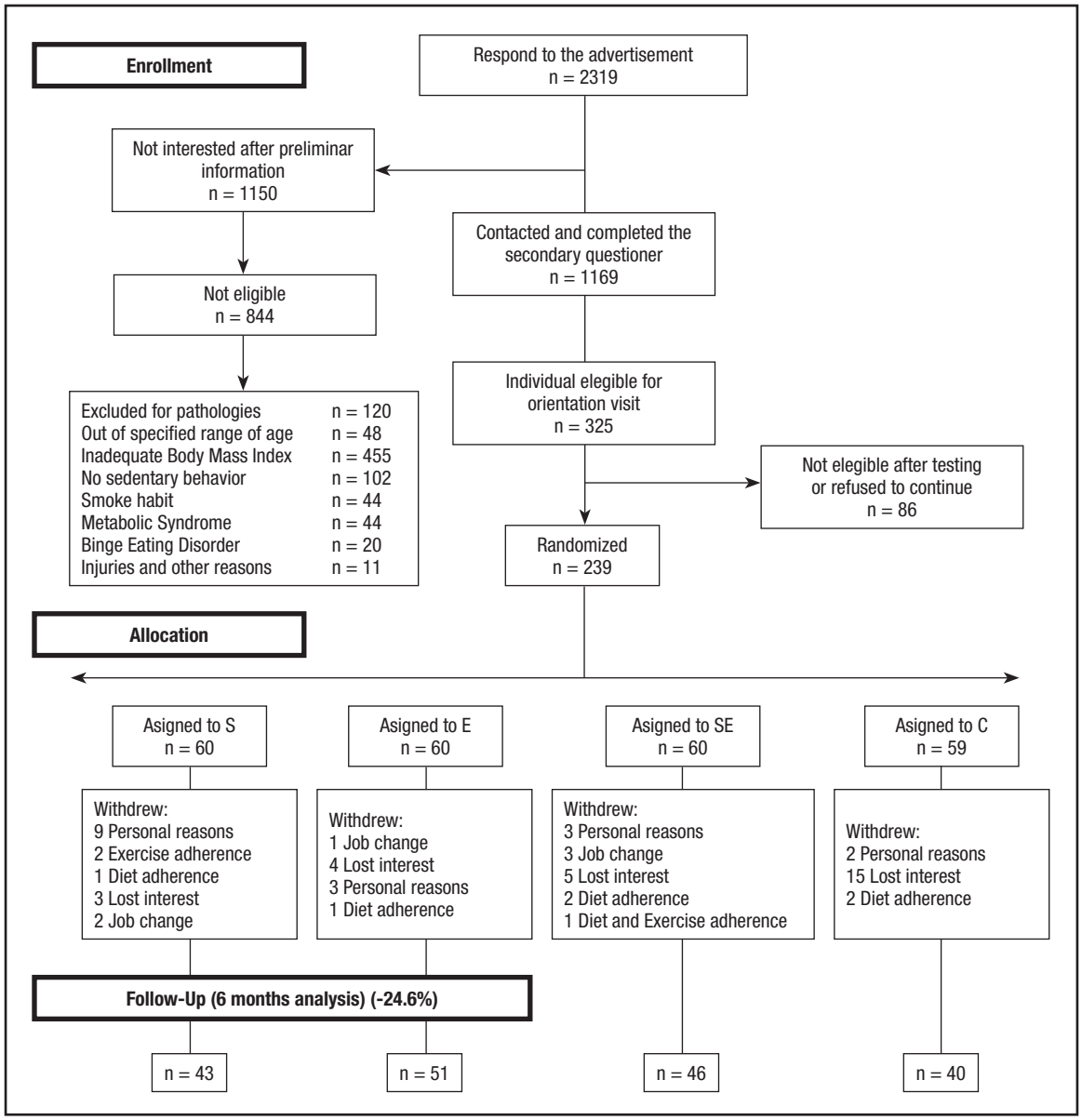

Figure 1.
Participant flow diagram.

At the beginning of the intervention the negative energy balance was calculated considering the daily energy expenditure and a 3-day food record, in order to decrease dietary energy intake by 25-30 % during the intervention. Adherence to the diet was calculated as the estimated kcal content of the diet divided by the actual kcal intake in percentage ([estimated kcal of diet / actual kcal intake] x 100), with 100 % being the highest adherence, following a methodology similar to that of other previous studies (20). Moreover, adherence to exercise was calculated by the number of sessions completed in relation to the theoretical number of sessions ([sessions performed / total sessions] x 100). Attendance of more than 90 % of training sessions, and an adherence to diet over 80 % were required.

DIET INTERVENTION

All participants followed an individualized hypocaloric diet with a 25-30 % caloric restriction (CR) from their own daily energy expenditure (21), which was measured by using the SenseWear Pro Armband™ (Body Media, Pittsburgh, PA, USA), which provides underestimates by a mean value of 8.8 % (22). Then, the macronutrient distribution was carried out according to the recommendatios issued by the *Sociedad Española de Nutrición Comunitaria* (23).

EXERCISE INTERVENTION

All exercise training groups (strength, endurance, and combined) followed an individualized training program, which consisted of exercise sessions three times a week for 22 weeks, carefully supervised by certified personal trainers. Details about the different protocols developed for these groups are described elsewhere (16).

CONTROL GROUP

Participants in the control group followed the dietary intervention and complied with the recommendations about physical activity issued by ACSM (24). Thus, control subjects were advised to undertake at least 200-300 min of moderate-intensity physical activity per week (30-60 min on most, if not all, days of the week).

OUTCOME

Body weight was measured in kilograms with a Tanita scale (TANITA BC-420MA. BioLógica Tecnología Médica SL, Spain) at baseline and just after the intervention period.

PREDICTORS

Body composition (fat mass and fat-free mass) was assessed by dual-energy X-ray absorptiometry (DXA) (GE Lunar Prodigy; GE Healthcare, Madison, WI, USA), and the scan analysis was performed using the GE Encore 2002, version 6.10.029, software to measure total fat mass in kg (FMD) and fat-free mass in kg (FFMD). Moreover, these parameters were also assessed by hand-to-foot bioelectrical impedance analysis (BIA) (OMRON BF 306W Analyzer, OMRON HEALTH-CARE Co., Ltd, Ukyo-ku, Kyoto, Japan), measuring fat mass in kg (FMB) and fat-free mass in kg (FFMB). All these predictors were measured just before and after the intervention period.

SAMPLE SIZE

The initial sample size was determined by the sample size estimation made in the clinical trial where the data for this work were obtained (25). Specifically for this study, the sample that completed the clinical trial (180 participants) was randomly divided into two subsets — with 70 % of the sample (134 participants) the prognostic model was developed, and later validated with the remaining 30 % of the sample (46 participants). In this way, the model was validated with a population that was different from the one it was developed with.

MISSING DATA

Participants who did not complete the intervention (for personal reasons, change of job, loss of interest, etc.), or whose adherence to the diet or exercise program was insufficient, had their information excluded from the analysis (Fig. 1).

STATISTICAL ANALYSIS METHODS

A one-way multivariate analysis of variance for repeated measures (MANOVA) was employed to compare the initial and final body composition variables between the development and validation subsets. Next, we applied a multivariable linear regression analysis to identify the most relevant variables associated with body weight from the development subset (70 % of the participants randomly sampled), to construct the best prognostic model for body weight estimation. These multivariable linear regression models were fitted to predict the final body weight. In each case, the dependent variable (predictor) was final body weight (in kilograms) and the independent variables were sex, initial body weight, height, type of treatment, fat mass, and fat-free mass for both the DXA and BIA models. A backward elimination approach was used to finalize the regression models. If the slope for an independent variable was not found to be significantly different than zero at $\alpha = 0.05$, that independent variable was excluded from the model. In addition, standardized coefficients of each variable and their 95 % confidence intervals were also obtained. To assess the fit of the prognostic model conventional linear regression models were used according to the coefficient of determination (R^2). After the prognostic models were fitted, they were applied to the remaining

30 % of the sample, carrying out a cross-validation and obtaining their predicted body weight measurements. Therefore, the models were validated by comparing the means from the measured and predicted body weight measurements using a paired Student's t-test. Pearson correlation coefficient (r) was used to assess the linear bivariate relationship among predicted and measured BW. In addition, mean differences, standard error of the mean (SEM), and 95 % confidence intervals were determined. Moreover, Bland-Altman plots were drawn to establish the limits of agreement for actual body weight against predicted weight, for both the DXA and BIA models. The data were statistically analyzed using the PASW Statistics software, version 18.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Data was presented as mean ± standard deviation (mean ± SD). For all tests a p-value < 0.05 was considered statistically significant.

RESULTS

PARTICIPANTS

Due to the reasons shown in figure 1 the final sample consisted of 180 participants. The characteristics of the 134 participants in the development subset, and the 46 participants in the validation subset are shown in table I. After the intervention, there were there no significant differences between groups (data not shown). At baseline, both the development and validation subsets had similar characteristics for all the measured variables ($p > 0.05$). After the intervention period, both the development and validation subsets had significant and similar reductions in BW (-8.49 ± 4.40 and -8.53 ± 4.48 kg, respectively, $F_{1,175} = 0.003$; $p = 0.958$), fat mass by DXA (FMD) (-6.83 ± 3.74 and -6.69 ± 3.03 kg, respectively, $F_{1,175} = 0.048$; $p = 0.826$), fat-free mass by DXA (FFMD) (-0.36 ± 1.50 and -0.50 ± 1.18 kg, respectively, $F_{1,175} = 0.294$; $p = 0.589$), fat mass by BIA (FMB) (-7.60 ± 3.80 and -7.71 ± 3.65 kg, respectively, $F_{1,175} = 0.029$; $p = 0.865$), and fat-free mass by BIA (FFMB) (-1.03 ± 1.69 and -0.84 ± 1.85 kg, respectively, $F_{1,175} = 0.391$; $p = 0.532$) (Table I).

MODEL DEVELOPMENT AND VALIDATION

In this study two prognostic models were developed and validated: the first one employing DXA data, and the second one using BIA data. In both cases, the dependent variable was the measured final body weight (in kilograms). The multivariable linear regression analysis revealed that the independent variables for the prognostic models were initial fat mass and fat-free mass in both models (DXA and BIA), thus discarding the rest of the variables introduced (sex, initial body weight, height, and type of treatment). In addition, coefficients of determination (R^2) over 0.9 were achieved for both models. The standardized coefficients from the multiple regressions and their 95 % confidence intervals are shown in table II. In this table, it may be observed that fat-free

Table I. Participant characteristics (n = 180). Values expressed as mean ± SD

	Development subset (n = 134)						Validation subset (n = 46)					
	Initial			Final			Initial			Final		
Age (years)	38.55	±	7.78	38.55	±	7.78	37.09	±	8.51	37.09	±	8.51
Body weight (kg)	88.52	±	13.6	80.03*	±	12.80	86.75	±	12.78	78.22*	±	11.13
Height (m)	1.70	±	0.09	1.70	±	0.09	1.67	±	0.10	1.67	±	0.10
Fat mass, DXA (kg)	34.37	±	6.90	27.55*	±	7.05	34.27	±	7.25	27.57*	±	7.69
Fat-free mass, DXA (kg)	50.15	±	9.66	49.79*	±	9.67	48.42	±	9.32	47.93*	±	9.28
Fat mass, BIA (kg)	31.35	±	7.83	23.75*	±	7.19	31.03	±	7.63	23.32*	±	7.33
Fat-free mass, BIA (kg)	57.50	±	10.86	56.46*	±	10.88	55.46	±	9.76	54.62*	±	9.91

**p < 0.05: significantly different from baseline.*

Table II. Standardized coefficients from the multiple regression models

Variable	Model 1 (DXA)	p-value	Model 2 (BIA)	p-value
Sex	-0.079 (-4.700-0.693)	0.144	-0.028 (-4.456-3.035)	0.708
Initial body weight	0.092 (-0.251-0.425)	0.611	0.134 (-0.308-0.561)	0.565
Height	0.013 (-13.436-16.964)	0.819	0.057 (-7.880-23.637)	0.324
Type of treatment	-0.046 (-1.123-0.070)	0.138	0.003 (-0.620-0.692)	0.914
Fat mass	0.486 (0.793-0.986)*	< 0.001	0.532 (0.787-0.965)*	< 0.001
Fat-free mass	0.741 (0.919-1.060)*	< 0.001	0.776 (0.855-0.984)*	< 0.001

**p < 0.001: significantly included in the models.*

Table III. Mean differences and standard errors between predicted and measured body weights using the paired t-test data

	Mean differences (kg)	Standard error (kg)	95 % confidence interval	Correlation	Paired Student's t-test
Development subset (n = 134)					
Model 1 (DXA)	-0.014	0.332	-0.671 to 0.642	0.954 ($p < 0.001$)	$t_{133} = -0.043$; $p = 0.965$
Model 2 (BIA)	-0.016	0.347	-0.704 to 0.672	0.951 ($p < 0.001$)	$t_{133} = -0.046$; $p = 0.963$
Validation subset (n = 46)					
Model 1 (DXA)	0.067	0.547	-1.036 to 1.170	0.947 ($p < 0.001$)	$T_{45} = 0.122$; $p = 0.903$
Model 2 (BIA)	-0.105	0.511	-1.134 to 0.924	0.954 ($p < 0.001$)	$t_{45} = -0.206$; $p = 0.838$

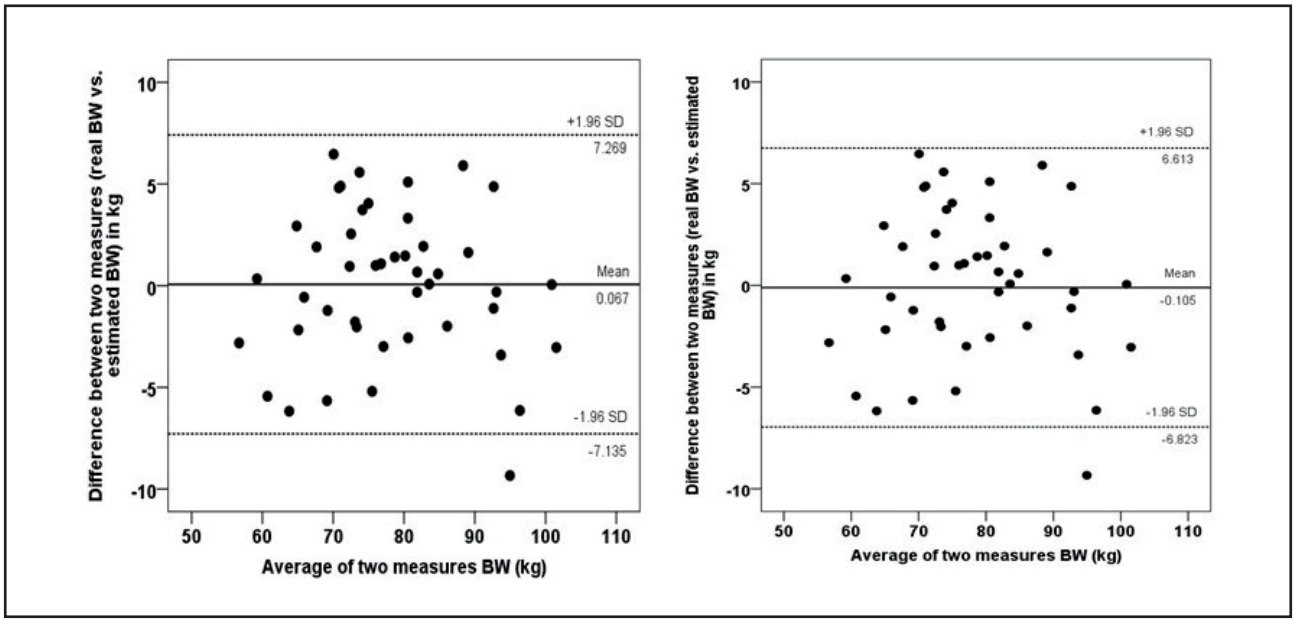

Figure 2.

Bland-Altman plot comparing the real body weight and the predicted body weight. Prognostic model with DXA data (left panel), and prognostic model with BIA data (right panel).

mass has more predictive power than fat mass in both models (0.741 vs. 0.486 for the DXA model; and 0.776 vs. 0.532 for the BIA model). Finally, the developed models were as follows:

- Model 1 (DXA, $R^2 = 0.909$; SEM = 3.87):
  Final BW (kg) = -0.379 + (0.89 x FMD) + (0.99 x FFMD)
- Model 2 (BIA, $R^2 = 0.903$; SEM = 4.01):
  Final BW (kg) = -0.344 + (0.876 x FMB) + (0.92 x FFMB)

Then, these models were validated by applying them to the remaining thirty per cent of the sample. Table III shows the mean differences between the values predicted by the models and the actual, measured weights with their standard errors and 95 % confidence intervals both in development and validation subsets. Furthermore, it may be observed that the prognostic models were developed and validated with a high correlation (over 0.95), with the paired t-tests not showing any significant differences between the predicted and measured body weights. Additionally, in the validation subset, the mean difference, standard error, and 95 % confidence interval of the DXA model were 0.067 ± 0.547 [-1.036-1.170], and those of the BIA model were -0.105 ± 0.511 [-1.134-0.924]. On the one hand, model 1 (DXA data) overestimated the change occurred in BW, which resulted in the mean predicted BW being lower than the measured one. On the other hand, model 2 (BIA) underestimated change in BW. The Bland-Altman agreement analysis for actual body weight as predicted by the two prognostic models is shown in figure 2. Finally, the standard error of the mean for the DXA model was 3.07 ± 2.21 kg, and for the BIA model was 3.19 ± 2.12 kg.

DISCUSSION

In this study we used data from a behavioral intervention program to develop prognostic models aimed at estimating final body weight after a six-month intervention, using as methodology baseline body

composition variables. Four different types of treatment were compared in this study, and this variable did not influence the analysis. Moreover, although several variables were added in the process of developing the prognostic models, only the body composition variables fat mass and fat-free mass were shown to have predictive power (Table II). The R^2 obtained in our study using the prognostic models in the validation subset were over 0.9, showing very small differences between actual and predicted BW means. The DXA model had an error of 0.82 % regarding total loss of BW, and the BIA model one of 1.29 % (Table III). These models could help health professionals estimate the loss of body mass (or weight) obtained at the end of this program, and propose more realistic strategies for their intervention, since weight loss is the primary concern of people who follow this program. With the baseline data of the participants and an intervention proposal similar to this one, similar results to those obtained in this study could be achieved, since the variables that most affect this result are the baseline body composition values and the energy balance during the intervention.

In this study we have reported values obtained using the DXA and BIA methods for assessing body composition. The most accurate method for assessing body composition is DXA (26-28). However, it is not as commonly accessible as the bioelectrical impedance method (which also has a lower cost). For this reason, both methods have been employed for the analyses. Since DXA is the most accurate method for assessing body composition, the prediction obtained based on DXA data should have been more accurate than that obtained with BIA. However, this was not the case since we could predict BW loss similarly with both methods.

We used multiple regressions to compare body composition variables in order to predict the final BW. According to the prognostic models developed, baselinel FM and FFM are the more predictive variables to estimate final BW in a weight loss program, whereas the variables sex, initial body weight, height, and type of treatment were excluded from the models (Table II). As Müller et al. reported, weight loss was associated with changes in the two major body components (FM and FFM) (5). Therefore, knowledge of the baseline FM and FFM measures would let us predict the final BW of any participant. This result was likely due to the fact that FM and FFM are the primary determinants of energy expenditure (29), and therefore the same intervention including diet and physical activity will result in a greater energy deficit in those with a higher FM and FFM, resulting in greater predicted weight loss.

In this study, it is noteworthy that final weight can be predicted based on only two variables of baseline body composition such as fat mass and fat-free mass. These models can predict final weight with a low standard error (0.55 kg), and a high correlation with actual weight (> 0.94).

The aim of weight loss is loss of FM, but inevitably a proportion of weight loss involves FFM (30,31). Loss of FFM may be undesirable if excessive, as non-adipose tissues are responsible for the majority of resting metabolic rate (RMR), regulation of core temperature, preservation of skeletal integrity, and maintenance of function and quality of life as the body ages (32,33). The fact of having a great amount of it could contribute to achieve a higher BW loss due to an increase in energy expenditure, with an increased RMR and a greater energy cost of physical activity (34-36). We suggest that any weight loss program should include exercise, especially strength training — because it maintains the FFM, contributing to the body's overall energy expenditure rate (29) —, has greater cardiometabolic health benefits (37), and prevents body weight regain (38,39). Redman showed that total daily energy expenditure was lower during weight loss with 25 % caloric restriction, and tended to be lower at weight loss maintenance (13). Brochu and Hunter showed this decreased RMR in a 6-month intervention (18,40). However, the strength trainers' group in Hunter's study did not have their RMR reduced, which led to maintenance of RMR following a return to energy balance, as this group trained at 65-80 % of the 1RM, an intensity higher than ours. This means that exercise intensity should be high in any weight loss program based on calorie restriction to maintain both the FFM and RMR.

Summarizing, the ability to estimate the loss of body weight at the end of a weight loss program represents an intellectual gap for health professionals. However, the prognostic models developed in this work make it possible to calculate the final BW of any participant engaged in an intervention using the PRONAF project methodology by only knowing their baseline body composition variables.

The use of these prognostic models could have advantages in the field of medicine and health because it would allow the prediction of the final body weight that a person could achieve at the end of his or her weight loss intervention, with non-invasive methods, in a rapid manner, and right there in the doctor's office. In addition, knowing the weight a patient could reach at the end of an intervention like that involved in the present study, a more restrictive intervention could be considered if the desired weight loss were greater. All of this could also contribute to evaluate the process at any time point throughout the intervention, allowing the health provider to redirect the intervention should body weight deviate from the established target. Further studies are needed to evaluate whether these models can be applied to other types of interventions. Moreover, it would be interesting to develop models to predict changes in the different components of body composition, beyond body weight.

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Trabajo Original

Valoración nutricional

Association of adductor pollicis muscle thickness and handgrip strength with nutritional status in hospitalized individuals

Asociación del espesor del músculo aductor del pulgar y la fuerza de prensión manual con el estado nutricional en individuos hospitalizados

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Abstract

Background: malnutrition is common in hospitalized patients and early diagnosis can contribute to better clinical and nutritional outcomes. Adductor pollicis muscle thickness (APMT) and handgrip strength (HGS) have been used to identify reductions in strength and muscle mass, associated or not with conventional methods.

Objective: we aimed to correlate APMT and HGS with conventional anthropometric variables in hospitalized patients, and assess their relationship with nutritional status as evaluated by the Patient-Generated Subjective Global Assessment (PG-SGA) method.

Methods: a cross-sectional study was conducted in patients of both sexes admitted to a University Hospital in Brazil. APMT, HGS, and conventional measures were used for anthropometric assessment. PG-SGA was used for the assessment of nutritional status.

Results: the sample included 73 patients (66.9 ± 9.6 years). Most patients were admitted for surgery procedures (53.4 %) and had an adequate body mass index (BMI) (47.9 %), while according to PG-SGA most patients (67.1 %) had some degree of malnutrition (B and C). Right-hand (R) APMT was significantly correlated with corrected arm muscle area (cAMA), calf circumference (CC), and HGS. Left-hand (L) APMT was significantly correlated with cAMA, arm circumference (AC), CC, PG-SGA score, and HGS. Both HGS values (R/L) were significantly correlated with CC, PG-SGA score, and APMT.

Conclusions: APMT and HGS were significantly correlated with the conventional anthropometric measure CC. In addition, the significant correlation observed between HGS, APMT, and PG-SGA highlights them as complementary assessments of nutritional status in clinical practice and for research purposes.

Keywords:

Handgrip strength. Nutritional status. PG-SGA.

Resumen

Introducción: la desnutrición es común en los pacientes hospitalizados y el diagnóstico temprano puede contribuir a obtener mejores resultados clínicos y nutricionales. El espesor del músculo aductor del pulgar (EMAP) y la fuerza de prensión manual (FPM) se han utilizado para identificar la reducción de la fuerza y la masa muscular, asociados o no a métodos convencionales.

Objetivo: nuestro objetivo fue correlacionar el EMAP y la FPM con las variables antropométricas convencionales en pacientes hospitalizados, y evaluar su relación con el estado nutricional evaluado por la valoración global subjetiva generada por el paciente (PG-SGA).

Métodos: se realizó un estudio transversal con pacientes de ambos sexos, ingresados en un hospital universitario de Brasil. Se utilizaron el EMAP, la FPM y medidas convencionales para la valoración antropométrica. Se utilizó el método PG-SGA para la valoración del estado nutricional.

Resultados: la muestra incluyó a 73 pacientes (66,9 ± 9,6 años). La mayoría de los pacientes ingresaron para someterse a procedimientos quirúrgicos (53,4 %) y tenían un índice de masa corporal (IMC) adecuado (47,9 %), mientras que según la PG-SGA, la mayoría de los pacientes (67,1 %) presentaban algún grado de desnutrición (B y C). El EMAP de la mano derecha se correlacionó significativamente con el área corregida del músculo del brazo (AMBc), la circunferencia de la pantorrilla (CP) y la FPM. El EMAP de la mano izquierda se correlacionó significativamente con las medidas AMBc, circunferencia del brazo, CP, puntuación PG-SGA y FPM. Ambas FPM, derecha e izquierda, se correlacionaron significativamente con las medidas CP, puntuación PG-SGA y EMAP.

Conclusiones: el EMAP y la FPM se correlacionaron significativamente con la medida antropométrica convencional CP. Además, la correlación significativa observada entre FPM, EMAP y PG-SGA destaca estos métodos como evaluaciones complementarias del estado nutricional en la práctica clínica y con fines de investigación.

Palabras clave:

Fuerza de prensión manual. Estado nutricional. PG-SGA.

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INTRODUCTION

Malnutrition can affect up to 50 % of hospitalized patients and is one of the main public health problems in developing countries. However, when malnutrition is not neglected by healthcare professionals, unfavorable clinical outcomes can be prevented 1).

Longer hospital stays, increased costs, impairment of the immune system, increased risk of pressure injuries, post-surgical complications, increased number of infections, delayed recovery, and increased risk of mortality are well-described consequences of malnutrition in the literature (1,2).

Thus, nutritional screening must be performed using validated tools, followed or not by detailed nutritional assessment, within 48 hours of patient admission in order to enable the multidisciplinary team to maintain a more assertive clinical approach and adequate clinical management (1).

The Patient-Generated Subjective Global Assessment (PG-SGA) instrument, available in Portuguese and culturally adapted to Brazil, is one of the most widely used subjective tools for patient screening and nutritional evaluation (3,4).

In addition to PG-SGA, objective methods such as conventional anthropometry are indicated for screening malnutrition. Among the most commonly used and available methods, especially in public hospitals, body mass index (BMI), calf circumference (CC), arm circumference (AC), tricipital skinfold (TSF), arm muscle circumference (AMC), and adductor pollicis muscle thickness (APMT) stand out (1).

Recently, APMT has emerged as an alternative nutritional status assessment as it is a direct measure, independent of adipose mass, and unaffected by hydration status. Moreover, APMT is a non-invasive, low-cost, easily applicable bedside method (5,6).

In the same way, handgrip strength (HGS) has also emerged as a highly used parameter by various healthcare professionals. Recently, HGS has been shown to be useful for assessing nutritional and functional status, especially in hospitalized patients (7).

Thus, considering the increasing need for improved nutritional care within hospitals, and the need to enhance the clinical prognosis of patients hospitalized for clinical and/or surgical procedures, this study aimed to assess whether APMT and HGS were correlated with conventional anthropometric variables in hospitalized patients, and to assess their relationship with nutritional status as determined by PG-SGA.

METHODS

STUDY DESIGN

A cross-sectional study with a non-probabilistic convenience sample design was conducted from June 2019 to September 2019 at the Department of Internal Medicine and Surgery at a University Hospital in Brazil.

ELIGIBILITY CRITERIA

Patients of both sexes admitted to the clinical or surgery ward within 48 hours of admission, aged 50 years or older, who were able to answer all PG-SGA items were invited to participate in this study. All patients signed an informed consent form after being consulted and informed about the research objective.

The following exclusion criteria were adopted: patients under respiratory precaution, with edema in the hands, with cognitive deficits, neurodegenerative diseases, rheumatic conditions or serious psychiatric disorders and indigenous population.

SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Sociodemographic variables were age, marital status, work status, and economic class according to the Brazilian Economic Classification criteria of the Brazilian Association of Research Companies (ABEP) (8).

The following clinical variables were assessed in the medical records of patients: clinical diagnosis, reason for hospitalization (clinical/surgical), and previous chronic diseases — diabetes mellitus, high blood pressure, and rheumatic diseases (none, 1 to 3, 3 or more).

NUTRITIONAL STATUS

Conventional anthropometry

The following measures were considered: current weight (kg), height (m), body mass index (BMI, kg/m^2), arm circumference (AC, cm), calf circumference (CC) (cm), and tricipital skinfold (TS, mm). Arm muscle circumference (AMC, cm) and corrected mid-upper arm muscle area (cAMA) were calculated. For measurement and classification we adopted the World Health Organization (WHO) criteria for BMI (9-11).

In order to minimize variability and increase reliability, all evaluators were trained, and the research equipment was calibrated as needed.

Adductor pollicis muscle thickness (APMT)

APMT was measured in each individual in a sitting position, with the arm flexed at approximately 90° and with the forearm and the hand resting on the knee, keeping the hand relaxed, as requested. We used a skinfold caliper, which exerted a continuous pressure of 10 g/mm^2 to pinch the adductor pollicis muscle at the apex of an imaginary triangle formed by the extension of the thumb and the index finger (5). The procedure was performed in both hands, in triplicate, using the mean value obtained as the final value. Cut-off points of 24.2 mm and 19.4 mm were adopted for men and women, respectively (12).

Handgrip strength (HGS)

A manual hydraulic dynamometer, which expressed values in kilograms, was used to assess HGS. Each individual was asked to sit with their feet flat on the ground, with their arm close to their chest and the elbow flexed at 90°, without being supported. Each measure was taken in triplicate, in both hands, considering the highest value as the result (13). The cut-off points used were those proposed by the European Working Group on Sarcopenia in Older People EWGSOP2 by sex (men: < 27 kg/f; women: < 16 kg/f) (14).

Patient-Generated Subjective Global Assessment (PG-SGA)

This study used the PG-SGA version validated for Brazilian Portuguese (3,4).

PG-SGA classifies individuals into: A (well nourished), B (suspicion of or moderate malnutrition), and C (severely malnourished). In addition, this method generates a score that helps the multidisciplinary team to define nutritional interventions, making specific decisions regarding patient and family guidance, symptom management, and adequate nutritional intervention: 0 to 1: no need for intervention; 2 to 3: requires nutritional education with the patient and family; 4 to 8: requires nutritional intervention; and total score ≥ 9: requires critical nutritional intervention and control of symptoms (3,4).

DATA ANALYSIS

Data were analyzed using the IBM SPSS Statistics® software (v.22, SPSS An IBM Company, Chicago, IL). A descriptive statistical analysis was performed using mean and standard deviation for continuous variables, and percentage for categorical variables. Pearson's correlation coefficient was used for the correlations of interest, setting the significance level at 5 %.

ETHICAL ASPECTS

This research complied with the rules and guidelines of Good Clinical Practice in accordance with Resolution 466/2012. The study was also approved by the Research Ethics Committee under CAAE 06426818.0.0000.5160.

RESULTS

The sample consisted of 73 patients with a mean age of 66.9 ± 9.6 years. Most patients were men (53.4 %), elderly (≥ 60 years) (79.1 %), married (64.4 %), belonged to economic class C (71.2 %), and were not working (69.9 %) (Table I).

Table I. Study sample characterization

Variables	Total n (%)
	73 (100.0)
Sex	
Male	39 (53.4)
Female	34 (46.6)
Marital status	
Married	47 (64.4)
Single	7 (9.6)
Widow(er)	14 (19.2)
Separated/divorced	5 (6.8)
*Economic class**	
A	-
B	9 (12.3)
C	52 (71.2)
D and E	12 (16.4)
Age group	
Adult (< 60 years)	16 (21.9)
Elderly (≥ 60 years)	57 (79.1)
Working status†	
No	51 (69.9)
Yes	20 (27.4)
Chronic diseases	
None	13 (17.8)
1 to 3	58 (79.5)
4 or more	2 (2.7)
Hospitalization	
Clinical condition	34 (46.6)
Surgery	39 (53.4)
Body mass index (BMI)	
Underweight	8 (11.0)
Normal weight	35 (47.9)
Overweight	30 (41.1)
PG-SGA score	
0-1	6 (8.2)
2-3	8 (11.0)
4-8	27 (37.0)
≥ 9	32 (43.8)
PG-SGA category	
Well nourished (A)	24 (32.9)
Suspicion of or moderate malnutrition (B)	35 (47.9)
Severely malnourished (C)	14 (19.2)

*PG-SGA: Patient-Generated Subjective Global Assessment; *Average household income: A = R$ 25,554.33; B = R$ 5,641.64 to 11,279.14; C = R$ 1,748.59 to 3,085.48; D and E= R$ 719.81; †2 missing values.*

Most patients were admitted to undergo surgical procedures (53.4 %), and 79.5 % had one to three chronic diseases when assessed.

Patients with an adequate BMI prevailed (47.9 %), whereas according to PG-SGA most patients (67.1 %) had some degree of malnutrition (B and C). Regarding the PG-SGA score, patients were predominantly classified with a score lower than 9 (56.2 %).

Patients mostly had a reduced APMT in both hands, while most patients had adequate HGS (Table II).

Table III outlines the mean and standard deviation of the continuous variables that were used to investigate the nutritional status of patients, such as conventional anthropometry, APMT, and HGS.

Table II. Distribution of individuals according to adductor pollicis muscle thickness and handgrip strength classification

Variables	Right hand	Left hand
APMT	**n (%)**	**n (%)**
Adequate	6 (8.2)	8 (11.0)
Reduced	67 (91.8)	65 (89.0)
HGS		
Adequate	38 (59.4)	36 (55.4)
Reduced	26 (40.6)	29 (44.6)

APMT: adductor pollicis muscle thickness; HGS: handgrip strength (right hand: 9 missing values; left hand: 8 missing values).

APMT (R) was significantly correlated with the measures cAMA, CC, APMT (L), FFP (R), and HGS (L). APMT (L) was significantly correlated with the measures cAMA, AC, AMC, CC, PG-SGA score, and right and left HGS. Both HGS (R) and HGS (L) were significantly correlated with the measures CC, PG-SGA score, and APMT in both hands (Table IV).

Table III. Mean and standard deviation of the continuous variables investigated for nutritional status by sex

Variables	Mean ± Standard deviation		
	Total	Women	Men
BMI (kg/m^2)	26.9 ± 6.0	28.7 ± 6.3	25.4 ± 5.3
cAMA (cm^2)	40.1 ± 13.2	40.3 ± 13.5	39.9 ± 13.2
AC (cm)	30.2 ± 4.1	31.3 ± 4.3	29.3 ± 3.8
TSF (mm)	18.5 ± 7.1	21.7 ± 6.4	15.7 ± 6.5
AMC (cm)	24.4 ± 3.4	24.5 ± 3.4	24.4 ± 3.5
CC (cm)	34.7 ± 4.1	34.7 ± 4.8	34.8 ± 3.4
PG-SGA score	9.3 ± 6.9	8.7 ± 6.3	9.8 ± 7.5
APMT R (mm)	16.0 ± 4.9	15.4 ± 5.1	16.6 ± 4.7
APMT L (mm)	15.8 ± 6.0	15.5 ± 5.4	16.2 ± 6.5
HGS R (kg)	25.0 ± 10.5	24.4 ± 9.9	25.4 ± 11.0
HGS L (kg)	24.2 ± 11.1	22.7 ± 9.6	25.4 ± 12.2

APMT: adductor pollicis muscle thickness; R: right; L: left; HGS: handgrip strength; BMI: body mass index; cAMA: corrected arm muscle area; AC: arm circumference; TSF: tricipital skinfold; CC: calf circumference.

Table IV. Adductor pollicis muscle thickness and handgrip strength correlation with anthropometric variables, dynamometry, and the Patient-Generated Subjective Global Assessment Score

Variables	APMT R (mm)	APMT L (mm)	HGS R (kg)	HGS L (kg)
	r (p)	r (p)	r (p)	r (p)
Age (years)	-0.025 (0.837)	0.064 (0.591)	-0.060 (0.636)	-0.116 (0.359)
BMI (kg/m^2)	-0.155 (0.196)	-0.182 (0.122)	-0.020 (0.873)	-0.068 (0.591)
cAMA (cm^2)	-0.319* (0.007)	-0.367* (0.001)	-0.118 (0.355)	-0.121 (0.336)
AC (cm)	-0.222 (0.063)	-0.233* (0.047)	-0.007 (0.955)	-0.074 (0.559)
TSF (mm)	-0.062 (0.608)	0.019 (0.872)	-0.014 (0.916)	-0.122 (0.333)
AMC (cm)	-0.228 (0.056)	-0.293* (0.012)	0.000 (1.000)	0.012 (0.924)
CC (cm)	0.375* (0.001)	0.275* (0.019)	0.276* (0.027)	0.251* (0.044)
PG-SGA score	-0.218 (0.068)	-0.255* (0.029)	-0.440* (< 0.001)	-0.408* (0.001)
APMT R (mm)				
APMT L (mm)	0.844* (< 0.001)			
HGS R (kg)	0.503* (< 0.001)	0.493* (< 0.001)		
HGS L (kg)	0.457* (< 0.001)	0.406* (< 0.001)	0.893* (< 0.001)	

*r: Pearson's correlation coefficient; p: p-value; *significant; APMT: adductor pollicis muscle thickness; R: right; L: left; HGS: handgrip strength; BMI: body mass index; cAMA: corrected arm muscle area; AC: arm circumference; TSF: tricipital skinfold; CC: calf circumference.*

DISCUSSION

Correlations of adductor pollicis muscle thickness and handgrip strength with CC and with the PG-SGA score were observed.

CC is the most commonly used measure to ascertain muscle depletion in the elderly, and has already been shown to predict performance and survival in this population when using the 31.0 cm cut-off point (15). Furthermore, CC can be used for muscle mass diagnosis in institutions lacking other muscle mass assessment methods (14).

An observational cross-sectional study conducted in 2015 with patients in anintensive care unit (ICU) found that APMT (R) was significantly correlated with BMI and CC. They reported that the lower values of APMT may have resulted from the sample composition, which included mostly elderly people (16). Conversely, a more recent epidemiological study conducted exclusively in elderly patients with chronic kidney disease (CKD) reported a significant correlation between APMT and conventional anthropometric measures such as CC, AC, TSF, and BMI (17). Including unconventional anthropometric measures in nutritional assessments is important considering their efficacy in detecting complications and risks of muscle depletion (14).

The PG-SGA tool is known to be a specific and sensitive instrument and is considered the gold standard for nutritional assessment in hospitalized patients. Thus, the significant correlation observed between PG-SGA and HGS and APMT highlight the latter two as complementary assessments of nutritional status in the hospital setting and for studies (3,18-20). Besides that, muscle strength can also be used to determine sarcopenia in adults and in the elderly (21). Our findings are supported by other studies. In a recent study with cancer patients APMT was significantly correlated with the PG-SGA score and with HGS in both hands (22). In the same way, another study conducted with 150 patients also showed significant associations between APMT, PG-SGA, and other conventional anthropometric measures (6). It should be noted that the cut-off points used by the authors in both studies were those proposed by Bragagnolo (23). Despite the fact that more stringent cut-off points were used in our study, our results were very similar. Schwanke et al., in a study to evaluate the association between APMT and nutritional parameters in hospitalized elderly patients in Brazil, reported that APMT was associated with all the investigated nutritional parameters, including MNA, BMI, AC, CC, and HGS (24).

Most participants in this study showed reduced APMT values and adequate HGS values. The sample of our study mainly consisted of elderly people, most of whom were not working, which may account for their loss of muscle mass. Physiologically, increased skeletal muscle mass losses are also inherent to age itself (25). It is important to highlight that although previous studies have reported that APMT could be used as a proxy of low lean mass in a clinical scenario, for epidemiological studies this measure cannot be used as single predictor of lean mass in health subjects (12).

Although HGS is also affected by the decrease in muscle mass, peripheral muscle strength is more related to the worsening of overall and cognitive function of the patient. Furthermore, in the elderly, this measure decreases with impairment of their daily living activities, functional dependence, risk of falls, and changes in gait (26,27). The prevalence of patients undergoing elective surgery in our sample, who possibly continued to perform their activities prior to hospitalization, may also explain the adequate HGS.

This study also underscores the use of objective and subjective parameters in clinical practice. Despite the fact that most patients were classified as 'adequate' or 'overweight' by their BMI, most were considered malnourished when assessed by APMT and PG-SGA. This finding shows that BMI should not be prioritized as an indicator of nutritional status in hospitalized individuals, especially when used alone. Factors which affect the functional decline of an individual, especially age-related changes such as those observed in the elderly population, and changes in muscle systems and strength, should be carefully monitored to establish preventive, recovery-related, and other interventions that may delay or prevent the functional decline of patients to improve their prognosis (28). A recent systematic review raised the question about the reliability of APMT measurement and that future studies should established cut-off values that are hand-, age-, sex-, and ethnic-specific before APMT can be used as a component of nutritional screening (29).

Our study is limited by its sample size and sample profile (mainly elective surgery). In addition, the cross-sectional design limits the evaluation of collected variables, especially of causal relationships. Despite including the number of chronic diseases, we did not use a validated comorbidity scale with prognostic value. We recommend that future research should use a expanded sample of hospitalized patients in order to provide more robust results. Furthermore, future research should investigate specific cut-off points for hospitalized patients with multiple morbidities.

CONCLUSION

APMT and HGS correlated with CC and PG-SGA in hospitalized patients. These measures should be implemented in clinical practice for the nutritional assessment of hospitalized patients to establish a reliable nutritional diagnosis and adequate nutritional therapy. They may boost the performance of the entire multidisciplinary team to outline strategies and interventions, including prevention and patient rehabilitation.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Cribado nutricional del paciente con patología vascular hospitalizado: relación del riesgo nutricional con los resultados clínicos y económicos en un servicio quirúrgico

Nutritional screening in hospitalized patients with vascular disease — The relationship of nutritional risk with clinical and economic outcomes in a surgery department

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Resumen

Introducción y objetivos: la desnutrición relacionada con la enfermedad produce un impacto negativo en la evolución del paciente quirúrgico. Nuestro objetivo es valorar la prevalencia del riesgo nutricional en el ámbito de la cirugía vascular y sus consecuencias en la evolución del paciente y el gasto sanitario.

Pacientes y métodos: estudio observacional prospectivo realizado durante 6 meses en la planta de cirugía vascular del Hospital Universitario de León. Se utilizó la herramienta *Malnutrition Universal Screening Tool* (MUST) para recoger datos al ingreso y cada 7 días hasta el alta hospitalaria. Se estudiaron las variables clínicas, la intervención quirúrgica realizada, las complicaciones médico-quirúrgicas, la estancia hospitalaria, los costes sanitarios y los reingresos precoces.

Resultados: el estudio contó con 104 pacientes, de los que el 84,6 % eran varones, cuya media de edad era de 69 años (DE: 13). El 46,2 % habían ingresado por enfermedad arterial periférica. El 10,6 % presentaban un MUST positivo al ingreso y el 19,2 % lo presentaban al alta; el 100 % de los pacientes desnutridos al ingreso permanecían en la misma situación al alta. Durante la hospitalización, en 29 pacientes (27,9 %) empeoró la situación nutricional. El 81,25 % de los pacientes que sufrieron empeoramiento del MUST habían ingresado de forma urgente ($p < 0,05$). Los pacientes que habían precisado una cirugía urgente empeoraron significativamente en términos de su estado nutricional ($p < 0,001$). Los pacientes con empeoramiento del estado nutricional obtuvieron mayores porcentajes de: reintervención quirúrgica ($p < 0,05$), gasto farmacéutico ($p = 0,017$), gasto hospitalario total (1000 €/paciente/ingreso), traslados a centros de cuidados crónicos ($p = 0,0002$) y número de reingresos precoces ($p = 0,017$).

Conclusiones: los pacientes en riesgo nutricional se asociaron a un incremento de las complicaciones médico-quirúrgicas, de la estancia hospitalaria, del coste sanitario y de la tasa de reingresos, por lo que consideramos necesaria la implantación de cribados y el desarrollo de estudios en el ámbito de la cirugía vascular.

Palabras clave:

Desnutrición relacionada con la enfermedad. Desnutrición hospitalaria. Riesgo nutricional. Cribado nutricional. Cirugía vascular. Paciente quirúrgico.

Abstract

Introduction: disease-related malnutrition has a negative impact on the outcome in surgical patients. Our objective was to assess the prevalence of nutritional risk in the field of vascular surgery, as well as its consequences on patient outcome and health expenditure.

Patients and methods: this is a prospective, observational study conducted during 6 months in a vascular surgery ward at the University Hospital of León, Spain. The Malnutrition Universal Screening Tool was used to obtain data on admission and then every 7 days until hospital discharge. Clinical variables, surgical intervention performed, medical-surgical complications, hospital stay, healthcare costs, and early readmissions were studied.

Results: a total of 104 patients, 84.6 % males, with a mean age of 69 (SD: 13) years were enrolled. Of these, 46.2 % were admitted due to peripheral arterial disease; 10.6 % had a positive MUST at the time of admission and 19.2 % at discharge; 100 % of malnourished patients at admission remained in the same situation at discharge. During hospitalization, in 29 patients (27.9 %) the nutritional situation worsened. In all, 81.25 % of patients who experienced worsening of their MUST score had been admitted urgently ($p < 0.05$). Patients who required urgent surgery significantly worsened in terms of their nutritional status ($p < 0.001$). Patients with worsening nutritional status obtained higher rates for: surgical reintervention ($p < 0.05$), pharmaceutical expense ($p = 0.017$), total hospital expense (€1,000/patient/admission), transfers to chronic care centers ($p = 0.0002$), and number of early readmissions ($p = 0.017$).

Conclusion: patients with nutritional risk suffered an increase in medical-surgical complications, hospital stay, healthcare costs, and re-admission rates. Therefore, we consider that an implementation of screening procedures and the development of further studies in the vascular surgery setting are necessary.

Keywords:

Disease-related malnutrition. Hospital malnutrition. Nutritional risk. Nutritional screening. Vascular surgery. Surgical patient.

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INTRODUCCIÓN

La desnutrición en el ámbito hospitalario fue definida por Caldwell en el año 1981 como un estado patológico, derivado del exceso o el defecto de uno o más nutrientes esenciales, que se detecta clínicamente mediante pruebas bioquímicas y antropométricas (1). Su incidencia se ha documentado ampliamente en las últimas tres décadas, oscilando entre el 19 % y el 80 % según el área geográfica y el método de detección utilizado (1-4).

Los datos del principal estudio multicéntrico sobre la desnutrición relacionada con la enfermedad (DRE) que se ha llevado a cabo en nuestro país, el llamado Prevalencia de Desnutrición y Costes Asociados (PREDyCES), en el que participaron 31 hospitales con una muestra de más de 1500 pacientes, demostraron que 1 de cada 4 pacientes hospitalizados (23,7 %) estaba en riesgo de desnutrición (5). El estudio PREDyCES estableció en un 17 % la prevalencia de la malnutrición en los pacientes quirúrgicos en el momento del ingreso (6).

En nuestra comunidad autónoma, un estudio llevado a cabo en pacientes hospitalizados en la planta de cirugía vascular del Hospital Clínico Universitario de Valladolid, detectó una prevalencia de la desnutrición al ingreso del 13 % (7). Asimismo, en otro estudio llevado a cabo en el Complejo Asistencial Universitario de León (CAULE), donde se incluyeron pacientes pertenecientes al servicio de cirugía vascular, asociados a otros servicios quirúrgicos del hospital, se obtuvo un riesgo nutricional (RN) del 34,7 % con la herramienta de cribado *Malnutrition Universal Screening Tool* (MUST) (8).

La etiología de la DRE es multifactorial. Si bien la propia enfermedad es un importante factor condicionante (9), los largos periodos de ayuno perioperatorios favorecen su desarrollo (10). A menudo pasa inadvertida en los distintos servicios quirúrgicos, por lo que no se administra el tratamiento necesario para su corrección (11). Un estado nutricional inadecuado afecta negativamente a las posibilidades de recuperación temprana del paciente quirúrgico, produciendo: aumento de las dehiscencias e infecciones de las heridas quirúrgicas, aumento de la aparición de úlceras por presión, ralentización de la cicatrización de las heridas, pérdida de masa muscular, aumento de los edemas, alteración de la eritropoyesis, etc. Por lo tanto, el éxito de la cirugía no solo va a depender de las habilidades quirúrgicas y técnicas, sino también de la terapia intervencionista metabólica y de la presencia de un soporte nutricional adecuado (1,12,13).

Teniendo en cuenta la elevada prevalencia del riesgo nutricional en el ámbito hospitalario, así como sus consecuencias clínicas y económicas (14), cabe pensar en la necesidad de implantar herramientas de cribado de uso sistemático en todos los servicios quirúrgicos. En el caso de los pacientes hospitalizados en un servicio de cirugía vascular, según sus características sociosanitarias (edad avanzada, hábitos tóxicos, comorbilidad cardiovascular, infecciones activas en lesiones cutáneas, etc.) cabría esperar una presencia no desdeñable del riesgo nutricional (RN). Por ello, nuestro estudio plantea valorar la prevalencia del RN en el servicio de cirugía vascular de un hospital terciario, así como las implicaciones que dicho RN puede suponer para la evolución clínica de los pacientes y, en consecuencia, del gasto sanitario.

MATERIAL Y MÉTODOS

Se trata de un estudio observacional prospectivo en el que se incluyeron pacientes con edades comprendidas entre los 18 y los 90 años, con ingreso hospitalario superior a 7 días en el Servicio de Cirugía Vascular del Complejo Asistencial Universitario de León, desde el 15 de junio al 15 de diciembre de 2016. Se excluyó a los pacientes con imposibilidad de colaboración (encamados, patología terminal, demencia y trastornos psiquiátricos), así como a aquellos otros con alteraciones de la conducta alimentaria (bulimia, obesidad mórbida o anorexia nerviosa). El estudio fue aprobado por el Comité Ético de Investigación del CAULE el 28/06/2016.

Se recogieron los hábitos tóxicos, los factores de riesgo cardiovascular (FRCV) y las patologías asociadas. Se tuvo en cuenta si el paciente estaba polimedicado (toma de más de cinco fármacos) y si presentaba comorbilidad, valorada mediante el índice de comorbilidad de Charlson (ICC) (15). Se registró el carácter urgente del ingreso y el tipo de tratamiento (quirúrgico o conservador).

Empleamos la herramienta MUST (16) para el cribado nutricional a través del sistema de información sanitario de cuidados de enfermería GACELA CARE (*Gestión Avanzada de Cuidados de Enfermería Línea Abierta*). Se talló y pesó a los pacientes durante las primeras 24 horas del ingreso y se le preguntó por su peso habitual en los últimos 3-6 meses, con el fin de detectar pérdidas involuntarias. Posteriormente se repitió la toma del peso semanalmente y al alta hospitalaria. Se recogió si el paciente no había podido recibir ninguna ingesta a consecuencia de su enfermedad en un periodo igual o superior a 5 días. Con todos estos datos, el paciente obtuvo una puntación automática basada en el MUST. Los pacientes con puntuación MUST ≥ 2 se consideraron de alto riesgo nutricional. Se repitió el cribado de forma semanal a todos los pacientes, de tal manera que pudiésemos distinguir entre los pacientes que ya presentaban RN al ingreso y aquellos otros que lo desarrollaban durante su estancia hospitalaria, evaluando las posibles diferencias evolutivas. Para la obtención del peso en aquellos pacientes que durante su estancia fueron sometidos a una amputación mayor utilizamos el método PIAMP (Tabla I), en el que el peso de un paciente amputado se calcula en relación al peso ideal (para la talla original), corregido por el porcentaje de amputación (Tabla I), de acuerdo con la siguiente ecuación (17): PIAMP = [(100 - % de amputación) / 100] x peso ideal.

Obtuvimos datos en relación con las complicaciones médico-quirúrgicas, la estancia hospitalaria, la mortalidad durante el ingreso, los reingresos prematuros (a los 3 meses tras el alta) y la derivación a centros de cuidados crónicos. Analizamos el gasto farmacéutico y, de forma aislada, el antibiótico de cada paciente, datos facilitados por el Servicio de Farmacología Clínica del CAULE. Así mismo, calculamos el gasto hospitalario total ajustado a la estancia media, según el gasto estimado por paciente/día ingresado en nuestro servicio en el año previo, facilitado por el Servicio de Contabilidad Analítica, resultando en 504 €/paciente-día.

El estudio estadístico se realizó mediante el paquete IBM SPSS Statistics 19. Los datos se expresaron mediante la media y la

Tabla I. Método PIAMP: cálculo del peso en pacientes con miembros amputados

Amputación	Cálculo
Pierna por debajo de la rodilla	Peso actual (kg) x 1,063
Pierna completa	Peso actual (kg) x 1,18
Antebrazo	Peso actual (kg) x 1,022
Brazo completo	Peso actual (kg) x 1,05

desviación estándar, comparándose mediante el test de la "t" de Student, con un valor de significación de $p < 0,05$, tras comprobar que siguieran una distribución normal (peso, índice de masa corporal [IMC], edad). Las variables que no seguían una distribución normal se expresaron como mediana y rango intercuartílico (RIC). Puesto que los datos de estancia y costes hospitalarios de los pacientes no seguían una distribución normal, se utilizaron pruebas no paramétricas (U de Mann Whitney) para su comparación.

RESULTADOS

Durante el periodo de estudio ingresaron 466 pacientes a cargo del Servicio de Cirugía Vascular del CAULE, de los cuales 104 fueron incluidos en nuestro estudio. De los 362 pacientes restantes, 323 correspondieron a ingresos inferiores a 7 días y otros 39 casos no cumplieron los criterios de inclusión por los siguientes motivos: 6 pacientes por fallecimiento precoz (antes de cumplirse los primeros 7 días de ingreso), 5 por obesidad mórbida, 6 pacientes por demencia, 12 pacientes por no ser colaboradores y 10 pacientes por tener una edad superior a los 90 años.

Los pacientes de nuestra muestra tenían una edad media de 69,41 años (DE: 13,12), siendo el 84,6 % de ellos varones. A continuación se reflejan las principales características de la población del estudio (Tabla II).

RIESGO NUTRICIONAL

La herramienta MUST detectó al ingreso 11 pacientes (10,6 %) con riesgo nutricional, cifra que ascendió a 20 (19,2 %) en el momento del alta. Estos 20 pacientes correspondían a los 11 casos iniciales que no mejoraron su estado inicial durante el ingreso, más 9 pacientes que accedieron al hospital sin riesgo nutricional y lo desarrollaron durante su estancia (Fig. 1).

Durante la hospitalización, 29 pacientes (27,9 %) vieron empeorada su situación nutricional, presentando un aumento de la puntuación MUST de tal forma que, entre los pacientes con MUST = 0 al ingreso, empeoran durante la hospitalización el 19,5 % (16/82), y entre los que tenían un MUST = 1, agravaron su situación un 54,5 % (6/11).

Únicamente 5 pacientes (4,8 %) del total con riesgo nutricional fueron derivados a la Unidad de Nutrición Clínica y Dietética del servicio de Endocrinología y Nutrición (UNCyD-SEYN).

Tabla II. Descripción global de la muestra

Variable	n	%
Género		
Hombre	87	84,6
Mujer	17	15,4
Edad		
< 70	47	48,8
≥ 70	57	59,2
Hábitos tóxicos/Toma de fármacos		
Tabaco	31	32,7
Alcohol	17	17,3
Polimedicación	64	66,3
FRCV		
Diabetes mellitus	43	45
Hipertensión arterial	67	70
Dislipemia	47	49
Hiperuricemia	14	14,4
Patologías asociadas		
Cardiopatía isquémica	22	25
Insuficiencia cardiaca	4	3,8
Enfermedad cerebrovascular	6	5,8
Insuficiencia renal crónica	29	27,9
Enfermedad pulmonar obstructiva	18	17,3
Índice de comorbilidad de Charlson		
Bajo (< 3 puntos)	6	5,8
Alto (≥ 3 puntos)	94	90,4
Características del ingreso		
Urgente	61	58,6
Características de la intervención quirúrgica		
Tratamiento quirúrgico	96	92,3
Carácter urgente	8	7,7
Infección de herida quirúrgica	8	7,7
Reintervención	9	33,8
Parámetros evolutivos		
Traslado a centro concertado	4	3,8
Fallecimiento	3	2,9
Reingreso hospitalario	24	20,2

CARACTERÍSTICAS DE LOS PACIENTES CON ALTO RIESGO NUTRICIONAL AL INGRESO

No se encontraron diferencias significativas en cuanto a la distribución por sexo, edad, polimedicación, índice de comorbilidad de Charlson, carácter urgente del ingreso, factores tóxicos y patologías en los pacientes que presentaban RN al ingreso. Tanto el peso

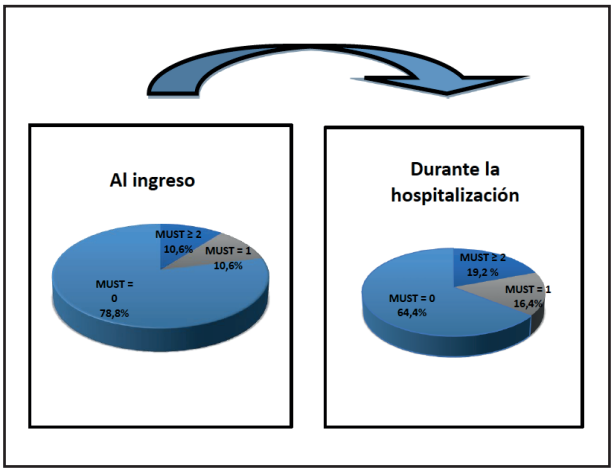

Figura 1.

Riesgo nutricional, según el MUST, al ingreso y durante la hospitalización. Los datos durante la hospitalización se refieren a la reevaluación de aquellos pacientes con MUST negativo al ingreso al cabo de una semana.

como el IMC eran significativamente más bajos en aquellos pacientes con RN al ingreso. Así mismo, los pacientes que presentaban esta condición se sometieron en mayor medida a cirugía abdominal abierta ($p < 0,05$) y presentaron una tasa de complicaciones médicas (cardiopatía isquémica, insuficiencia renal, infecciones del tracto urinario y respiratorio, etc.) significativamente mayor. En este grupo, la estancia media se vio aumentada en 8,5 días, aunque con una $p > 0,05$. Tanto el gasto antibiótico como el gasto farmacéutico y el hospitalario total se vieron incrementados en 15,18 €, 52,52 € y 2627 €, respectivamente, aunque este aumento no fue estadísticamente significativo.

En cuanto a las complicaciones quirúrgicas, hubo un aumento porcentual considerable de la infección de la herida quirúrgica (de 5,4 % a 27,3 %) y de la reintervención (de 6,5 % a 23,3 %), aunque con una $p > 0,05$. En los pacientes con RN alto inicial, la tasa de mortalidad durante el ingreso no fue superior, como tampoco lo fueron los reingresos precoces y las derivaciones a centros de estancia larga (Tabla III).

CARACTERÍSTICAS DE LOS PACIENTES QUE EMPEORARON SU SITUACIÓN NUTRICIONAL DURANTE EL INGRESO

Al igual que en el grupo anterior, no se detectaron diferencias significativas en términos de sexo, edad, polimedicación, ICC, factores tóxicos y distribución de patologías en relación con el empeoramiento de la puntuación MUST durante el ingreso. Sin embargo, encontramos que el carácter urgente del ingreso sí se relaciona con un mayor empeoramiento de la situación nutricional ($p < 0,05$). Aquellos pacientes que presentaban un peso más bajo y un menor IMC presentaron con mayor frecuencia empeoramiento del RN ($p < 0,05$). Así mismo, los pacientes que presentaron esta condición fueron sometidos en mayor medida a cirugía de carácter urgente ($p = 0,001$).

Tabla III. Características de los pacientes según su riesgo nutricional al ingreso

Variable	MUST < 2	MUST ≥ 2	Valor de p
Sexo (% de varones)	79 (84,5 %)	9 (81,8 %)	0,786
Edad (años)	69,33	70,09	0,857
Peso (kg)	73,12	59,82	0,002
IMC	26,07	22,20	0,004
ICC	4,87	4,91	0,857
Polimedicación	62 (66,7 %)	7 (63,6 %)	0,841
Ingreso urgente	57 (61,3 %)	4 (36,4 %)	0,112
Cirugía abdominal	2 (22,6 %)	7 (63,6 %)	0,004
Complicaciones médicas	17 (18,4 %)	5 (45,5 %)	0,001
Infección de herida quirúrgica	5 (5,4 %)	3 (27,3 %)	0,010
Reintervención quirúrgica	6 (6,5 %)	3 (27,3 %)	0,020
Estancia hospitalaria (días)	18,31	26,82	0,018
Gasto antibiótico (euros)	60,21	75,39	0,313
Gasto farmacéutico (euros)	135,61	188,13	0,107
Gasto hospitalario (euros)	5.678,59	8.305,99	0,017
Fallecimientos	2 (2,2 %)	1 (9,1 %)	0,193
Derivación a centro de larga estancia	4 (4,3 %)	0	0,346
Reingresos precoces	19 (20,5 %)	2 (18,2 %)	0,861

Tabla IV. Características de los pacientes que empeoraron su estado nutricional durante el ingreso

Variable	MUST < 2	MUST ≥ 2	Valor de p
Sexo (% de varones)	59 (89,4 %)	13 (81,25 %)	0,372
Edad (años)	68,68	72,25	0,326
Peso al alta (kg)	73,79	67,19	0,042
IMC al alta	26,10	23,99	0,032
ICC	4,85	4,69	0,948
Polimedicación	42 (63,6 %)	12 (75 %)	0,390
Ingreso urgente	36 (54,5 %)	13 (81,25 %)	0,049
Cirugía urgente	3 (4,55 %)	5 (31,25 %)	0,001
Tasa de amputación	11 (16,6 %)	7 (43,75 %)	0,046
Complicaciones médicas	10 (15,2 %)	5 (31,25 %)	0,245
Infección de herida quirúrgica	2 (3 %)	2 (12,5 %)	0,115
Reintervención quirúrgica	3 (4,5 %)	3 (18,7 %)	0,049
Estancia hospitalaria (días)	17,95	20,88	0,093
Gasto antibiótico (euros)	59,16	88,11	0,065
Gasto farmacéutico (euros)	116, 41	253,66	0,017
Gasto hospitalario (euros)	5.551,26	6.572,49	0,072
Fallecimientos	2 (3 %)	0	0,481
Derivación a centro de larga estancia	0	3 (18,8 %)	0,001
Reingresos precoces	11 (16,7 %)	4 (25 %)	0,017

Este grupo de pacientes presentó un incremento significativo de la tasa de complicaciones, con aumento de la tasa de amputaciones (del 16,6 % al 3,75 %, con una $p = 0,046$) y del porcentaje de reintervenciones quirúrgicas (del 4,5 % al 18,7 %, con una $p < 0,05$), así como con aumento de la tasa de complicaciones médicas (del 15,2 % al 31,25 %, aunque en este caso con una $p > 0,05$).

En los pacientes con empeoramiento de la situación nutricional, la estancia media se vio aumentada en 3 días, aunque con una $p > 0,05$, es decir, sin significación estadística. En este grupo hubo un incremento de todos los gastos: gasto antibiótico (de 28,95 €, $p = 0,065$), gasto farmacéutico (de 137,25 €, $p = 0,017$) y gasto hospitalario total (de 1019,23 €, $p = 0,072$). Al igual que en el grupo anterior, no hubo diferencias en cuanto a la cifra de fallecimientos; sin embargo, sí hubo un aumento significativo de la tasa de reingresos precoces (del 16,7 % al 25 %, $p = 0,017$) y de las derivaciones a centros de larga estancia (del 0 % al 18 %, $p = 0,001$) (Tabla III).

DISCUSIÓN

Los datos del estudio PREDYCES (5,18) demostraron una prevalencia del riesgo nutricional del 23,7 % en el momento del ingreso, según la herramienta de cribado *Nutritional Risk Screening* (NRS). Al separar la muestra global en servicios médicos y quirúrgicos, se obtuvo una prevalencia del 29 % y el 17 %, respectivamente, poniendo de manifiesto una incidencia superior en los pacientes pertenecientes a los departamentos médicos. En nuestro estudio obtuvimos una prevalencia inicial algo inferior, del 10,6 %. Esta diferencia puede deberse, por un lado, al menor porcentaje de ingresos de carácter urgente (un 59,65 % en comparación con un 71,2 % en el PREDYCES), ya que estos pacientes suelen tener un proceso clínico más grave, con mayor repercusión sobre su estado nutricional, y por otro lado, a la inclusión de patologías quirúrgicas que condicionan una disminución de la ingesta y estados inflamatorios crónicos, como el cáncer y las enfermedades digestivas, patologías frecuentemente tratadas por los servicios de cirugía general, no pertenecientes a nuestra especialidad.

Dicha cifra también fue sustancialmente inferior en comparación con otras series quirúrgicas publicadas en los últimos años a escala mundial, como la de Thomas y colaboradores (19), estudiada en Alemania, con una prevalencia de malnutrición del paciente quirúrgico —evaluada mediante el NRS— del 24 %, o la de Lin Lim y colaboradores (20), estudiada en Singapur, con una prevalencia —evaluada mediante la valoración subjetiva global— del 15 %. Estas series se basaron en la inclusión de

patologías quirúrgicas correspondientes a la cirugía general; por tanto, podemos explicar las diferencias al igual que anteriormente en el caso del PREDYCES.

Son escasas las series publicadas en el ámbito concreto de la cirugía vascular a nivel mundial. En el estudio australiano desarrollado por Jolene Thomas y colaboradores (21), llevado a cabo en una unidad de cirugía vascular desde 2014 hasta 2016 y que contó con 322 pacientes de características similares a las de nuestro estudio en términos del alto porcentaje de varones, la edad media cercana a los 70 años y los altos porcentajes de hipertensión, diabetes y dislipemia, utilizando también la herramienta MUST obtuvieron un riesgo nutricional al ingreso del 12,5 %, muy similar al de nuestra investigación. Este grupo de pacientes sufrió un aumento de su estancia hospitalaria de 13 a 7 días, una mayor tasa de complicaciones quirúrgicas (7,23 % frente a 6,91 %) y un aumento de los costes sanitarios de 1979 € por paciente e ingreso.

En la serie quirúrgica de Leandro Merhi y colaboradores (22), llevada a cabo en un hospital terciario de Sao Paulo, donde se incluía un pequeño porcentaje de pacientes pertenecientes a cirugía vascular, los autores describieron una prevalencia de la malnutrición del 9,8 % en nuestra especialidad, casi idéntica a la nuestra. Los pacientes malnutridos sufrieron un aumento significativo de la estancia hospitalaria (de 5,9 a 8,1 días) y las complicaciones posquirúrgicas (de un 5,6 % a un 9,4 %).

En Castilla y León se han llevado a cabo numerosos trabajos sobre desnutrición hospitalaria que nos han servido como guía para la realización del nuestro. En el estudio de Ballesteros Pomar y cols. (23), realizado en el Complejo Asistencial Universitario de León en 2015, se detectó —mediante la herramienta MUST— un 26,9 % de pacientes con riesgo de desnutrición al ingreso, porcentaje sustancialmente más alto que el de nuestra muestra, al tratarse de pacientes pertenecientes al Servicio de Medicina Interna. Los pacientes cuya situación nutricional empeoró durante el ingreso tuvieron una estancia significativamente mayor (2,5 días). Además, ocasionaron un sobrecoste de 767 € por ingreso (35 % superior), lo que implica un exceso de gastos relacionados con la desnutrición de 646.419,93 € anuales en el servicio estudiado.

En el estudio multicéntrico de Luis y colaboradores (24), que incluyó pacientes pertenecientes a los servicios de medicina interna de nueve hospitales de Castilla y León, se obtuvo un porcentaje de malnutrición del 23,9 % al ingreso mediante cribado con la herramienta *Mini Nutritional Assessment* (MNA). En el grupo con malnutrición hubo un aumento de la estancia hospitalaria de 2,6 días.

En el CAULE, asimismo, se desarrolló un estudio comparativo de las principales herramientas de cribado nutricional, realizado por Calleja Fernández y colaboradores (8), donde se incluyeron pacientes pertenecientes a cirugía vascular, asociados a un grupo de servicios quirúrgicos excepto de cirugía general, que se evaluó como servicio independiente. Encontraron un riesgo nutricional —mediante la herramienta MUST, medido durante los cuatro primeros días de ingreso— del 34,7 %, con un porcentaje de malnutrición del 8,2 %. La herramienta que alcanzó mejores resultados de sensibilidad y especificidad de los métodos de cribado nutricional a nivel global y por servicios de hospitalización fue el MUST, método elegido para la realización de nuestro trabajo, basándonos en las recomendaciones de la Sociedad Europea de Nutrición Parenteral y Enteral (ESPEN) (25), así como en diferentes publicaciones —como el mencionado artículo— que manifiestan su efectividad (26,27).

Actualmente, el único estudio sobre desnutrición hospitalaria en cirugía vascular que se ha publicado hasta la fecha en nuestro país es el trabajo realizado por Torres Torres y colaboradores (7) en el Hospital Clínico Universitario de Valladolid. Este estudio es el más comparable con el nuestro hoy en día y sobre el que hemos basado gran parte de la sistemática de desarrollo de nuestra investigación. Torres Torres y colaboradores obtuvieron un riesgo nutricional inicial —mediante la herramienta de cribado MUST— del 15,6 %, cercano a nuestro 10,6 %. En el mencionado trabajo, los pacientes que ingresaron con carácter urgente tenían una mayor prevalencia de desnutrición (19 % *vs.* 4 %) al igual que en nuestro grupo, donde encontramos una asociación significativa entre el empeoramiento del estado nutricional durante el ingreso y el carácter urgente del mismo (54,5 % *vs.* 81,35 %), dato reflejado también en el estudio PREDYCES, donde el ingreso programado presentaba una menor prevalencia de la DRE.

En nuestro trabajo, los pacientes con alto riesgo nutricional al ingreso desarrollaron más complicaciones médicas (18,3 % con MUST < 2 frente a 45,5 % con MUST ≥ 2 al ingreso) y más predisposición a la infección quirúrgica (5,4 % con MUST < 2 frente a 27,3 % con MUST ≥ 2 al ingreso), al igual que en estudio PREDYCES de casos y controles, donde la presencia de desnutrición suponía un aumento del desarrollo de complicaciones y procesos infecciosos, incluyendo la infección de la herida quirúrgica. Así mismo, los autores asociaron el mayor porcentaje de reintervenciones quirúrgicas (6,5 % con MUST < 2 frente a 27,3 % con MUST ≥ 2 al ingreso) y el incremento de la estancia hospitalaria, con una media de 7 días, a los casos que habían presentado riesgo nutricional al ingreso, siendo la cifra de 7 días ligeramente superior a los 3 días encontrados en el estudio PREDYCES.

Al igual que en los estudios más relevantes, mencionados con anterioridad, encontramos un incremento importante del gasto hospitalario total, con un aumento de 2627 €, lo que representa un 58 % más. En el PREDYCES se describe un incremento de 1505 € por paciente, siendo este del 65 % en el estudio de Torres Torres. Por otra parte, en nuestro estudio, el MUST positivo al ingreso no se asoció a un aumento de la mortalidad, al igual que en las series de Ballesteros Pomar y Torres Torres.

El empeoramiento de la situación nutricional tuvo un impacto muy negativo sobre la evolución de los pacientes de nuestra serie, observándose un mayor número de reintervenciones quirúrgicas (18,75 % con MUST ≥ 1 frente a 4,5 % con MUST $= 0$) y un incremento de la estancia hospitalaria de 4,5 días, similar al encontrado por otros estudios, como el multicéntrico canadiense de Allard y colaboradores (28), en el cual el deterioro del estado nutricional durante el ingreso aumentaba la estancia

hospitalaria en 3 días, y el trabajo de Ballesteros Pomar y cols. (23), donde el empeoramiento del estado nutricional fue del 18 %, con un aumento de la estancia de 2,5 días y un aumento de los reingresos hospitalarios (16,7 % con MUST = 0 frente a 31,5 % con MUST ≥ 1). Como consecuencia de lo anterior, se produjo en este grupo un incremento del gasto antibiótico del 400 %, del gasto farmacéutico del 100 % y del gasto hospitalario total del 47,24 %. En el estudio de Torres Torres, los costes de la hospitalización se incrementaron en un 127 % en los pacientes que sufrieron deterioro del estado nutricional durante el ingreso, siendo este porcentaje del 35 % para Ballesteros y colaboradores.

Nuestro estudio presenta limitaciones, al haberse realizado en un hospital terciario en España, con una muestra pequeña y en un servicio quirúrgico concreto, por lo que los resultados no pueden extrapolarse a la población hospitalaria general, ni a la de otros países. No obstante, hemos seguido la sistemática de trabajo de otros estudios principales, basándonos en la importancia del cribado nutricional positivo al ingreso y del desarrollo del riesgo nutricional, evaluando el pronóstico del paciente. Así mismo, los resultados obtenidos con respecto a la patología, las intervenciones y las complicaciones propias del paciente vascular, no podemos compararlos en gran medida con los de otros estudios a fin de poder sacar conclusiones adecuadas, ya que no hay estudios suficientes publicados hasta la fecha que los describan.

CONCLUSIONES

El 10,6 % de los pacientes que ingresaron en el servicio de cirugía vascular presentaban riesgo nutricional al ingreso y este ni se detectó ni se trató adecuadamente ya que, en el momento del alta, el 100 % de estos pacientes permanecían en el mismo estado. Así mismo, el 9,7 % de los pacientes que ingresaron con buen estado nutricional desarrollaron riesgo de desnutrición durante el ingreso. El carácter urgente del ingreso parece tener relación con un mayor empeoramiento del estado nutricional, probablemente por el carácter agudo de la patología, que en muchos casos condiciona una cirugía urgente. La cirugía abdominal abierta se asocia a un mayor empeoramiento de la situación nutricional, probablemente por los largos periodos de ayuno perioperatorio. Observamos una relación significativa entre el riesgo nutricional elevado y el aumento de las complicaciones médicas, las infecciones de la herida quirúrgica, la tasa de reintervenciones y la tasa de amputaciones. Todo ello supone un incremento de los costes sanitarios, la estancia hospitalaria, la tasa de reingresos y los traslados a centros de larga estancia.

Por tanto, creemos necesaria una mayor implicación y un mayor control del estado nutricional en los pacientes ingresados en los servicios quirúrgicos mediante el empleo de herramientas de cribado, favoreciendo la detección precoz, y el seguimiento periódico de cada paciente para detectar el posible empeoramiento del estado nutricional durante el ingreso. Con la implantación de estas medidas se podrían reducir las complicaciones médico-quirúrgicas, la estancia hospitalaria y los reingresos precoces, y favorecer el alta al domicilio, todo lo cual se traduciría en una reducción de los costes sanitarios. Sería necesaria la realización de más estudios en nuestra especialidad, así como en el resto de especialidades quirúrgicas, para ver la implicación real del problema y concienciarnos sobre esta realidad, muchas veces inadvertida.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Does nutritional treatment in patients with dysphagia affect malnutrition and anxiety?

Afecta el tratamiento nutricional de los pacientes con disfagia a la desnutrición y la ansiedad?

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Abstract

Introduction: dysphagia is common in patients with cerebrovascular disease (CVD), with an incidence reported to be 35 %-50 %. Dysphagia can result in malnutrition, dehydration, and death, and negatively affects anxiety levels.

Objectives: this study aimed to evaluate the effects of recommended nutritional treatment (NT) on nutritional status and anxiety levels in patients with dysphagia based on clinical and fiber-optic endoscopic evaluation of swallowing (FEES) tests.

Methods: seventy-five patients over the age of 50 who were diagnosed with CVD, hospitalized at the Mersin City Research and Training Hospital, Neurology Clinic, from October 2019 to January 2020 were followed up for the study. The FEES test was performed to diagnose dysphagia in CVD patients. Anthropometric measurements of the patients were taken to calculate their body mass index (BMI) values. To determine a patient's daily energy and food intake, 24-h food recalls were taken, and the Nutritional Risk Screening 2002 (NRS 2002) test was used to identify patients at risk of malnutrition. State (SAI)-Trait Anxiety Inventories (TAI) were used to determine instant and general anxiety levels. After patient evaluations NT was provided. All evaluations were repeated 8 weeks after NT. Our study was carried out based on a longitudinal design since we worked with the same units at two different time points.

Results: post-NT SAI scores were significantly lower than pre-NT scores ($p < 0.05$). A moderate correlation was found between pre- and post-NT SAI scores and daily energy and fluid intake status, and between TAI scores and daily energy, fat, and fluid intake amounts ($p < 0.05$). Post-NT SAI scores significantly decreased with both NRS 2002 and BMI values ($p < 0.05$).

Conclusions: this study highlights the importance of NT in improving rehabilitation outcomes of patients with dysphagia. Since exercises such as postural techniques or maneuvers, and muscle strengthening to reduce swallowing difficulties are an important part of NT for dysphagia, a multidisciplinary study is required for the management of dysphagia, and further studies are needed on this subject.

Keywords:

Anxiety. Dysphagia. Malnutrition. Nutritional status.

Resumen

Introducción: la disfagia es común en los pacientes con enfermedad cerebrovascular (ECV). Se ha informado de que aparece entre el 35 % y el 50 % de estos pacientes. La disfagia puede provocar desnutrición, deshidratación y muerte, y afecta los niveles de ansiedad.

Objetivos: este estudio tuvo como objetivo evaluar los efectos del tratamiento nutricional recomendado (TN) sobre el estado nutricional y los niveles de ansiedad en pacientes con disfagia diagnosticada a partir de pruebas clínicas y de la evaluación endoscópica de la deglución por fibra óptica (FEES).

Métodos: se realizó un seguimiento para el estudio de 75 pacientes mayores de 50 años con diagnóstico de ECV, hospitalizados en la Clínica de Neurología del Hospital de Investigación y Capacitación de la Ciudad de Mersin desde octubre de 2019 hasta enero de 2020. La prueba FEES se realizó para diagnosticar la disfagia en los pacientes con ECV. Se tomaron medidas antropométricas de los pacientes para calcular los valores del índice de masa corporal (IMC). Para determinar la ingesta diaria de energía y alimentos de los pacientes, se realizaron recuerdos de alimentos de 24 horas y se utilizó la prueba de evaluación del riesgo nutricional 2002 (NRS 2002) para identificar a los pacientes en riesgo de desnutrición. Se utilizaron los inventarios de ansiedad como estado (SAI) y como rasgo (TAI) para determinar los niveles de ansiedad instantánea y general. Después de las evaluaciones de los pacientes se les proporcionó TN. Todas las evaluaciones se repitieron 8 semanas después del TN. Nuestro estudio se realizó sobre la base de un diseño longitudinal, ya que trabajamos en las mismas unidades con dos tiempos diferentes.

Resultados: las puntuaciones del SAI post-TN fueron significativamente más bajas que las puntuaciones previas al TN ($p < 0,05$). Se encontró una correlación moderada entre las puntuaciones del SAI antes y después del TN y el estado de ingesta diaria de energía y líquidos, y entre las puntuaciones del TAI y las cantidades de ingesta diaria de energía, grasas y líquidos ($p < 0,05$). Las puntuaciones del SAI posteriores al TN disminuyeron significativamente tanto para los valores del NRS 2002 como para los valores del IMC ($p < 0,05$).

Conclusiones: este estudio destaca la importancia del TN para mejorar los resultados de la rehabilitación de los pacientes con disfagia. Dado que los ejercicios como las técnicas/maniobras posturales y el fortalecimiento muscular para reducir las dificultades para tragar son una parte importante del TN de la disfagia, se requiere un estudio multidisciplinario sobre el manejo de la disfagia y se necesitan más estudios sobre este tema.

Palabras clave:

Ansiedad. Disfagia. Desnutrición. Estado nutricional.

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INTRODUCTION

Cerebrovascular disease (CVD) is characterized by dysphagia (1). The prevalence of dysphagia is 10 % among individuals over 50 years of age — it increases with age and is reported to be 35 % to 50 % in patients with CVD (2,3). The most important changes that may cause dysphagia with increasing age are decreased chewing power because of decreased face muscle strength, tooth loss, decreased saliva production, and low fluid intake (4). In patients with CVD, dysphagia may result in malnutrition, dehydration, penetration, aspiration, pneumonia, and death (5), and may adversely affect an individual's anxiety status and quality of life (6).

In dysphagia, the risk of aspiration increases with age and malnutrition (7). Decreased protein intake due to malnutrition leads to muscle loss, which increases the risk of aspiration, causing a decrease in cough and respiratory power (8). About half of the patients with dysphagia aspirate. Silent aspiration occurs when food goes down the vocal cords without cough. Silent aspiration can be overlooked in clinical tests; therefore, advanced instrumental methods are used to evaluate dysphagia. The fiber-optic endoscopic evaluation of swallowing (FEES) test is the most commonly used assessment tool in clinical practice. Using the FEES test, the anatomical and physiological structures involved in the swallowing phases were examined, and nutritional treatment (NT) strategies were determined using a fiber-optic camera and providing the patient with foods with different bolus consistencies (liquid/semisolid) (9). The evaluation is easy and standardized as it is based on scales. The most commonly used scale is the Penetration-Aspiration Scale (PAS). The degree of dysphagia was determined based on the score obtained in this scale (10).

Nutritional treatment is important to increase swallowing efficacy and safety, one of the basic approaches to dysphagia treatment. Nutritional treatment in patients with dysphagia is based on changes in the amount and density of the foods consumed by the patient after clinical and instrumental evaluation. For patients to swallow these foods without aspiration, they need to eat slowly in a sitting position (11).

This study was planned and conducted to evaluate the effects of NT, which is routinely recommended for patients with dysphagia based on clinical and FEES tests, on the nutritional status and anxiety levels of the patients included. The hypotheses determined for this study may be described as follows — First, there is a relationship between the nutritional status of dysphagia patients and their anxiety levels. Second, nutritional therapy provides an increase in food intake and a reduction in risk of malnutrition in patients with dysphagia.

MATERIALS AND METHODS

THE ETHICAL ASPECT OF THE RESEARCH AND DATA COLLECTION

The Toros University Scientific Research and Publication Ethics Committee approved the study (#43-25.09.2019), and an informed consent was obtained from the individuals who participated in this study. Seventy-five patients over the age of 50, who were diagnosed with CVD and hospitalized at the Mersin City Research and Training Hospital, Neurology Clinic, from October 2019 to January 2020, were followed up for the study. Patients diagnosed with CVD for at least 2 weeks and those with dysphagia who could be fed orally were included, and those who were fed only via enteral nutrition (EN), except for oral enteral support, and total parenteral nutrition (TPN) were excluded. Our study was carried out based on a longitudinal design since we worked with the same units at two different time points.

Consent was obtained from all patients who volunteered to participate in the study. First, a FEES test was administered routinely to diagnose dysphagia, and PAS scores were obtained. Then, anthropometric measurements (height and weight) of the patients were taken to calculate their BMI. To determine their daily food intake, 24-h dietary recalls were taken, the NRS-2002 was used to identify patients at risk of malnutrition, and both State and Trait Anxiety Inventories (SAI and TAI, respectively) were used to determine instant and general anxiety levels. They were informed about the importance of consuming food in an upright position. The amounts of energy, nutrients, and fluids specific for each patient were calculated. NT, as modified based on food consistency, was administered. In the second study visit, which took place 8 weeks after the first interview, anthropometric measurements and 24-h dietary recalls were taken again. The NRS 2002 and SAI-TAI assessments were readministered.

ASSESSMENT OF THE SWALLOWING DISORDER

To standardize the FEES and PAS assessments, evaluations were made by a doctor specialist experienced in laryngology-swallowing conditions. During the FEES test, patients were given food in liquid/semisolid form with green food dye, and their food swallowing was monitored with a fiber-optic camera and scored with the PAS.

PAS is reliable and easy to use. It includes a scoring system that allows to obtain a numerical dysphagia level based on the images obtained via the FEES test. There are eight scores on the scale regarding patient penetration and aspiration severity. Higher scores on the scale indicate a higher severity (1, no-penetration-aspiration; 2-5, penetration; 6-8, aspiration) (12).

EVALUATION OF ANTHROPOMETRIC MEASUREMENTS

The body weights of the participants were measured with a sensitive scale, and their height was measured without stretching. Body mass index was calculated using the formula BMI (kg/m^2) = body weight (kg) / height (m^2) using their body weight and height. If the value obtained was < 18.5 kg/m^2, the subject was underweight; if between 18.5 and 24.9 kg/m^2, the subject

was normal weight; if between 25.0 and 29.9 kg/m^2, the subject was overweight; if between 30.0 and 34.9 kg/m^2, the subject was included in obesity class 1; if between 35.0 and 39.9 kg/m^2, in obesity class 2; if ≥ 40.0 kg/m^2, in obesity class 3 (13).

EVALUATION OF NUTRITIONAL STATUS AND POTENTIAL MALNUTRITION

The NRS 2002 test was used to identify patients at risk of malnutrition. An NRS 2002 score ≥ 3 indicates a nutritional high risk (14). To determine daily food intake, 24-h dietary recalls were taken. The data were entered into the Nutrition Information Systems (BEBIS), and daily energy, macronutrient, and liquid consumption status were determined (15). These data, which were collected at the beginning of the study, were recorded again at the end of the study.

The daily energy requirements of the patients were calculated using a practical formula (20-30 kcal/kg of body weight) (16). Energy calculations in patients with body weight below normal (BMI < 18.5 kg/m^2) provided a result of > 25-30 kcal/kg of body weight (16). When assessing the energy requirements of obese patients (body mass index [BMI] of 30 kg/m^2), their ideal body weight was calculated (17) as: adjusted body weight = [IBW + (ABW – IBW x 0.25)], with IBW = ideal body weight, amd ABW = actual body weight. Daily protein needs were 1-1.5 g/kg, and daily fluid needs were 30 mL/kg (18). Accordingly, appropriate NTs were given considering the safe consistency patterns that they could receive based on FEES results (11).

ASSESSMENT OF ANXIETY LEVELS

In this study, SAI-TAI were used to determine instant emotional and general anxiety levels. A Turkish adaptation, as well as validity and reliability studies were performed in 1985 (19). These inventories contain short statements (20 each) for self-reporting. The SAI evaluates "instant emotional" anxiety levels, and the TAI evaluates the "general" anxiety status. The score ranges from 20 to 80. Although the scales do not have a definite cut-off point, it is generally accepted that 39-40 points are the cut-off point for anxiety (19). Higher scores indicate increased anxiety (20). These scales, which were administered at the beginning of the study, were repeated at the end of the study.

STATISTICAL ANALYSIS OF THE DATA

In the study, a paired-sample t-test, Pearson's correlation analysis, and a reliability analysis were used. We used Pearson's correlation analysis to assess the relationship between energy, macronutrients, and anxiety scores. Shapiro-Wilks normality tests were conducted for quantitative score variables, and it was observed that normality conditions were met. The reliability of state and trait anxiety scales was evaluated according to Cronbach's alpha coefficients. Analyses were applied by considering the total scores of the scale items. The IBM SPSS 20 software was used for the statistical analyses. In addition, correlation difference tests were used to test differences between correlations. At this stage, the psych package included in the R Project software was used (21).

RESULTS

A total of 75 patients with dysphagia, 24 women (32.0 %) and 51 men (68.0 %), with a mean age of 71.15 ± 10.34 years were recruited. The mean body mass index (BMI) of these patients was 26.14 ± 5.57. Although the mean NRS 2002 score was 2.20 ± 0.86, 31 patients (41.3 %) were found to have a NRS 2002 score ≥ 3. Based on the FEES scores, for liquid nutrients 60 patients (80.0 %) had a PAS score of 2-5, and 15 patients (20.0 %) had a PAS score of 6-8. For semisolid foods 72 patients (96.0 %) had a PAS score of 2-5, and 3 (4.0 %) had a PAS score of 6-8 (Table I).

The comparison of these patients pre- and post-NT based on their PAS scores and rates of meeting their energy and macronutrient needs is shown in table II. According to these results, for liquids there are significant differences between patients with a PAS score of 2-5 and those with a score of 6-8 in terms of the

Table I. General characteristics of patients with dysphagia

		Patients with dysphagia n = 75	
		n	%
Age (mean ± SD)		71.15 ± 10.34	
Gender			
Female		24	32.0
Male		51	68.0
BMI (mean ± SD)		26.14 ± 5.57	
NRS 2002 (mean ± SD)		2.20 ± 0.86	
< 3		44	58.7
≥ 3		31	41.3
PAS			
Liquid	(2-5)	60	80.0
	(6-8)	15	20.0
Semi solid	(2-5)	72	96.0
	(6-8)	3	4.0
Use of ONS			
Pre-NT		14	18.6
Post-NT		21	28.0

BMI: body mass index; NRS 2002: Nutritional Risk Screening 2002; NT: nutritional treatment; PAS: Penetration-Aspiration Scale; ONS: oral nutritional support.

Table II. Evaluation of percentages of meeting energy and macronutrients and liquid intake according to PAS in patients with dysphagia before and after nutritional treatment

PAS (liquid)		Pre-NT	Post-NT	p
		$\bar{X}$ ± SD	$\bar{X}$ ± SD	
Energy %	(2–5)	61.77 ± 14.98	70.92 ± 21.13	< 0.001***
	(6–8)	59.42 ± 19.71	76.33 ± 30.71	0.001**
Protein %	(2–5)	58.06 ± 17.68	66.81 ± 19.68	< 0.001***
	(6–8)	56.73 ± 13.69	75.78 ± 20.57	< 0.001***
CHO %	(2–5)	45.93 ± 6.96	44.68 ± 7.77	0.175
	(6–8)	39.06 ± 7.61	41.20 ± 4.64	0.245
Fat %	(2–5)	35.45 ± 6.012	36.73 ± 6.77	0.098
	(6–8)	41.53 ± 7.92	38.86 ± 3.50	0.007**
Liquid intake	(2–5)	767.56 ± 123.70	887.78 ± 134.82	< 0.001***
	(6–8)	506.46 ± 45.32	640.40 ± 75.27	< 0.001***
PAS (semi solid)		**Pre-NT**	**Post-NT**	**p**
		$\bar{X}$ ± SS	$\bar{X}$ ± SS	
Energy %	(2–5)	64.21 ± 18.41	76.85 ± 26.49	< 0.001***
	(6–8)	59.94 ± 3.79	67.71 ± 11.26	0.466
Protein %	(2–5)	59.49 ± 17.75	72.20 ± 20.62	< 0.001***
	(6–8)	62.33 ± 7.74	74.51 ± 11.17	0.359
CHO %	(2–5)	43.57 ± 7.80	44.80 ± 7.61	0.391
	(6–8)	44.66 ± 2.08	41.33 ± 2.08	0.109
Fat %	(2–5)	37.91 ± 6.93	36.94 ± 6.02	0.262
	(6–8)	36.00 ± 2.64	36.00 ± 2.64	0.184
Liquid intake	(2–5)	710.02 ± 164.91	840.85 ± 174.51	< 0.001***
	(6–8)	515.33 ± 26.63	628.66 ± 41.23	0.006**

CHO, Carbohydrate; NT, Nutritional Treatment; PAS, Penetration-Aspiration Scale.
***p < 0.01, ***p < 0.001.*

rate of meeting energy, protein, and fluid intake needs pre- and post-NT ($p < 0.05$). When the scoring for semisolid foods was analyzed pre- and post-NT, there was a significant difference in patients with a PAS score of 2-5 in terms of the percentage that met energy, protein, and fluid intake needs ($p < 0.05$). There was a significant difference in patients with a PAS score of 6-8 only in terms of their pre- and post-NT fluid intake status ($p < 0.05$).

The comparison of results in terms of NRS-2002 and BMI scores pre- and post-NT are given in table III. According to the results, there is a statistically significant difference between BMI and NRS 2002 scores pre- and post-NT ($p < 0.05$). In addition, there was no significant relationship between NRS 2002 score groups before and after nutritional treatment ($p > 0.05$).

Cronbach's alpha values for the scales, according to the reliability analysis results applied to the SAI and TAI, were found to be 0.845 and 0.903 pre-NT, respectively, and 0.902 and 0.888 post-NT, respectively. The reliability coefficients of the scales were determined. In this study, while the SAI scores of patients with dysphagia were determined before and after nutritional treatment (51.33 ± 6.88; 48.46 ± 7.39, respectively), the TAI scores were determined as 51.42 ± 7.12 and 51.42 ± 4.79, respectively; this appears to be higher than the generally accepted cutoff point. Mean post-NT SAI scores were significantly lower ($p < 0.05$) than pre-NT values, but there was no significant difference between mean TAI scores ($p > 0.05$).

Correlations regarding the meeting of daily energy, protein, carbohydrate (CHO), fat, and fluid intake needs, and pre-and post-NT SAI and TAI scores are given in table IV. There is a negative moderate relationship between pre- and post-NT SAI scores and the rate of meeting daily energy and fluid needs, and there is a weak negative relationship between SAI and the rate of meeting daily protein, CHO, and fat needs. There was a negative moderate relationship between TAI scores and the meeting of daily energy, fat, and fluid needs, and a negative poor relationship between TAI scores and the rate of meeting daily protein and CHO needs ($p < 0.05$). In addition, according to the significance of the differences between pre- and post-NT SAI and TAI scores and nutritional parameters, none of the post-NT correlation increases were significant ($p > 0.05$).

Table III. Evaluation of NRS 2002 and BMI values of patients with dysphagia before and after nutrition treatment

	Pre-NT		Post-NT		P
BMI ($\bar{X}$ ± SS)	26.14 ± 5.57		25.90 ± 6.04		< 0.001***
NRS 2002	**n**	**%**	**n**	**%**	
> 3	44	58.3	48	64.0	0.502
≥ 3	31	41.3	27	36.0	
$\bar{X}$ ± SS	2.20 ± 0.86		2.13 ± 0.92		< 0.001***

****BMI, body mass index; NT, nutritional treatment; NRS 2002, Nutritional Risk Screening 2002; p < 0.001.*

Considering the anxiety scale scores in relation to BMI and NRS 2002 values, it was seen that post-NT SAI scores significantly decreased in terms of NRS 2002 and BMI values ($p < 0.05$), but there was no significant decrease in TAI scores (Table V).

DISCUSSION

Dysphagia is a disease symptom that requires multidisciplinary treatment, of which a proper dietary intake is an important part. In NT, it is essential to regulate the intake of energy, protein, and fluid in the amount that patients can optimally absorb, and to maintain an optimal consistency to prevent aspiration as well as macro-micronutrient deficiencies (22). In patients with CVD, the

Table IV. The relationship between energy and macronutrients and anxiety scores of patients with dysphagia before and after nutritional treatment

		SAI			TAI		
		Pre-NT	**Post-NT**	**Difference**	**Pre-NT**	**Post-NT**	**Difference**
Energy	r	-0.467	-0.522	0.055	-0.470	-0.508	0.038
	p	< 0.001***	< 0.001***	0.577	< 0.001***	< 0.001***	0.702
Protein	r	-0.315	-0.388	0.073	-0.359	-0.395	0.036
	p	< 0.001***	< 0.001***	0.524	< 0.001***	< 0.001***	0.748
CHO	r	-0.355	-0.389	0.034	-0.313	-0.321	0.008
	p	< 0.001***	< 0.001***	0.763	< 0.001***	< 0.001***	0.946
Fat	r	-0.373	-0.408	0.035	-0.405	-0.461	0.056
	p	< 0.001***	< 0.001***	0.752	< 0.001***	< 0.001***	0.598
Liquid	r	-0.659	-0.709	0.050	-0.584	-0.688	0.104
	p	< 0.001***	< 0.001***	0.472	< 0.001***	< 0.001***	0.179

*CHO, carbohydrate; NT, nutritional treatment; SAI, State Anxiety Inventory; TAI, Trait Anxiety Inventory ***p < 0.001.*

Table V. Comparison of anxiety scores in relation with NRS 2002 and BMI values before and after nutritional treatment

	SAI		p	TAI		p
	Pre-NT	**Post-NT**		**Pre-NT**	**Post-NT**	
	Mean ± SD	**Mean ± SD**		**Mean ± SD**	**Mean ± SD**	
NRS 2002						
< 3	42.65 ± 10.50	38.31 ± 10.86	< 0.001***	42.97 ± 10.56	42.27 ± 9.97	0.188
≥ 3	51.31 ± 8.73	48.62 ± 10.14	< 0.001***	52.45 ± 8.860	52.02 ± 6.69	0.617
BMI (kg/m²)						
< 18.5	51.55 ± 6.54	47.11 ± 8.52	0.010*	51.44 ± 8.60	50.44 ± 7.26	0.590
18.5-24.9	45.97 ± 11.49	43.00 ± 12.88	< 0.001***	47.53 ± 11.78	47.26 ± 10.71	0.704
25.0-29.9	45.45 ± 9.88	40.62 ± 10.53	< 0.001***	44.86 ± 9.57	44.51 ± 8.70	0.653
30.0-34.9	40.57 ± 11.34	36.85 ± 11.59	0.001**	42.14 ± 11.49	39.90 ± 11.21	0.094
35.0-39.9	44.37 ± 9.45	40.37 ± 9.28	0.048*	42.75 ± 10.89	43.50 ± 7.89	0.634
≥ 40.0	-	-	-	-	-	-

BMI, body mass index; NT, nutritional treatment; NRS 2002, Nutritional Risk Screening 2002; SAI, State Anxiety Inventory; TAI, Trait Anxiety Inventory.
**p < 0.05, **p < 0.01, ***p < 0.001.*

frequency of dysphagia increases, and nutritional deficiencies are common (23). The use of oral nutritional supplements to correct nutritional deficiencies in patients with dysphagia, and the use of thickened enteral products to facilitate swallowing are the most effective ways to prevent nutritional deficiency and dehydration in these patients (11). In this study we observed that inadequate pre-NT energy, macronutrient, and fluid intake increased with NT. It may be seen that the increase in the rate of meeting energy and protein fluid intake needs by patients with a PAS score of 2-5 and 6-8 for both liquid and semisolid foods was significant (Table II). In an adequate and balanced diet, in addition to total energy and protein intake, the patterns of other macronutrients such as fat and CHOs in the diet should be taken into consideration. The amount of fat in the diet can increase the severity of dysphagia by changing serum cholesterol, triglyceride, and lipoprotein levels, and by setting the ground for chronic degenerative diseases with increasing age (24). In this study a significant increase was observed in the rate of meeting dietary fat needs in patients with dysphagia (Table II). Increases in energy and nutrient intake are thought to be due to an increase in the consumption of those foods that can be swallowed by patients, awareness of energy-nutrients, and an increase in the consumption of the oral nutritional supports that are recommended to correct the energy and nutrient deficiencies that nutrition cannot amend.

There is a strong link between dysphagia and malnutrition (25). In the available studies the prevalence of malnutrition following CVD was found to be 8 % to 49 % (25,26). In another study involving patients with dysphagia, it was reported that the rate of malnutrition, which was approximately 50 % at 2 weeks after a stroke, decreased to 19 % in the following 4 months (8). NT has a positive effect on weight gain and malnutrition in patients with dysphagia (27). The current NRS 2002 results that changed post-NT also support this outcome (Table III). The decrease in NRS 2002 scores is due to an increase in food intake as a result of the nutritional treatment that patients with dysphagia received at a consistency suitable for their swallowing function status. We think that the decrease in BMI of patients with dysphagia is due to the fact that these patients have different periods of cerebrovascular disease (number of weeks) — rehabilitation at different stages, different course or severity of disease in this period, and presence of an additional chronic disease (DM, etc.). If the nutritional treatment applied to these patients had continued, we think that nutritional treatment would also have had a positive effect on weight gain.

The complications that may occur in patients with CVD also increase the anxiety levels of patients with dysphagia (28). Studies have shown that patients with CVD have higher levels of both state and trait anxiety (29,30). This outcome can be explained by various possible reasons. First, neurological disorders cause physical, physiological, and psychological problems, causing changes in the daily lifestyle of patients. Difficulty in chewing and swallowing may cause additional anxiety due to malnutrition, pneumonia, and fear of death (31). Another possible reason for increased anxiety may be the increased time spent eating due to difficulty in swallowing, which may deteriorate the relationship between patient and caregiver (32). The last possible reason is that patients with dysphagia are embarrassed during eating, so they avoid eating with others (33). It is important to determine the anxiety levels of patients, which also play a vital role in the management of dysphagia. It was reported that 37 % of patients with dysphagia were found to have high anxiety levels (34). NT increases the level of knowledge about safe food intake in both patients and caregivers and thus reduces anxiety levels (35). In this study, a significant decrease was found in post-NT SAI scores. We can attribute this decrease in the scores that reflect immediate anxiety states to the fact that nutritional treatment, which is modified to facilitate chewing and swallowing, both reduces the time spent by the patient with food, and makes the patient feel more secure during this period.

As a result of postural disturbances, visual-perceptual disorders, decreased mobilization, and communication problems in patients with dysphagia and cerebrovascular disease, food consumption begins to decrease, and this situation causes weight loss and malnutrition (25-27), which may be associated with depression and increased anxiety levels (36). In a study examining this relationship, it was found that malnutrition caused increased complications, length of hospital stay/rehabilitation period, and anxiety levels (37). In the present study there was a significassnt relationship between pre- and post-NT SAI/TAI scores and energy and nutrient parameters ($p < 0.05$) (Table IV). However, according to the significance tests performed on the differences between SAI/TAI scores and nutritional parameters, none of the post-NT correlational increases were statistically significant ($p > 0.05$). Even if the differences between correlations were not significant, it was seen that NT improved anxiety levels (Table IV). We think that this positive effect on the anxiety levels of patients with dysphagia is due to an increase in the food consumed by the patients, a decrease in risk of complications due to malnutrition, and a decrease in the length of the hospital stay-rehabilitation period, thanks to the consistency changes made to ensure that food intake is safe for each specific patient.

Nutritional status, anxiety level, and quality of life affect each other in neurological patients (38). Nishioka et al. (39) reported that maintaining body weight by improving nutritional status increased quality of life. Serious weight loss or decrease in BMI was associated with anxiety levels (40). In the present study SAI scores decreased post-NT significantly for both NRS 2002 and BMI values ($p < 0.05$), but no significant decrease was observed in TAI scores (Table V). We think that nutritional treatment, which is given in a consistency that the patient is able to ingest, especially affects the state of anxiety, and that a decrease in the state of continuous anxiety may occur in the future by continuing the same nutritional treatment.

This is an exemplary study showing the effects of nutritional therapy as based on safe food intake on both nutritional status and anxiety levels in patients with dysphagia; however, it has also some limitations. First, no swallowing therapist/physiotherapist experienced in the treatment of dysphagia was included in the study. Second, the patients were at different rehabilitation stages. Another limitation is that the blood parameters that reflect the nutritional status of patients were not examined. Finally, some patients could not be included in the study because they could

not be reached. The data of the patients not included in the study could have led to different results, and more patients would have increased the reliability of the results.

Consequently, in this study NT, as based on safe food intake, led to an increase in the meeting of energy and protein requirements, as well as in fluid intake, in patients with dysphagia, which resulted in improvements in patient nutritional status, and a decrease in the risk of malnutrition by causing a decrease in NRS 2002 scores. In addition to the nutritional results, it also showed a positive secondary effect on the state anxiety levels of patients. While these results support the hypotheses of the study, they also emphasize the importance of NT in improving rehabilitation outcomes for patients with dysphagia. Since appropriate posture movements during swallowing, and exercises to reduce swallowing difficulties are important parts of NT for dysphagia, a multidisciplinary approach is required for the management of dysphagia, and more studies are needed on this subject.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

High nutritional risk using NUTRIC-Score is associated with worse outcomes in COVID-19 critically ill patients

Asociación entre el riesgo nutricional evaluado a través de NUTRIC-Score y los desenlaces clínicos en pacientes en estado crítico con COVID-19

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Abstract

Background: nutritional risk has been associated with worse outcomes at the critical care unit. The aim of this study was to describe the association between nutritional risk and length of stay, days on mechanical ventilation, and in-hospital mortality in patients infected with SARS-CoV-2.

Methods: a retrospective cohort of ventilated, critically ill patients. We assessed nutrition risk at baseline using NUTRIC-score. Logistic and linear regression models were used to analyze the association between NUTRIC-score and clinical outcomes (days on mechanical ventilation, hospital length of stay, and in-hospital mortality). A survival analysis was performed using Kaplan-Meier curves.

Results: a total of 112 patients were included, 39.3 % were overweight and 47.3 % were obese. Based on NUTRIC-Score, 66 % and 34 % of patients were at high and low nutritional risk, respectively. High nutritional risk was associated with increased mortality risk (OR: 2.4, 95 % CI, 1.06-5.47, p = 0.036) and higher 28-day mortality (HR: 2.05, 95 % CI, 1.01-4.23, p = 0.04) in comparison with low risk.

Conclusion: high nutritional risk is related to mortality in SARS-CoV-2 critically ill patients. Overweight and obesity are common in this sample. More studies are needed to elucidate the impact of nutritional therapy on infection course and outcomes.

Keywords:

Enteral nutrition. Nutritional risk. COVID-19. Critically ill patient. Mechanical ventilation.

Resumen

Introducción: el riesgo nutricional se asocia a peores desenlaces en los pacientes en estado crítico. El objetivo de este estudio es describir la asociación entre el riesgo nutricional y los días de estancia hospitalaria, los días de ventilación mecánica y la mortalidad en pacientes infectados por el SARS-CoV-2.

Métodos: cohorte retrospectiva de pacientes en estado crítico bajo ventilación mecánica invasiva. Se evaluó el riesgo nutricional utilizando la herramienta NUTRIC-Score. Se utilizaron regresiones lineares y logísticas para evaluar la asociación entre el riesgo nutricional y los desenlaces clínicos (días de ventilación mecánica, días de estancia hospitalaria y mortalidad hospitalaria). Se utilizaron curvas de Kaplan-Meier para analizar la sobrevivencia.

Resultados: se incluyeron 112 pacientes, el 39,3 % con diagnóstico de sobrepeso y el 47,3 % con obesidad de acuerdo con el IMC. Utilizando la herramienta NUTRIC-Score, el 66 % tenían riesgo nutricional alto y el 34 % riesgo nutricional bajo. El riesgo nutricional alto se asoció a un mayor riesgo de mortalidad (OR: 2,4; IC 95 %: 1,06-5,47; p = 0,036) y mayor mortalidad a 28 días (HR: 2,05; IC 95 %: 1,01-4,23; p = 0,04) en comparación con los individuos con riesgo nutricional bajo.

Conclusión: el riesgo nutricional alto se asocia con mortalidad en los pacientes con infección por SARS-CoV-2 en estado crítico. El sobrepeso y la obesidad son comunes en este grupo de pacientes. Se necesitan más estudios que evalúen el impacto de la terapia nutricional sobre el curso de la infección y los desenlaces clínicos.

Palabras clave:

Nutrición enteral. Riesgo nutricional. COVID-19. Paciente crítico. Ventilación mecánica.

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BACKGROUND

Over 109 million patients worldwide have been affected by Coronavirus Disease 2019 (COVID-19), caused by the SARS-COV-2 virus (1). Studies have shown that approximately 30 % of hospitalized patients require admission to intensive care units (ICUs) and ventilatory support (2).

In Latin American countries, 40-60 % of patients are malnourished at the time of hospital admission (3). This condition seems to impair immune response (4) with increased susceptibility to infection (5,6), which may have a deleterious impact on length of stay, days on mechanical ventilation, and in-hospital mortality (7).

Nutrition screening is defined as the process that allows identifying individuals who are at nutritional risk or already malnourished who would benefit from early nutritional support in order to predict and prevent adverse clinical outcomes. For this purpose, multiple nutritional screening tools have been validated in different clinical settings. However, all of them must be practical, reliable, and quickly appliable in the first 24-48 hours of hospital admission (7).

NUTRIC-Score was the first designed and standardized tool for use in critically ill patients. The original score was modified by excluding IL-6, because of high-cost measurement and low availability in the clinical setting. Global results showed a positive association between nutritional provision and survival at 28 days in patients with a higher NUTRIC-Score. Furthermore, this score is useful to identify the critically ill patients who will benefit most from optimal nutritional support (8).

During the COVID-19 pandemic, some authors have reported an increased prevalence of high nutritional risk in critically and non-critically ill patients from China when using nutrition screening tools such as NRS-2002 and NUTRIC-Score. Nutritional risk as identified by these tools has been associated with higher mortality and longer hospital stay in COVID-19 patients; however, there are no previous reports of associations between nutritional risk and clinical outcomes in Latin-American countries (9-11).

The aim of this study was to describe the association between nutritional risk and length of stay, days on mechanical ventilation, and in-hospital mortality in patients infected with SARS-CoV-2.

METHODS

In a retrospective cohort study, critically ill patients over 18 years of age, with a documented diagnosis of COVID-19, requiring mechanical ventilation from March 1, 2020 to June 30, 2020 at the National Institute of Respiratory Diseases were included. This center is a tertiary respiratory-disease exclusive hospital in Mexico City, Mexico.

ETHICAL CONSIDERATIONS

This study was reviewed and approved by the Institutional Review Board of the National Institute of Respiratory Diseases (Register #C51-20).

DATA COLLECTION

Demographic data included sex, age, height, weight, and body mass index (BMI). Prescribed drugs with nutritional implications (steroids, benzodiazepines, opioids, neuromuscular blocking agents [NBA], sedatives, peripheral nerve blockers, insulin regimens, and vasopressors), as well as PaO_2/FiO_2 ratio, medical history of non-communicable diseases, and biochemical parameters (acid-base status, electrolytes, glucose, and lipid levels) during the first 24-48 h of mechanical ventilation were collected.

NUTRITIONAL RISK ASSESSMENT

The nutritional risk of each patient was calculated using a modified NUTRIC-Score that includes age, APACHE II, and SOFA scores at admission, number of comorbidities and pre-ICU hospital length of stay during the first 48 hours of mechanical ventilation. High nutritional risk was stablished with a score ≥ 5.

CLINICAL ENDPOINTS

The main endpoint was the number of days under mechanical ventilation. Secondary endpoints included hospital length of stay (LOS) in-hospital mortality and 28-day mortality.

STATISTICAL ANALYSIS

Categorical variables were expressed as frequency rates (%), and continuous variables were expressed as means and standard deviation or median and interquartile range (IQR) values (P25-P75). Means for continuous variables were compared using independent group t-test when data were normally distributed between severe and critically ill groups, or using the Mann-Whitney U-test otherwise. Proportions for categorical variables were compared using the χ^2 test between two groups. Logistic regression models and linear regression models were used to analyze the association between NUTRIC-Score (treated as a categorical variable) and clinical outcomes (ventilator days, length of stay, and in-hospital mortality) after sex adjustment. Survival at 28 days was assessed using Kaplan-Meier curves with log-rank test, and a Cox proportional hazards model. The statistical analysis was performed using the packages Stata Intercooled (Version 14, STATA Corporation, College Station, TX, USA) and GraphPad Prism (GraphPad Software Inc., San Diego, USA). Statistical significance was defined as $p < 0.05$.

RESULTS

A total of 112 patients on mechanical ventilation were included in the analysis. The demographic characteristics and clinical fea-

tures of patients are listed in table I. Average age was 56.1 ± 12.6 years, and 34.8 % of the sample was over 60 years. There was a male predominance overall (71.4 %), and the mean age of females (60.7 ± 13.5 years) was higher than that of males (54.3 ± 11.9 years; p = 0.01). The average BMI of patients was 30.1 ± 5 kg/m^2; 39.3 % were overweight and 47.3 % were obese. The most common comorbidities were hypertension (n = 31, 27.6 %) and diabetes (n = 38, 34 %). Based on NUTRIC-Score, 74 (66 %) were at high nutritional risk and 38 (34 %) were at low nutritional risk. The mean APACHE II and SOFA scores were 21 ± 5 and 9 ± 2, respectively. Any degree of acute kidney injury was diagnosed in 45.5 % of patients.

Table I. Demographics, clinical, and nutritional characteristics of COVID-19 critically ill patients at the onset of mechanical ventilation

	n = 112
Age, years	56.1 ± 12.6
> 60 years (%)	39 (34.8 %)
Male gender (%)	80 (71.4 %)
Weight (kg)	80.5 ± 14.5
Ideal body weight (kg)	60.8 ± 9.4
BMI (kg/m^2)	30.1 ± 5.0
Normal weight, 18.5-24.9 kg/m^2	13.4 %
Overweight, 25-29.9 kg/m^2	39.3 %
Obesity, > 30 kg/m^2	47.3 %
NUTRIC-Score	
Low nutritional risk	38 (34 %)
High nutritional risk	74 (66 %)
Comorbidities (%)	
Diabetes	38 (34 %)
Hypertension	31 (27.6 %)
Diabetes + hypertension	18 (15.9 %)
Severity of disease	
PaO_2/FiO_2 ratio	128 (101-162)
SOFA score	9 ± 2
APACHE II score	21 ± 5
Acute kidney injury (%)	51 (45.5 %)
Renal replacement therapy (%)	9 (8 %)
Biochemicals	
Sodium (mmol/L)	141.6 ± 4.6
Potassium (mmol/L)	4.3 ± 0.6
Magnesium (mg/dL)	2.3 ± 0.4
Phosphorus (mg/dL)	3.9 ± 1.7
Triglycerides (mg/dL)	268 (201-337)
Total cholesterol (mg/dL)	140 (104-169)
Lactate (mmol/L)	1.5 (1.0-2.1)
Glucose (mg/dL)	161 (113-231)
C-Reactive protein (mg/dL)	13.7 (7.7-22.1)
Drugs	
Steroids	73 (65.2 %)
Benzodiazepines	85 (76.5 %)
Opioids	101 (91 %)
Neuromuscular blocking agents	85 (76.5 %)
Sedatives (propofol)	50 (45 %)
Peripheral nerve blockade	26 (23.4 %)
Rapid-acting insulin regimen	61 (55 %)
NPH insulin with rapid-acting regimen	36 (32.4 %)
Vasopressors	57 (51.3 %)

OUTCOMES ASSOCIATED TO NUTRITIONAL RISK

In- hospital mortality was 48.2 % in the whole sample. Patients with high nutritional risk had higher mortality than low-risk patients (p = 0.03). The average LOS was 25 days (IQR, 16-41), and the duration of mechanical ventilation (MV) was 17 days (IQR, 9-27) in discharged patients (Table II)

In logistic regression models, high nutritional risk was associated with increased mortality risk (OR: 2.38, 95 % CI, 1.06-5.38, p = 0.036). No associations for hospital length of stay and ventilation days were observed (Table III).

TWENTY-EIGHT-DAY MORTALITY RISK

A survival analysis at 28 days was performed. A total of 73 patients had been discharged or had died on day 28 (48 with high nutritional risk and 25 with low nutritional risk). The number of patients who died on the first 28 days was 33 in the high nutrition risk group and 11 in the low nutrition risk group. Differences (p = 0.04) were observed with a higher 28-day mortality in the group at high nutritional risk (Fig. 1). In the Cox model adjusted for sex the high nutritional risk group was associated with a higher 28-day mortality (HR: 2.05, 95 % CI: 1.01-4.23, p = 0.04) when compared to the low risk group.

DISCUSSION

This study is the first one to describe an association between nutritional risk and clinical outcomes in Latin-American critically ill patients with COVID-19. Patients affected by this pandemic disease are at nutritional risk. According to Liu et al., nutritional risk is present in 85.8 % of non-critically ill patients (11). In critically ill COVID-19 patients, Zhang et al. reported a prevalence of high nutritional risk in 61 % of the patients in a retrospective study with data from three ICUs in Wuhan, China (n = 136). In our study, we found that 66 % of critically ill COVID-19 patients were at high nutritional risk according to NUTRIC-Score calculations at ICU admission, which is similar to the findings by Zhang et al.

Additionally, patients in the study by Zhang et al. were predominantly elderly, with 63 % of participants being older than 65 years of age, in comparison with only 34.8 % of patients in our

Table II. Clinical outcomes of COVID-19 critically ill patients by nutritional risk

Outcome	Total (n = 112)	NUTRIC-Score		
		High risk (n = 74)	Low risk (n = 38)	p-value
Mortality (%)	54 (48.2 %)	41 (55.4 %)	13 (34.2 %)	0.03[a]
LOS (days)				
Discharged	25 (16-41)	25 (18-41)	25 (16-39)	0.46[b]
MV (days)				
Discharged	17 (9-27)	17 (12-28)	17 (9-25)	0.47[b]
Died	16 (9-22)	16 (10-22)	12 (7-20)	0.14[b]

Median (IQR). [a]X^2 test; [b]Mann-Whitney U-test; LOS: hospital length of stay; MV: mechanical ventilation.

Table III. Association between high nutritional risk using NUTRIC-Score and clinical outcomes in COVID-19 patients

Model	In-hospital mortality	Hospital length of stay (days)	Mechanical ventilation (days)
Model 1	OR: 2.38, 95 % CI, 1.06 to 5.38, p = 0.036	β: 3.4, 95 % CI, -4.4 to 11.3, p = 0.38	β: 1.8, 95 % CI -3.2, 6.9, p = 0.46
Model 2	OR: 2.40, 95 % CI, 1.05 to 5.47, p = 0.036	β: 3.4, 95 % CI, -4.4 to 11.3, p = 0.38	β: 1.8, 95 % CI, -3.2 to 7.0, p = 0.46

Model 1, crude. Model 2, adjusted for sex.

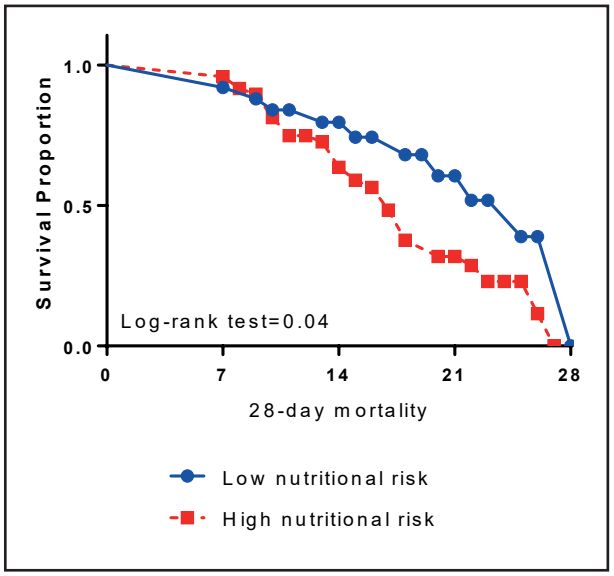

Figure 1.

Survival curves for high and low nutritional risk using NUTRIC-Score in critically ill patients with COVID-19.

sample being over the age of 60 years. Hypertension and diabetes were the most commonly reported comorbidities in both studies. The prevalences of hypertension and diabetes were 50 % and 41 %, respectively, in the study by Zhang et al., in comparison with prevalences of 27.6 % and 34 %, respectively, in our study. Hemodynamic instability with vasopressor requirements and acute kidney injury (AKI) were present in 51.3 % and 45.5 %, respectively, of the participants in our study, which does not differ from the 66 % and 41 % reported by Zhang et al. Older age, multiple comorbidities, and disease severity contribute to increased nutritional risk detection using tools such as NUTRIC-Score.

Higher nutritional risk was associated with adverse clinical outcomes in similar patients. Zhao et al. demonstrated in critically ill patients with COVID-19 that higher nutritional risk (using the NRS score) was associated with a higher risk of mortality (OR: 2.23, 95 % CI, 1.10-4.51, p = 0.026); they also did not observe any association between nutritional risk and LOS (9). Using NUTRIC-Score in 136 critically ill COVID-19 patients, Zhang et al. reported a higher mortality in the high nutritional risk group (HR: 2.01, 95 % CI, 1.22-3.32, p = 0.006) (10). In our sample, high nutritional risk was associated with mortality risk (OR: 2.4, 95 % CI, 1.05-5.47, p = 0.046); however, we observed a high prevalence of overweight and obesity in this sample, which may have influenced the association.

Our study has some limitations. First, all data were obtained from a single center, which may result in concerns regarding the generalization of our conclusions. Second, we only assessed critically ill patients. Third, long-term survival outcomes were not accessible due to the impact of COVID-19 on the workload of the nutrition department. More studies are needed to elucidate the impact of nutritional therapy on nutritional status, infection course, and clinical outcomes.

CONCLUSION

Nutritional risk is associated with a higher risk of mortality in critically ill patients with SARS-CoV-2 infection. Further studies

should be performed to establish an early nutritional intervention and its impact on the course of this infection.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Epidemiología y dietética

Exercise and fruit/vegetable intake, and their associations with body weight status in university students

Ejercicio físico y consumo de frutas/verduras, y sus asociaciones con el estado del peso corporal en estudiantes universitarios

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Abstract

Background: evidence suggests that exposure to risk factors related to excess body weight is more frequent in the second and third decades of life. Thus, one of the most propitious environments for the acquisition of habits that can inhibit overweight is the university.

Objective: to identify the frequency of aerobic and strength exercises and of fruit/vegetable intake in university students, and subsequently establish associations between both health behaviors and excess body weight.

Methods: the sample was comprised of 5,310 university students. An online questionnaire was used to collect the frequency of exercises and fruit/vegetable intake. The body mass index was used to define body weight status. The data were analyzed statistically by employing a bivariate analysis and binary logistic regression.

Results: the practice of aerobic and strength exercises was reported by 80.4 % and 51.6 % of the sample, respectively. Only 13 % of the surveyed university students had an adequate fruit/vegetable intake. The proportion of excess body weight was 39.1 %, the condition being significantly higher in men. The risk for excess body weight identified in the university students who reported not consuming fruits/vegetables daily was two to three times higher than in their peers who reported an adequate intake (women: OR = 2.92 [95 % CI 2.07-4.12]; men: OR = 1.98 [95 % CI 1.41-3.02]). Exposure to the risk for excess body weight was progressively lower as the reported frequency of aerobic exercise became higher.

Conclusion: these findings suggest the need to promote initiatives aimed at the preparation and implementation of health education and promotion programs in the university context, through actions of guidance about exercise and food intake that may help to minimize the risks of onset and development of excess body weight.

Keywords:

Physical activity. Food intake. Overweight. University health. Health promotion.

Resumen

Antecedentes: las evidencias sugieren que la exposición a factores de riesgo relacionados con el exceso de peso se produce con mayor frecuencia en la segunda y tercera décadas de la vida. Por lo tanto, uno de los entornos más propicios para la adquisición de hábitos que puedan inhibir el sobrepeso es la universidad.

Objetivos: identificar la frecuencia de los ejercicios aeróbicos y de fuerza y del consumo de frutas/verduras en estudiantes universitarios, y posteriormente establecer asociaciones entre los dos comportamientos de salud y el exceso de peso.

Métodos: la muestra estaba compuesta de 5310 estudiantes universitarios. Las frecuencias de los ejercicios físicos y del consumo de frutas/verduras se recopilaron mediante la aplicación de un cuestionario *online*. El exceso de peso se estableció a partir del índice de masa corporal. Los datos se analizaron estadísticamente empleando análisis bivariados y de regresión logística binaria.

Resultados: la práctica de ejercicios aeróbicos y de fuerza fue relatada por el 80,4 % y el 51,6 % de la muestra, respectivamente. Solamente el 13 % de los estudiantes universitarios presentaron un consumo adecuado de frutas/verduras. La proporción del exceso de peso fue equivalente al 39,1 %, siendo dicha proporción significativamente más elevada en los hombres. El riesgo de padecer exceso de peso identificado en los estudiantes universitarios que relataron no consumir frutas/verduras diariamente fue de dos a tres veces mayor que el de sus pares que refirieron un consumo adecuado (mujeres: OR = 2,92; IC 95 %, 2,07-4,12; hombres: OR = 1,98; IC 95 %, 1,41-3,02). La exposición al riesgo del exceso de peso fue progresivamente menor conforme mayor era la frecuencia reportada de ejercicios aeróbicos.

Conclusión: los hallazgos sugieren la necesidad de promover iniciativas dirigidas al diseño e implementación de programas de educación y promoción de la salud en el contexto universitario a través de acciones de orientación sobre ejercicio físico y consumo de alimentos que puedan ayudar a minimizar los riesgos de aparición y desarrollo del exceso de peso.

Palabras clave:

Actividad física. Consumo de alimentos. Sobrepeso. Salud universitaria. Promoción de la salud.

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INTRODUCTION

Non-communicable diseases such as cardiovascular diseases, some types of cancers, respiratory diseases, and diabetes cause 71 % of all deaths globally, and over 85 % in low- and middle-income countries (1). Unhealthy lifestyles characterized by physical inactivity and inadequate eating habits are seen as the main risk factors for chronic diseases and premature deaths (2-5). Individually, they account for a significant amount of preventable deaths worldwide, with physical inactivity alone claiming 3.2 million annual deaths, and dietary risks 11.3 million (6). The impact of these individual issues is exacerbated by the interactions with other risk factors, which further endanger the health of the population. For instance, physical inactivity, poor diet, and excess body weight are linked to an increased risk for countless chronic diseases (7).

In this context, overweight and obesity have been an important factor of concern in the area of public health. Estimates indicate that, in keeping with current trends, in 2030 there will be approximately 2.2 billion overweight adults worldwide, and more than 1.1 billion obese people, which should account for 60 % of the world's population (8). Particularly in Brazil, a survey carried out in 2018 reveals that, depending on the region considered, between 32 % and 59 % of the population over 18 years of age are overweight or obese (9). This implies higher rates of morbidity in the population, a significant increase in the need to use medical services, and a great economic impact on the health system (10).

Evidence suggests that the exposure to risk factors related to excess body weight is more frequently emerging in the second and third decades of life (11). Thus, one of the most propitious environments for the acquisition of habits that can inhibit overweight and obesity is the university. University life is where young people undergo various changes in terms of biological, psychological, social, and economic changes. When young people enter university they face numerous challenges, such as being away from home, adjustment to independent living, the need to establish new friendships in addition to coping with higher-level studies and academic stress (12). Moreover, researchers have shown that the academic years lead to major changes in risk behaviors such as decreased levels of physical activity and inadequate eating habits (13). These unhealthy behaviors represent a negative impact not only during the academic cycle but may continue after the university period, becoming highly detrimental in adult age (14).

Thus, investigating physical activity and eating habits in the academic environment can help in detecting the most vulnerable groups to overweight and obesity, and provide interventions aimed at reducing exposure to excess body weight. In Brazil few studies have sought to investigate physical activity, eating habits, and their association with variations of body weight in representative samples of the university population, leaving an important gap in knowledge in the area. The few studies identified so far have focused on exclusive samples of specific courses from a single institution and with participants selected for convenience or another non-probabilistic method (15-17). Most studies on the topic among college students were conducted in developed countries (11,18-21), and tend to show findings and perspectives that are different from those of developing countries.

Therefore, the objective of this study was to identify the frequency of practice of aerobic and strength exercises and of fruit/vegetable intake in university students in the State of Paraná, Southern Brazil, and subsequently establish associations between both health behaviors and excess body weight.

METHODS

This is a cutout of the University Promoting Health Project, a population-based cross-sectional study designed and implemented by the Federal Technological University of Paraná (UTFPR). To illustrate the size of the population universe addressed, the UTFPR attends approximately 30 thousand university students in 105 courses, distributed over 13 campuses located in cities of different geographic regions of the State of Paraná, Brazil.

SAMPLE

The sample size was established assuming a prevalence of unknown success (p = 50 %), 95 % confidence level, and sampling error of three percentage points. However, considering that the sample planning involved a cluster, the design effect was defined to three, adding 20 % to address possible losses during data collection, thus initially foreseeing a minimum sample of five thousand university students. However, the final sample used in the treatment of the collected information comprised 5,310 university students. The composition of the sample was the result of stratified random sampling involving a three-stage cluster: campuses, course, and course year, with probability proportional to size.

DATA COLLECTION

The data were collected between September and November 2018. The information about the frequency of aerobic and strength exercises, and of fruit/vegetable intake were obtained through the online questionnaire known as the National College Health Assessment II (NCHA IIc) as translated, adapted, and validated for use in the Brazilian university population (22), with additional questions about demographic data including gender, age, marital status, housing type, and course year. The reliability and validity of the Brazilian version of the NCHA IIc questionnaire were originally confirmed through psychometric properties equivalent to Cronbach's alpha, indicators of confirmatory factor analysis, factor invariance, and kappa agreement index (23).

The NCHA-IIc involves questions about health-risk and protective behavior, including seven sections: a) health, health education, and safety; b) alcohol, tobacco, and other drug use; c) sex behavior and contraception; d) weight, nutrition, and exercise; e) mental health; f) physical health; and g) impediments to academic performance

(24,25). However, the present study used data made available specifically in the "weight, nutrition, and exercise" section. In this case, our university students reported the frequency with which they practiced aerobic and strength exercises, and consumed fruits/vegetables using the week prior to data collection as their reference.

Based on the frequency of aerobic and strength exercises the following indicators were adopted: no practice; low level of practice for frequencies equivalent to 1-2 days/week; moderate level of practice for frequencies equivalent to 3-4 days/week; and high level of practice for frequencies equivalent to ≥ 5 days/week. Regarding the fruit/vegetable intake reported by university students, according to the recommendations from the World Health Organization (26) the following indicators were taken into consideration: no intake; low intake for frequencies equivalent to 1-2 servings/day; moderate intake for frequencies equivalent to 3-4 servings/day; and adequate intake for frequencies equivalent to ≥ 5 servings/day.

In terms of body weight status, body mass index (BMI) was calculated through the ratio between body mass in kilograms and the square of height in meters (kg/m^2). The measures of body weight and height were self-reported by the university students when answering the questions: a) What is your body weight in kilograms? and b) What is your height in meters? Based on these BMI values, the body weight status of university students was obtained from the cut-off points recommended by the World Health Organization (27), considering the following four strata: low body weight (BMI < 20 kg/m^2), eutrophic (20 kg/m^2 ≤ BMI < 25 kg/m^2), overweight (25 kg/m^2 ≤ BMI < 30 kg/m^2), and obesity (BMI ≥ 30 kg/m^2).

We visited the classrooms selected for the study and explained the objectives of the research and the principles of secrecy, non-identification, and non-influence on academic performance to the university students. We then invited them to participate in the study and those who initially agreed received individual guidelines and a password to access the electronic platform, thus confirming anonymity. We instructed the participants on how to access the platform and self-complete the questionnaire within a deadline of seven days after releasing the individual password. The rights of all participants were guaranteed by a Free and Informed Consent Term signed by an electronic procedure before the initiation of the NCHA IIc self-completion process in the online format.

The exclusion criteria for any university student belonging to the selected classroom included: a) absence from classes on the day scheduled for the invitation to participate in the study and the distribution of the individual password to access the electronic platform; b) refusal to participate in the study; c) being subjected to any specific medical treatment or diet; d) pregnancy; e) failure to complete the questionnaire on the electronic platform within seven days, and f) age under 18 or over 35 years.

STATISTICAL ANALYSIS

The data were processed using the computerized Statistical Package for the Social Sciences (SPSS®, version 24). The exact proportions and respective confidence intervals (95 % CIs) of indicators associated with the aerobic and strength exercises, and with fruit/vegetable intake, stratified according to demographic data and nutritional status, were identified. Statistical differences between the strata under investigation were analyzed with a table of contingencies and the chi-square non-parametric test (χ^2). Established through binary logistic regression, odds ratios (ORs) were calculated to identify associations between excess body weight and indicators of exercise and fruit/vegetable intake. Models were established separately for each sex, and controlled for age, marital status, housing type, and course year.

RESULTS

Table I provides descriptive data on the sample selected for the study. Approximately one-third of the sample were women (38.2 %) and 39.1 % were aged between 21 and 25 years. At the time of data collection, 78.2 % of the university students were single, 24.2 % lived in students residences, and 52.8 % lived with their families. Regarding the course years, 32.1 of the university students who participated in this study were in the first year of study and 31.5 % in the last year. Moreover, 39.1 % of the sample selected had excessive body weight, with higher proportions of overweight and obesity among men (35.5 % and 12.1 %, respectively), whereas low body weight totaled 15.1 % of the sample, with a higher proportion among women (26.5 %).

The statistical information about the frequency of aerobic and strength exercises is shown in tables II and III. The proportion of university students selected in this study who reported not practicing any type of aerobic exercise during the week prior to the data collection was 19.6 % [95 % CI, 18.2 to 21.1]. In contrast, approximately half (48.4 % [95 % CI, 45.2 to 51.7]) of our university students reported practicing no strength exercises. When the χ^2 values were analyzed, males reported a higher weekly frequency of exercise, especially when this frequency was ≥ 5 times/week (aerobic exercises [$\chi^2 = 19.29$; $p < 0.001$] and strength exercises [$\chi^2 = 18.63$; $p < 0.001$]). With the advance of age, the proportion of university students who did not practice any aerobic exercises ($\chi^2 = 40.41$; $p < 0.001$) or strength exercises ($\chi^2 = 59.48$; $p < 0.001$) tended to increase significantly. In contrast, a significantly higher proportion of university students aged ≤ 20 years reported a frequency ≥ 5 times/week for aerobic exercises ($\chi^2 = 18.74$; $p < 0.001$) and strength exercises ($\chi^2 = 20.04$; $p < 0.001$).

In terms of marital status, a significantly greater proportion of married university students reported performing no aerobic exercises ($\chi^2 = 25.76$; $p < 0.001$) or strength exercises ($\chi^2 = 45.62$; $p < 0.001$), whereas those who said that they lived in a students residence exercised less frequently than those others who reported living with their family. Furthermore, the results revealed a statistically significant trend towards a reduction in the frequency of exercise with the advance of course years, especially for strength exercises.

Body weight status was closely associated with the frequency of exercise among university students. The findings from this

Table I. Demographic data and body weight status of the sample analyzed in the study

	Female n = 2,029 (38.2 %)	Men n = 3,281 (61.8 %)	Both genders n = 5,310 (100 %)
Age			
≤ 20 years	564 (27.8 %)	979 (29.8 %)	1,543 (29.1 %)
21-25 years	854 (42.1 %)	1,224 (37.3 %)	2,078 (39.1 %)
≥ 26 years	611 (30.1 %)	1,078 (32.9 %)	1,689 (31.8 %)
Marital status			
Single	1,494 (73.6 %)	2,658 (81.0 %)	4,152 (78.2 %)
Married/Partnered	535 (26.4 %)	623 (19.0 %)	1,158 (21.8 %)
Housing type			
Student residence	377 (18.6 %)	908 (27.7 %)	1,285 (24.2 %)
Parent's home	1,242 (61.2 %)	1,562 (47.6 %)	2,804 (52.8 %)
Homestay	363 (17.9 %)	731 (22.3 %)	1,094 (20.6 %)
Alone	47 (2.3 %)	80 (2.4 %)	127 (2.4 %)
Course year			
1st	694 (34.2 %)	1010 (30.8 %)	1,704 (32.1 %)
2nd-3rd	753 (37.1 %)	1180 (36.0 %)	1,933 (36.4 %)
4th or more	582 (28.7 %)	1091 (33.2 %)	1,673 (31.5 %)
Body weight status			
Low body weight	538 (26.5 %)	266 (8.1 %)	804 (15.1 %)
Eutrophic	980 (48.3 %)	1,453 (44.3 %)	2,433 (45.8 %)
Overweight	369 (18.2 %)	1,165 (35.5 %)	1,534 (28.9 %)
Obesity	142 (7.0 %)	397 (12.1 %)	539 (10.2 %)

study enable one to infer that the frequency with which university students reported practicing both types of exercise is inversely proportional to their nutritional status. Thus, 31.4 % [95 % CI, 28.9 to 34.0] of eutrophic students reported practicing aerobic exercises ≥ 5 times/week, compared to 5.7 % [95 % CI, 5.2 to 6.4] of those categorized as obese ($\chi^2 = 31.86$; $p < 0.001$). Moreover, 19.4 % [95 % CI, 18.0 to 21.0] of eutrophic students reported practicing strength exercises with the same weekly frequency, while only 2.2 % [95 % CI, 1.9 to 2.7] of obese students reported an identical frequency ($\chi^2 = 22.31$; $p < 0.001$).

Based on the information shown in table IV, 20.7 % [95 % CI, 19.1 to 22.4] of the university students selected for this study reported a moderate frequency, and only 13.0 % [95 % CI, 12.1 to 14.2] mentioned an adequate frequency of fruit/vegetable intake. In contrast, 51.8 % [95 % CI, 48.4 to 55.3] and 14.5 % [95 % CI, 13.4 to 15.8] of students reported a low or nil frequency of fruit/vegetable intake, respectively. The adequate proportion of frequency of fruit/vegetable intake was higher in female ($\chi^2 = 17.98$; $p < 0.001$), and increased with age ($\chi^2 = 6.38$; $p = 0.024$) and in the strata that included married students ($\chi^2 = 14.52$; $p < 0.001$) and those who lived with their family ($\chi^2 = 13.03$; $p < 0.001$). Additionally, the adequate frequency of fruit/vegetable intake was significantly higher with the advance in course year ($\chi^2 = 5.98$; $p = 0.021$). With regard to nutritional status, a significantly lower proportion of students categorized with excess body weight (overweight and obese) reported an adequate frequency of fruit/vegetable intake when compared to those who were eutrophic or had low body weight ($\chi^2 = 14.23$; $p < 0.001$).

Table V shows the associations between exercise, fruit/vegetable intake, and variations in the occurrence of excess body weight found in the sample selected. Through the analysis of odds ratio values, considering that adjustments will be made for the remaining variables in the study, the estimates found in both sexes indicated that the exposure to risk of excess body weight was inversely proportional to the frequencies of aerobic exercises. Compared to individuals who performed exercise ≥ 5 days/week, men who reported not practicing this type of exercise had double the risk of excess body weight (OR = 2.05 [95 % CI, 1.59 to 3.25], whereas the same risk for women was one and a half times (OR = 1.56 [95 % CI, 1.16 to 2.18]).

Regarding strength exercises, significant associations were found for the frequencies of practice of 3-4 days/week. In this case, there was a lower risk for the presence of excess body weight equivalent to 68 % and 62 % among both women and men, respectively (females – OR = 0.68 [95 % CI, 0.44 to 0.98]; males – OR = 0.62 [95 % CI, 0.35 to 0.97]). The remaining situations of frequency of practice of strength exercises did not indicate statistically significant associations with the variations in the presence of excess body weight.

Table II. Proportion (95 % CI) of aerobic exercise practice, with stratification for demographic data and body weight status, among university students

	No practice	1-2 days/week	3-4 days/week	≥ 5 days/week
Overall	19.6 (18.2-21.1)	29.9 (27.5-32.4)	26.4 (24.3-28.6)	24.1 (22.0-26.3)
Gender	$\chi^2 = 18.28$; $p < 0.001$	$\chi^2 = 22.38$; $p < 0.001$	$\chi^2 = 20.87$; $p < 0.001$	$\chi^2 = 19.29$; $p < 0.001$
Female	25.7 (23.6-27.8)	37.8 (34.8-40.9)	19.1 (17.7-20.6)	17.4 (16.2-18.7)
Male	15.8 (14.6-17.1)	25.0 (22.9-27.2)	30.9 (28.4-33.5)	28.3 (26.1-30.6)
Age	$\chi^2 = 40.41$; $p < 0.001$	$\chi^2 = 19.23$; $p < 0.001$	$\chi^2 = 23.48$; $p < 0.001$	$\chi^2 = 18.74$; $p < 0.001$
≤ 20 years	5.7 (5.2-6.4)	33.2 (30.5-36.0)	31.9 (29.3-34.6)	29.2 (26.9-31.6)
21-25 years	18.4 (17.1-19.8)	30.7 (28.2-33.3)	26.1 (23.9-28.4)	24.8 (22.7-27.0)
≥ 26 years	36.5 (33.5-39.6)	23.9 (21.9-26.1)	20.3 (18.8-21.9)	19.3 (17.9-20.8)
Marital status	$\chi^2 = 25.76$; $p < 0.001$	$\chi^2 = 10.78$; $p < 0.001$	$\chi^2 = 4.89$; $p = 0.048$	$\chi^2 = 8.81$; $p < 0.001$
Single	16.3 (15.1-17.6)	31.5 (28.9-34.2)	26.8 (24.6-29.1)	25.4 (23.3-27.6)
Married/Partnered	34.4 (31.6-37.3)	24.2 (22.1-26.4)	21.8 (20.0-23.7)	19.6 (18.1-21.2)
Housing type	$\chi^2 = 27.82$; $p < 0.001$	$\chi^2 = 8.46$; $p < 0.001$	$\chi^2 = 6.09$; $p = 0.024$	$\chi^2 = 5.93$; $p = 0.029$
Students residence	30.9 (28.4-33.5)	26.0 (23.8-28.3)	22.1 (20.3-24.0)	21.0 (19.4-22.7)
Parent's home	11.8 (10.9-12.8)	33.2 (30.5-36.0)	28.2 (26.0-30.5)	26.8 (24.6-29.1)
Homestay	31.7 (29.1-34.4)	25.6 (23.5-27.8)	21.9 (20.1-23.8)	20.8 (19.2-22.5)
Alone	24.3 (22.3-26.4)	28.5 (26.2-30.9)	24.1 (22.1-26.2)	23.1 (21.1-25.2)
Course year	$\chi^2 = 28.59$; $p < 0.001$	$\chi^2 = 5.64$; $p = 0.027$	$\chi^2 = 5.77$; $p = 0.030$	$\chi^2 = 5.61$; $p = 0.034$
1st	11.4 (10.6-12.3)	32.6 (29.9-36.4)	28.7 (26.4-31.1)	27.3 (25.0-29.7)
2nd-3rd	19.7 (18.2-21.3)	29.6 (27.2-32.1)	26.0 (23.9-28.2)	24.7 (22.6-26.9)
4th or more	27.8 (25.6-30.1)	27.2 (25.0-29.3)	23.1 (21.1-25.2)	21.9 (20.1-23.8)
Body weight status	$\chi^2 = 56.38$; $p < 0.001$	$\chi^2 = 6.83$; $p = 0.019$	$\chi^2 = 26.84$; $p < 0.001$	$\chi^2 = 31.86$; $p < 0.001$
Low body weight	10.1 (9.7-11.0)	32.1 (29.5-34.8)	29.6 (27.2-32.1)	28.2 (26.0-30.5)
Eutrophic	8.7 (7.9-9.6)	27.4 (25.2-29.8)	32.5 (29.8-35.3)	31.4 (28.9-34.0)
Overweight	28.9 (26.6-31.3)	32.8 (30.1-35.6)	20.7 (19.1-22.4)	17.6 (16.3-19.0)
Obesity	56.2 (52.5-60.1)	25.9 (23.7-28.2)	12.2 (11.3-13.2)	5.7 (5.2-6.4)

The risk of excess body weight, regardless of the simultaneous contribution of age, marital status, housing type, course year, and exercise, was increasingly higher in parallel with the reduction in the frequency of fruit/vegetable intake. Compared to those who mentioned an intake of ≥ 5 servings/day, the women who reported not consuming fruits/vegetables were approximately three times more likely to have excess body weight (OR = 2.92 [95 % CI, 2.07 to 4.12]). Among males, this proportion was nearly two times higher (OR = 1.98 [95 % CI, 1.41 to 3.02]). Moreover, the exposure to the risk of excess body weight among the university students who reported a frequency of fruit/vegetable intake equivalent to 1-2 portions/day remained significant in both sexes (females – OR = 1.97 [95 % CI, 1.31 to 2.96]; males – OR = 1.54 [95 % CI, 1.07 to 2.43]).

DISCUSSION

Initially, the present study aimed to identify specific information about the frequency of practice of aerobic and strength exercises, and of fruit/vegetable intake in a representative sample of Brazilian university students. Subsequently, it sought to establish possible associations between both health behaviors and the occurrence of excess body weight (overweight + obesity), adjusted for control variables.

The specialized literature includes few cases of population-based studies that deal with the frequency of exercise and food intake. Furthermore, there is no consensus regarding the measurement instruments to be used to estimate these types of health behavior among these studies. Differences in sample

Table III. Proportion (95 % CI) of strength exercise practice, with stratification for demographic data and body weight status, among university students

	No practice	1-2 days/week	3-4 days/week	≥ 5 days/week
Overall	48.4 (45.2-51.7)	20.3 (18.8-21.9)	16.8 (15.6-18.2)	14.5 (13.5-15.7)
Gender	$\chi^2 = 32.68$; $p < 0.001$	$\chi^2 = 3.98$; $p = 0.109$	$\chi^2 = 16.73$; $p < 0.001$	$\chi^2 = 18.63$; $p < 0.001$
Female	60.8 (56.6-65.1)	22.1 (20.3-24.0)	11.2 (10.4-12.2)	5.9 (5.4-6.7)
Male	40.7 (37.6-43.9)	19.2 (17.8-20.7)	20.3 (18.8-22.0)	19.8 (18.3-21.5)
Age	$\chi^2 = 59.48$; $p < 0.001$	$\chi^2 = 25.89$; $p < 0.001$	$\chi^2 = 22.79$; $p < 0.001$	$\chi^2 = 20.04$; $p < 0.001$
≤ 20 years	28.1 (25.9-40.4)	28.3 (26.1-30.6)	23.4 (21.4-25.6)	20.2 (18.7-21.9)
21-25 years	38.4 (35.4-41.5)	24.2 (22.1-26.4)	20.1 (18.6-21.8)	17.3 (16.1-18.7)
≥ 26 years	79.3 (74.7-84.1)	8.2 (7.5-9.1)	6.7 (6.1-7.6)	5.8 (5.3-6.6)
Marital status	$\chi^2 = 45.62$; $p < 0.001$	$\chi^2 = 19.82$; $p < 0.001$	$\chi^2 = 17.05$; $p < 0.001$	$\chi^2 = 14.89$; $p < 0.001$
Single	40.5 (37.4-43.7)	23.8 (21.7-26.0)	19.2 (17.8-20.8)	16.5 (15.3-17.9)
Married/Partnered	72.7 (68.2-77.3)	10.3 (9.5-11.3)	9.7 (8.9-10.7)	7.3 (6.7-8.2)
Housing type	$\chi^2 = 12.48$; $p < 0.001$	$\chi^2 = 5.61$; $p = 0.034$	$\chi^2 = 3.83$; $p = 0.121$	$\chi^2 = 4.10$; $p = 0.084$
Students residence	55.3 (51.8-58.9)	17.4 (16.2-18.7)	14.6 (13.5-15.9)	12.7 (11.8-13.9)
Parent's home	41.9 (38.8-45.1)	22.9 (20.9-25.0)	18.9 (17.5-20.5)	16.3 (15.1-17.7)
Homestay	54.3 (50.7-58.0)	18.1 (16.8-19.5)	15.1 (14.0-16.4)	12.5 (11.6-13.6)
Alone	50.6 (47.3-54.0)	19.5 (18.0-21.1)	16.0 (14.8-17.4)	13.9 (12.9-15.1)
Course year	$\chi^2 = 48.38$; $p < 0.001$	$\chi^2 = 22.42$; $p < 0.001$	$\chi^2 = 17.54$; $p < 0.001$	$\chi^2 = 14.78$; $p < 0.001$
1st	33.4 (30.7-36.2)	26.2 (24.1-28.4)	21.7 (19.9-23.6)	18.7 (17.3-20.3)
2nd-3rd	42.7 (39.6-45.9)	22.7 (20.7-24.8)	18.2 (16.9-19.7)	16.4 (15.2-17.8)
4th or more	68.9 (64.5-73.4)	11.7 (10.8-12.8)	10.2 (9.4-11.2)	8.1 (7.4-9.1)
Body weight status	$\chi^2 = 50.69$; $p < 0.001$	$\chi^2 = 6.34$; $p = 0.015$	$\chi^2 = 21.98$; $p < 0.001$	$\chi^2 = 22.31$; $p < 0.001$
Low body weight	47.5 (44.3-50.8)	22.1 (20.3-24.0)	16.4 (15.2-17.8)	14.1 (13.1-15.3)
Eutrophic	38.9 (35.9-42.0)	19.2 (17.8-20.7)	22.5 (20.5-24.7)	19.4 (18.0-21.0)
Overweight	57.3 (53.5-60.2)	18.5 (17.1-20.1)	13.0 (12.1-14.1)	11.2 (10.4-12.3)
Obesity	76.9 (72.3-81.7)	15.4 (14.3-16.6)	5.5 (5.0-6.3)	2.2 (1.9-2.7)

composition and selection procedures must also be taken into consideration as factors that hinder comparative analyses.

When the information about the frequency of exercise reported by university students was analyzed, the results showed a trend towards a reduction with age and towards men being more committed to their practice, as compared to women. Although certain differences in type of exercise can be found, the studies available in the literature agree that this practice tends to be negatively associated with age, especially beginning in the last years of adolescence (28,29). Although several studies have sought to identify the reasons for such decrease, the proportion of the contribution of biological and environmental factors and their interaction to the reduction in exercise with age remains unclear.

Previous studies showed that adult males exercise more frequently than females (30), corroborating the results found in the present study. However, if, on the one hand, the practice of aerobic and strength exercises predominated in women and men, on the other hand, there were important differences in the distribution of frequency of aerobic and strength exercises between sexes. Among young adults, the ratios to identify differences in physical activity between women and men are not clear. However, some studies have revealed the existence of a combination of socio-cultural and biological factors with the potential to encourage both sexes to practice exercise. The greater involvement with exercise shown by men can be partly explained by the fact that males are encouraged to practice highly physical activities since an early age, whereas women are directed towards activities that are more

Table IV. Proportion (95 % CI) of fruit/vegetable intake, with stratification for demographic data and body weight status, among university students

	No intake	Low intake[1]	Moderate intake[2]	Adequate intake[3]
Overall	14.5 (13.4-15.8)	51.8 (48.4-55.3)	20.7 (19.1-22.4)	13.0 (12.1-14.2)
Gender	*$\chi^2 = 19.06$; $p < 0.001$*	*$\chi^2 = 49.87$; $p < 0.001$*	*$\chi^2 = 48.27$; $p < 0.001$*	*$\chi^2 = 17.98$; $p < 0.001$*
Female	6.2 (5.7-7.0)	38.9 (35.8-42.1)	33.7 (30.9-36.6)	21.2 (19.6-23.0)
Male	19.6 (18.1-21.3)	59.8 (55.6-64.1)	12.7 (11.8-13.9)	7.9 (7.2-9.0)
Age	*$\chi^2 = 23.87$; $p < 0.001$*	*$\chi^2 = 5.49$; $p = 0.038$*	*$\chi^2 = 14.79$; $p < 0.001$*	*$\chi^2 = 6.38$; $p = 0.024$*
≤ 20 years	23.5 (21.4-25.7)	48.4 (45.2-51.7)	16.2 (15.0-17.6)	11.9 (11.0-13.1)
21-25 years	16.9 (15.7-18.3)	52.6 (49.1-56.2)	19.9 (18.4-21.6)	10.6 (9.8-11.8)
≥ 26 years	4.7 (4.2-5.6)	53.8 (50.2-57.5)	25.0 (22.9-27.3)	16.5 (15.3-18.0)
Marital status	*$\chi^2 = 13.52$; $p < 0.001$*	*$\chi^2 = 22.32$; $p < 0.001$*	*$\chi^2 = 21.84$; $p < 0.001$*	*$\chi^2 = 14.52$; $p < 0.001$*
Single	16.6 (15.4-18.0)	55.1 (51.6-58.8)	17.5 (16.2-19.0)	10.8 (10.0-11.9)
Married/Partnered	7.1 (6.5-7.9)	39.8 (36.7-43.0)	32.3 (29.7-35.1)	20.8 (19.2-22.6)
Housing type	*$\chi^2 = 15.73$; $p < 0.001$*	*$\chi^2 = 41.08$; $p < 0.001$*	*$\chi^2 = 39.81$; $p < 0.001$*	*$\chi^2 = 13.03$; $p < 0.001$*
Students residence	21.0 (19.4-22.8)	58.7 (54.6-62.9)	12.4 (11.5-13.6)	7.9 (7.2-9.0)
Parent's home	9.2 (8.4-10.2)	43.8 (40.7-47.0)	29.1 (26.8-31.6)	17.9 (16.6-19.5)
Homestay	19.4 (18.0-21.0)	62.3 (58.0-66.7)	10.2 (9.4-11.3)	8.1 (7.4-9.2)
Alone	20.3 (18.8-22.0)	54.5 (50.9-58.2)	15.5 (14.3-16.9)	9.7 (8.9-10.9)
Course year	*$\chi^2 = 6.43$; $p = 0.014$*	*$\chi^2 = 16.42$; $p < 0.001$*	*$\chi^2 = 13.49$; $p < 0.001$*	*$\chi^2 = 5.98$; $p = 0.021$*
1st	10.4 (9.6-11.5)	45.6 (42.4-48.9)	26.7 (24.5-29.1)	17.3 (16.1-18.8)
2nd-3rd	17.2 (16.0-18.6)	53.3 (49.8-56.9)	18.1 (16.8-19.7)	11.4 (10.6-12.6)
4th or more	16.4 (15.2-17.7)	55.5 (51.8-59.3)	17.6 (16.3-19.2)	10.5 (9.7-11.7)
Body weight status	*$\chi^2 = 22.54$; $p < 0.001$*	*$\chi^2 = 39.78$; $p < 0.001$*	*$\chi^2 = 18.41$; $p < 0.001$*	*$\chi^2 = 14.23$; $p < 0.001$*
Low body weight	10.1 (9.3-11.2)	50.6 (47.3-54.0)	24.2 (22.1-26.5)	15.1 (14.0-16.5)
Eutrophic	10.7 (9.9-11.8)	44.1 (41.0-47.3)	27.3 (25.1-29.7)	17.9 (16.6-19.5)
Overweight	18.1 (16.8-19.7)	63.9 (59.6-68.3)	11.1 (10.2-12.4)	6.9 (6.3-7.9)
Obesity	29.7 (27.5-32.2)	55.3 (51.4-59.0)	9.2 (8.4-10.4)	5.8 (5.3-6.7)

[1]Frequency of intake equivalent to 1-2 servings/day. [2]Frequency of intake equivalent to 3-4 servings/day. [3]Frequency of intake equivalent to ≥ 5 servings/day.

physically passive. Likewise, the more effective participation of men in the practice of exercise can be the result of the greater positive reinforcement and promotion of such practice received by them since childhood (28).

Another possible explanation for the lower participation of women in exercise is the different concept of body, capacity, and attitude required to make more intense physical efforts. From a socio-cultural perspective, the concept of body which is usually associated with physical activity is not adjusted to current female models of corporeality. Effectively, in modern times, the ideal female body is characterized by grace, elegance, beauty, and relative fragility, which does not seem to adjust to the image of a body involved with physical efforts. This factor can cause women to show some reservations concerning the possibility of practicing exercise, as this may affect their femininity (31).

In addition to socio-cultural factors, differences in the practice of exercise between sexes can be equally due to biological factors. Lower muscle resistance and strength, higher level of body fat, greater diameter and depth of the pelvic area, and discomfort during menstruation could be good reasons for women's lower involvement with exercise (32). The presence of sexual dimorphism should be seriously considered by managers of intervention programs in public health, especially aiming to eliminate social prejudices against the participation of women in the practice of exercise, which are culturally emphasized and valued from an individual perspective.

Table V. Odds ratios and respective confidence intervals (95 % CI) for the association between excess body weight (overweight + obesity) and frequency of exercise and fruit/vegetable intake among university students

	Female		Male	
	OR Adjusted (95 % CI)	p-value	OR Adjusted (95 % CI)	p-value
Aerobic exercise				
≥ 5 days/week	Reference	0.019	Reference	0.001
3-4 days/week	1.23 (0.94-1.65)		1.31 (0.97-1.93)	
1-2 days/week	1.36 (1.01-1.87)		1.47 (1.08-2.28)	
No practice	1.56 (1.16-2.18)		2.05 (1.59-3.25)	
Strength exercise				
≥ 5 days/week	Reference	0.037	Reference	0,041
3-4 days/week	0.68 (0.44-0.98)		0.62 (0.35-0.97)	
1-2 days/week	0.92 (0.64-1.37)		0.84 (0.51-1.44)	
No practice	1.18 (0.85-1.72)		1.17 (0.69-1.98)	
Fruit/vegetable intake				
≥ 5 servings/day	Reference	< 0.001	Reference	0.001
3-4 servings/day	1.43 (0.94-2.18)		1.26 (0.91-2.11)	
1-2 servings/day	1.97 (1.31-2.96)		1.54 (1.07-2.43)	
No intake	2.92 (2.07-4.12)		1.98 (1.41-3.02)	

Values adjusted for age, marital status, housing type, course year, and/or frequency of fruit/vegetable intake and exercise.

The high proportions of university students who reported not performing aerobic and strength exercises were one of the alarming findings. Previous studies showed that, apart from being an important factor that predisposes young adults to organic and psychological disorders, the risk of insufficient and inadequate physical activity tends to increase with age. This suggests a higher possibility that such behavior, harmful to health, will remain during more advanced adult stages of life (28).

Regarding the frequency of fruit/vegetable intake, the results found showed that only 13 % of the study sample met the recommendations for adequate intake (≥ 5 portions/day). Although possible methodological differences and influences resulting from cultural characteristics, climate, and food production and commercialization conditions can be found, this result corroborates previous estimates found in studies involving the Brazilian population in general and, more specifically, the population of university students (15-17). However, this was significantly lower than the findings of studies performed in developed countries (18,19). In this sense, assuming that the eating habit is one of the priority actions in the thematic agenda of public health, in view of the results found, there is the great challenge of education and health promotion in our reality.

Consistent with the results found in Brazilian studies (9,15-17) and different regions worldwide (18,19,21), the frequency of fruit/vegetable intake was higher among women and older university students. In fact, culturally speaking, a greater interest in questions related to diet, health, and beauty generates more concern about the consumption of low-calorie foods, which can have a positive influence on women's eating habits (33), thus justifying the differences in fruit/vegetable intake between genders. The higher fruit/vegetable intake found in older university students may be analyzed as a result of differences in the formation of eating habits in younger generations. In theory, this should consider the fact that they are more exposed to the eating pattern that predominates in modern society, which includes a larger amount of processed foods and high levels of fat and sugar, to the detriment of vegetable foods. Healthier eating habits at more advanced ages can also be associated with greater concern and health care and, consequently, older subjects may follow the instructions provided by health professionals in a more effective way.

The association between frequency of fruit/vegetable intake and marital status, housing type, and university course year found in the present study is in agreement with some findings from the literature (9,15-21). In this sense, possible causal mechanisms must be taken into consideration when seeking an explanation for this association, as is the case of knowledge about nutrition and motivation to adopt a healthy diet. In fact, marketing and educational nutrition interventions are actions that have proven highly effective in the search for a healthier diet (34).

Regarding excess body weight, in general, it could be observed that its occurrence was higher than identified in university students from middle income and emerging economy countries (11); however, lower than found in the United States (35) and similar to the rates reported in some European countries (19,20). The results indicate that excess body weight was more prevalent in men, coinciding with the findings from certain studies (19,20,35);

however, this diverges from other studies that show similarities between both sexes (11). In this case, the differences found among studies can probably be attributed to the variousl criteria used to define excess body weight, since there is no consensus regarding the use of only one criterion.

Another finding from the present study was the statistically significant and inverse association between frequency of exercise and fruit/vegetable intake, and excess body weight as identified in both sexes. It should be emphasized that both outcomes remained significantly associated, even after adjustments were made for control variables. In this case, the lower risk of exposure for the occurrence of excess body weight among those university students who most frequently perform exercise and consume fruits/vegetables is consistent with the evidence shown by other studies involving different experimental designs and statistical treatments (19).

Fruit/vegetable intake with an adequate frequency influences the occurrence of excess body weight through a specific effect on the greater proportion of complex carbohydrates and insoluble fibers found in plant foods, causing an increase in satiety and a reduction in the caloric support of food intake. Contrary to diets in which manufactured products and high levels of fat and sugar predominate, diets with a more frequent fruit/vegetable intake tend to show lower amounts of simple carbohydrates and fats, which is inversely associated with greater calorie intake, a known component of excess body weight (36).

Among the limitations of the study, it is noteworthy that the investigation method employed involves self-reported responses, thus allowing for possible memory biases or even biased statements towards the desirable. However, self-reporting is the current procedure in studies such as this one, as it is the most viable way to gather data in population-based surveys. Normally, certain procedures minimize this limitation, which are also adopted here: anonymous questionnaire, voluntary participation, filling out the questionnaire without the presence of the researchers, and the guarantee of the confidential nature of the information provided. Besides, the larger sample size allows for minimizing any inaccuracy of the calculated estimates in some way. Additionally, the cross-sectional approach to data does not allow inferences of causality in the associations due to the outcomes and the independent variables that can be modified having been identified simultaneously, increasing the risk of a reverse causality bias. Therefore, the identified associations should not be considered conclusive, and further longitudinal studies are needed to address this limitation, which are currently being conducted by the authors of this manuscript. Another limitation refers to the adequate fruit/vegetable intake being ≥ 5 servings/day, instead of being expressed in grams or size of portions consumed. Nonetheless, the measure of the frequency of food intake, without considering the size of portions, is very common in the international (18,21) and national literature (15-17).

The main strengths of the study relate to the concept, design, and conduct of the University Health Promoter project. The project meets a comprehensive cultural and geographic diversity, and provides robust and up-to-date data on exercise, fruit/vegetable intake, and weight status of university students from a representative state in southern Brazil, which allows for the generalization of its results to a larger population universe. Its findings may add new evidence to the scarce body of knowledge about the association of exercise and fruit/vegetable intake with weight status, considering that studies involving Brazilian university students and those from other regions in the world are rare. Since this population is composed of young adults, it is important to identify these associations and to invest heavily in the prevention and control of excess body weight. Regarding the methodology used, possible seasonal interferences in the reports of university students were minimized as data collection was carried out over a short period (three months) and within the same season of the year (spring), which, along with a minimum refusal rate to participate in the study, ensures more reliability to the findings.

CONCLUSIONS

The results found in this study mainly point to habits of exercise and fruit/vegetable intake that do not meet current recommendations. Approximately one third of the university students included in the sample showed excess body weight. Variations in the occurrence of excess body weight was inversely and significantly associated with a higher frequency of aerobic exercise and fruit/vegetable intake. In the case of strength exercises, lower chances of university students being categorized with excessive body weight occurred with a frequency of practice equivalent to 3-4 days/week. These findings indicate there is a need to promote initiatives aimed at the preparation and implementation of health education and promotion programs in the university context, through actions of guidance on exercise and food intake that can help to minimize the risks of onset and development of excess body weight.

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Nutrición Hospitalaria

Trabajo Original

Otros

The importance of knowing and listening to all those involved in the design and use of nutrition mobile apps. Getting to know the Great GApp

La importancia de conocer y escuchar a todos los implicados en el diseño y uso de las aplicaciones móviles de nutrición. Dando a conocer el Gran GApp

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Keywords:

mHealth. eHealth. Mobile applications. Health promotion. Healthy diet.

Abstract

Almost every country worldwide suffers from one or more types of malnutrition. Mobile technology (mHealth) interventions seem to represent a promising approach to this problem because they help share information about healthy eating patterns, offer motivation for behavioral change, etc. From this perspective we introduce a theoretical model that attempts to explain the gap that currently prevails between the elements involved in the development of nutritional mHealth strategies (which we have called the Great GApp). Evidence tells us that it is necessary to consider all the parts involved to ensure positive outcomes of an mHealth-based nutritional intervention: patients, health care providers, and stakeholders (technological companies). If these elements are not considered in the design of mHealth strategies a Great GApp arises, which may lead to lack of adherence to the proposed change, and decrease the potential for improving the quality of health outcomes.

Palabras clave:

mHealth. eHealth. Aplicaciones de móvil. Promoción de la salud. Dieta saludable.

Resumen

Casi todos los países del mundo sufren uno o más tipos de malnutrición. Las intervenciones con tecnología móvil (mHealth) parecen representar un enfoque prometedor para este problema porque son útiles para compartir información sobre patrones de alimentación saludable y ofrecer motivación para el cambio de comportamiento, entre otras posibilidades. Desde esta perspectiva, introducimos un modelo teórico que intenta explicar la brecha que prevalece actualmente entre los elementos que participan en el desarrollo de estrategias nutricionales de mHealth (que hemos denominado el Gran GApp). La evidencia nos dice que es necesario tener en cuenta a todos los interesados en el proceso para asegurar los resultados positivos de una intervención de nutrición basada en la mHealth: los pacientes, los proveedores de atención de la salud y las empresas tecnológicas. Si estos elementos no se tienen en cuenta en el diseño de las estrategias de mHealth, surge el Gran GApp, que puede conducir a falta de adherencia al cambio propuesto y disminuir el potencial de mejora de la calidad de los resultados en materia de salud.

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MALNUTRITION IS A SIGNIFICANT PROBLEM WORLDWIDE

Almost in every country worldwide people suffer from one or more malnutrition types, and facing this in all its forms may be considered the most significant global health challenge. Evidence has demonstrated that malnutrition (in the forms of wasting, stunting, overweight, or obesity) is globally the leading risk factor of sickness and death. It represents a significant problem for public health because it increases the risk of morbidity and mortality, from the wealthiest to the poorest countries, and represent a substantial burden from the medical, social, and economic points of view, harming families, communities, and states (1).

THE PROBLEM OF OVERWEIGHT AND OBESITY

On the one hand, obesity increases the risk of developing multiple chronic conditions, including cardiovascular disease, diabetes mellitus, etc., which leads to a decrease in quality of life and work productivity, and an increase in healthcare costs (2). In Europe, it is estimated that the total direct and indirect cost attributable to overweight and obesity was higher than 0.50 % of the Global Burden of Disease (3) in 2014. In the US, the health costs linked to obese individuals was US$149.4 billion per annum in the same period (4).

However, the worldwide prevalence of overweight and obesity has doubled since 1980 (2). In 2018, 1.9 billion adults suffered from overweight and 462 million from underweight. Furthermore, 52 million under-fives were wasted, 17 million severely wasted, and 155 million stunted, whereas 41 million infants were obese or overweight (5).

THE PROBLEM OF UNDERNOURISHMENT

On the other hand, wasting and stunting are the most important reasons for child mortality in developing countries, especially during the first five years of life (6). It is estimated that 6.3 million deaths in under-fives were preventable in 2013 (7) through nutritional programs. Besides, disease-related malnutrition is a significant public health problem in America, Europe, and Asia. It is related to higher morbidity (infections, suture dehiscence, delayed fracture healing, etc.), prolonged hospital stay, and increased readmission rates, mortality, and associated costs (8-11).

mHEALTH AND NUTRITIONAL MANAGEMENT

MOBILE TECHNOLOGY AS A GLOBAL SOLUTION FOR MALNUTRITION

Since malnutrition is due to an interaction between environmental, political, cultural, and socio-economic factors (1), several authors have evidenced the need for finding global solutions. These have to be based on effective theory-driven tools to help individuals manage their eating patterns (12) (and, obviously, on ensuring access to food resources).

In this sense, mobile technology interventions seem to represent a promising approach to this problem because they are useful for sharing healthy eating patterns and offering motivation for behavioral change while being scalable, low-cost, with high acceptance rates (5,12,14,15). Nowadays, these technologies are part of our daily lives, and their role in society has become crucial. Nobody doubts how technical improvements in mobile devices (with larger screens, higher resolution, increasing browsing speed, and development of mobile applications or "apps") have changed the way we live, work, and interact with others (15,16).

WHAT IS mHEALTH?

The term mHealth was first defined at the beginning of the 21st century (17). At the mHealth Summit 2010, organized by the Foundation for National Health Institutes, it was defined as "the delivery of health care services using mobile communication devices" (18). Today, mHealth is globally understood as medical practice and public health based on mobile devices (19). About 40 % of the more than 300,000 applications available on the market are related to health issues, with those for monitoring and managing chronic conditions deserving special mention (20). In other words, mHealth encompasses any strategy based on mobile devices (cell phones, PDAs, activity monitoring bands, etc.) to provide or facilitate health care. Many of the strategies included in mHealth, from simple phone calls or text messages to the use of applications to support clinical decision-making or telemedicine (20), have demonstrated high effectiveness in communication between patients and health professionals, in the adoption of healthy lifestyles, and in increasing adherence to treatments in chronic conditions (21,22).

For instance, a national survey in the US evidenced that 58.23 % of respondents had installed at least one health app in their phones, mainly focused on nutrition and physical activity. However, many had not used these apps, or had uninstalled them, due to lack of usability, interest, or time to introduce the necessary data, among other reasons (23). This high abandonment rate has been stated by other researchers (24,25). They have evidenced the importance of any public or private entities involved in the design and development of a health app considering every part connected in the mHealth strategy since the earliest stage. This approach may ensure that the designed app will demonstrate proper functionality, usability, safety, and capacity to solve and manage different pathologies in real settings (12,15,16).

INCONSISTENCIES IN THE APPLICATION OF mHEALTH STRATEGIES IN REAL SETTINGS

mHealth strategies have been demonstrated to be effective in various studies focused on dietary self-monitoring (26), long-term weight loss (27), managing of type 1 diabetes mellitus (28),

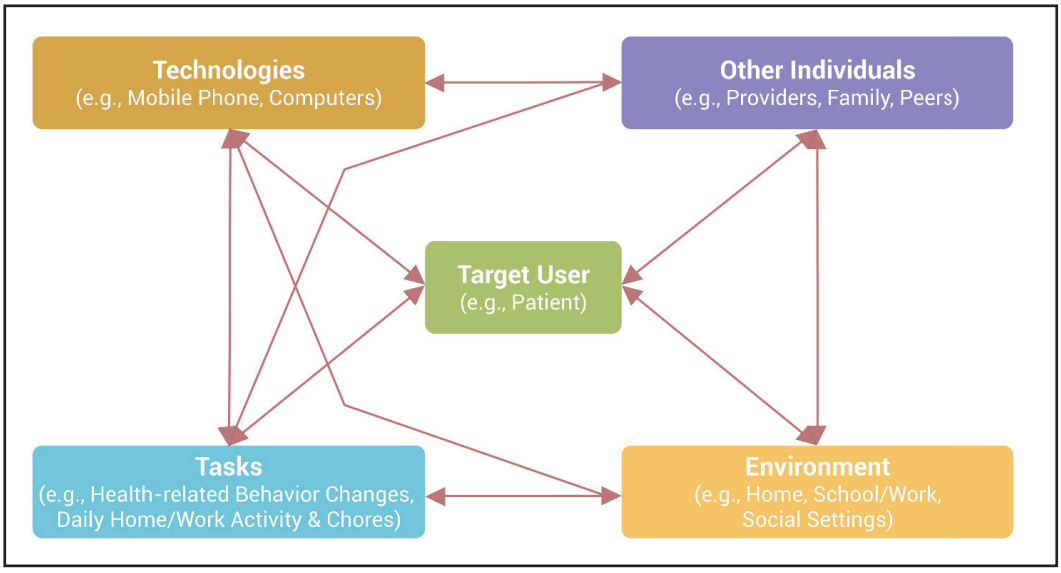

Figure 1.

Sociotechnical system demonstrating the relationship between stakeholders, processes, environments, and technologies (adapted from Graham et al. (43).

improving lipid profile markers in patients with metabolic syndrome (16), offering behavioral change in low- and middle-income countries (29), etc. In addition, it seems that some functionalities such as establishing weight-loss goals (30), self-monitoring (14), granting access to reliable information on healthy eating patterns (13), controlling enteral or parenteral nutrition for undernourishment prevention (31,32), and tracking energy intake (12) have a determinant role.

However, translating to the community setting successful dietary intervention experiences based on mHealth strategies that were effective in experimental studies (12-14,26-30) seems tremendously complicated (29). There are only a few experiences where an mHealth strategy has been evaluated at the population level (33,34). Meanwhile, most research and systematic reviews carried out to evaluate the efficacy of developed apps conclude that further investigations with larger sample sizes or longer interventions are needed (6,12,13,27-30,35-39). Also, most of the apps developed for each of these investigations, even though they showed positive results, are not available in the leading app stores.

On the other hand, we found that mobile nutrition applications on iTunes or PlayStore, with a higher number of downloads and better user ratings (12,26), lack efficacy studies and are often criticized by researchers for lacking a scientific basis to support their contents (12,13,16,40).

Therefore, from this perspective, we would like to introduce a theoretical model that attempts to explain the gap existing between the elements involved in the development of nutritional mHealth strategies. We have called it the Great GApp. However, before going any further into describing this model, it is necessary to have a proper understanding of the processes involved in developing a mobile health application.

DESIGN AND DEVELOPMENT OF A MOBILE HEALTH APPLICATION

The massive development of information and communication technologies has made it possible that any intervention we may wonder about can be implemented in a mobile application. In summary, it is stated that the process should be organized in five stages: i) conceptualization, ii) definition, iii) design, iv) development, and v) publication (41). According to Berlanga et al. (42): i) conceptualization implies generating an application idea considering the users' needs or problems; ii) the definition stage aims to specify the characteristics of users and the objective of the mobile application; iii) the design stage refers to the conceptual, content, and visual design of the app through prototyping; iv) the development stage focuses on programming the source code and performing user tests; and v) in the publication stage, after testing, the application is published in mobile application stores.

However, this approach involves several socio-cultural and technological relationships and interactions between the actors in each phase, which were defined in the model proposed by Graham et al. (43) (Fig. 1). Since the end-user is the focus of the mHealth intervention, it is essential that he/she be placed at the center of the process. That is, consideration must be given to how the designed app fits into the subject's day-to-day life. Furthermore, we must acknowledge that any patient interacts with other actors (health professionals, family, etc.) who directly affect their behavior and, therefore, the application's success. Besides, the user interacts with his or her environment, which may also exert negative or positive influences on adherence to a specific food pattern. The relationship of individuals with technology (including their mobile phones) can also modulate the success of a mHealth intervention.

Last but not least, it should be considered that the patient will be influenced by the number and difficulty of the tasks that are part of the proposed behavior change, and how these may interfere with other mundane aspects such as daily tasks at home or work (43).

This model can be extrapolated to the health professionals (30,43) involved in a mHealth-based intervention. They also need to interact with other individuals (patients, family members, etc.), technologies (e.g., databases with digital medical records), the environment (depending on where they use the technology for work), and tasks of varying complexity (text messages, writing notes, monitoring alarm symptoms or signs, etc.). Although it is unlikely that all potential relationships and interactions will occur in all mHealth experiences, taking them into account in the design and development phases of a mobile health application can remove barriers and increase engagement. Furthermore, there is evidence that attention to user needs through design leads to greater acceptance, understanding, adoption, and commitment rates regarding technology (25,43-46), and increases the potential for improving outcomes (47,48).

GETTING TO KNOW THE GREAT GApp

Therefore, to ensure the positive outcomes of a mHealth-based nutrition intervention it is necessary to take into consideration all stakeholders in the process (25,30,43,46): i) the people who will receive the service (e.g., patients); ii) those who provide it (e.g., health care providers); and iii) other stakeholders who may be affected by the service (technology companies). This approach is crucial because these stakeholders are committed to the service and therefore affect the intervention's scope and outcomes. It is also necessary to consider the legislation and regulatory policies of each region or country, as they may also influence how mobile health applications are designed and distributed. Regulatory frameworks and legislation provide assurances of safety and increase the mHealth instruments' credibility among patients and providers (49). For all these reasons, it is necessary to understand how all the parties involved interact, from their respective points of view, with each other in this technological process (50,51). If these elements are not considered in the design of mHealth strategies, what we have called the Great GApp may develop (Fig. 2).

Firstly, it is common for health care providers to attempt to develop mHealth-based interventions through the "digital translation" of conventional treatments or high scientific evidence papers (such as clinical practice guidelines), expecting the same results that those traditional interventions have shown (43). In other words, an application's content has a factual scientific basis and possibly responds to real needs that they have detected in real clinical settings. However, these apps may exhibit several deficiencies: these care providers usually do not have technology companies that guarantee adequate implementation and continuity over time (52), they do not have graphics and product designers that favor an adequate user experience (53), and in

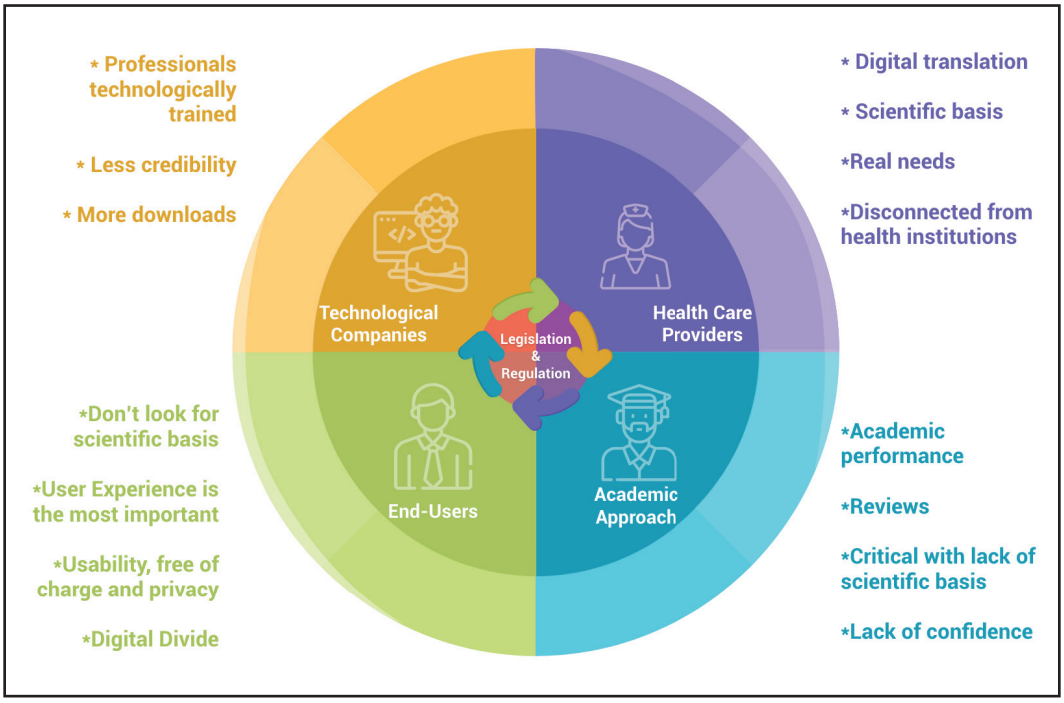

Figure 2.
The Great GApp.

some cases their attempts respond to personal initiatives that are disconnected from public or private health services. This fact makes it difficult for them to be integrated into regular clinical practice (54). In other cases, these public or private health services, without considering the professionals who will have to use these mobile applications, implement them, causing discomfort and poor adherence to using them (47).

A different component of the Great GApp is represented by health professionals who have an academic approach and who, far from seeking to modify clinical practice, focus on evaluating apps already published in application stores and on looking for academic performance (55,56). These researchers point out the lack of scientific basis and of usability of the available apps (13,39,40), or the risk of bias in RCTs carried out in small samples (6,15,16,26,28,37,38). In these cases, they may conclude that an app seems effective and that further research is needed with a larger sample size and longer interventions.

Technological companies are the executing component of the Great GApp. They have technologically trained personnel to design and develop health applications and implement their publication and maintenance in application stores. For this reason, the apps designed and developed by them guarantee that the user experience will be well valued (12,40). However, these applications have less credibility (especially on the part of health professionals, who could recommend them) because they do not usually specify either the scientific grounds they used to develop their content, the professionals who participated, or the scientific degree of evidence their proposals may have. However, these applications represent the most widely downloaded apps on nutrition and physical activity (39,40). Based on this situation, open innovation models have been proposed that allow professionals, users, and technology companies to work together (57).

Another component of the Great GApp, and one which represents the reason for the development of mHealth-based nutritional strategies, is the end user. End users do not usually look for scientific evidence or alignment with international recommendations by scientific societies. For the end user, functionalities and ease of use (especially in data entry), free-of-charge downloading, and to a lesser extent privacy are usually the most critical variables for selecting and using a health app (14,23, 25,30,39,40,45,48,51,52). Another relevant aspect that must be considered during the design phase of a mobile health app focused on the end user is the digital divide. This term refers to the differential rate of cell phone ownership associated with social, cultural, and economic indicators. It is more pronounced in low- and middle-income countries, and highlights the inequality that exists in access to technologies and subsequent technical services (58). Furthermore, this digital divide may also refer to the digital competencies of different generations, and their ability or preference to adhere to mHealth strategies (59). Some authors have proposed focus group sessions before the design and development of mobile health applications where aspects such as studying previous experiences in mHealth or the barriers to adopting this technology as a therapeutic strategy can be addressed (25).

The final component of the Great GApp that can be determinant in how mHealth strategies can reach populations is the legislation and regulatory framework of the region or country where the mHealth-based approach is developed (49). As shown in figure 2, the regulatory framework and legislation on health apps have been placed at the center of the conceptual model. Rather than being a key element in the development and implementation of mHealth apps, what stands out is its potential to influence the attitudes and behavior of all those involved, from the need to trust professionals for prescribing health apps to the reliability or safety perceived by end users. Moreover, traditional methods of evaluating medical devices to establish safety and efficacy are costly, time consuming, and assume that the approved device will not undergo significant changes in content or use (60). Although this framework could be useful for specific medical devices, it is not for applications that are continually being updated with new forms of navigation, functionalities, etc. This situation represents a challenge for clinical evaluation and for establishing the application's version and platform, mainly because the standards apply to the application and not to its associated device. Ultimately, it seems likely that traditional evaluation methods will only be appropriate for a small number of applications that run as traditional medical devices (wearables) and will become barriers to most software developments and innovations (60).

For these reasons, international and national organizations are permanently working on the development of accreditation and certification systems for mobile health applications (42). For instance, the Food and Drug Administration (FDA) has proposed a Policy for Device Software Functions and Mobile Medical Applications (61). The European Commission (EC), in 2015, published the Green Paper on mHealth as a consultation book for citizens, health professionals, public authorities, mobile device manufacturers, and other stakeholders on how to use mobile technology to improve health services in Europe (62). Following this consultation, EC encouraged industry stakeholders to draft and adhere to a code of conduct on mobile health apps, especially on their associated privacy issues. After several revisions, this code is still pending approval and is focused on: user consent, purpose limitation and data minimization, privacy by design and by default, data subject rights and information requirements, data retention, security measures, advertising in mHealth apps, use of personal data for secondary purposes, disclosing data to third parties for processing operations, data transfers, personal data breach, and data gathered from children (63). Once again, regulations move away from essential concepts such as usability, veracity of contents, or the app's effectiveness.

However, the Strategy for Quality and Safety in Mobile Health Applications of the *Junta de Andalucía* (Andalusian government) stands out in Spain at a national level. This initiative has elaborated a list of recommendations for the design, use, and evaluation of health apps, and a quality label called AppSaludable, which recognizes the quality and safety of health apps from public and private initiatives, both Spanish and international. The label ensures that an app complies with a series of recommendations on design and relevance, quality, security of information, service provision,

Table I. Some examples of mHealth strategy development evaluating whether they considered the Great GApp elements and their current availability

Paper	Year	Strategy or mobile application developed	Did the authors consider the elements included in the Great GApp?	Is it currently available in the Apps Stores or in use?	Searching sources
Active 10 - A new approach to increase physical activity in inactive people in England (33)	2019	Active 10 mobile application for Android	Yes	Yes	Play Store
FoodSwitch: a mobile phone app to enable consumers to make healthier food choices and crowdsourcing of National Food Composition Data (34)	2014	FoodSwitch mobile application for Android and iOS	Yes	Yes	Play Store App Store
User-centered design of a tablet waiting room tool for complex patients to prioritize discussion topics for primary care visits (50)	2016	Kaiser Permanente mobile application for Android and iOS (visit planner)	Yes	Yes	Play Store App Store
A smartphone app to promote an active lifestyle in lower-educated working young adults: development, usability, acceptability, and feasibility study (49)	2018	Active coach mobile application for Android	Partially (user-centered design)	No	Play Store
Integrating mobile technology with routine dietetic practice: the case of myPace for weight management (62)	2015	Developed specifically to be embedded into and to support dietetic practice, a platform called myPace (http://mypaceapp.com/)	No	No	http://mypaceapp.com/ Play Store App Store
User-centered design of Learn to Quit, a smoking cessation smartphone app for people with serious mental illness (48)	2018	Learn to Quit application for Android	Partially (experts, user-centered design)	No	Play Store
Push notifications from a mobile app to improve the body composition of overweight or obese women: a randomized controlled trial (14)	2020	Private mobile application for Android	No	No	Play Store App Store

confidentiality, and privacy (64). With the same objectives, the same initiative was launched in 2016 in Catalonia under the name TicSalut (65). It also offers a repository of health apps that have been approved after a quality accreditation process structured in four blocks: usability and design, functionality, technology, and security.

As we indicated above, when these five elements are not connected and involved in the whole process of developing a health app, adherence to the use of a mobile application and, consequently, its impact on health outcomes is reduced. However, different initiatives have tried to connect all the elements of this Great GApp with positive results. Examples include user-centered approaches (25), the Active10 program (33), the FoodSwitch (34) and myPace (66) mobile apps, the creation of The Yale Center for Biomedical Innovation and Technology (CBIT) (52), and cooperative development models based on Crowdsourcing (67) or Open Innovation (57). They all show approaches that allow involvement of all the actors connected, and therefore avoid the negative effect of the Great GApp (Table I).

CONCLUSIONS

This theoretical model, named the Great GApp, seems to contain and explain the main circumstances that usually occur during the design and development of mobile health applications. These circumstances lead to a disconnection between the elements involved in the implementation of mHealth strategies (end users, health professionals — whether in the clinical or academic field — and technological companies), which results in a gap between the scientific and healthcare settings, and the daily life of the subjects to whom these measures are eventually addressed. As a result, a limited efficiency of these measures is perceived (low effectiveness concerning the high cost that any technological

development usually entails). Taking into account this GApp, and trying to involve all the associated elements from the early stages of design and development of mobile health applications, could increase their success through greater use adherence and better health outcomes.

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Trabajo Original

Otros

Basal metabolic rate for high-performance female karate athletes

Tasa metabólica basal de deportistas de karate femenino de alto rendimiento

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Abstract

Introduction: karate is a millennial martial art, currently inserted in the context of Olympic Combat Sports. However, important scientific gaps still persist in monitoring high-performance athletes, including the basal metabolism measurement of female karate athletes.

Aim: to contribute to understanding the applicability of equations for predicting basal metabolic rate in this population.

Methods: this is a cross-sectional study with a retro-analytical component, in which data were obtained from the medical records of seven athletes participating in the project "Karate São Paulo Olímpico" (São Paulo Olympic Karate) (KSPO) during their nutrition counseling, including body composition and indirect calorimetry testing, with the aim of comparing these data to basal metabolic rate prediction equations.

Results: only one out of the five evaluated equations did not have a significant statistical difference relative to the value obtained by open-circuit indirect calorimetry.

Conclusion: in case basal metabolism cannot be measured through standard methodology (calorimetry), Cunningham's prediction equation (1980) would be appropriate to obtain total energy expenditure for high-performance female karate athletes.

Keywords:

Basal metabolism. Calorimetry. Martial arts. Energy metabolism. Sports nutrition sciences.

Resumen

Introducción: el karate es un antiguo arte marcial que actualmente encaja en el contexto de los deportes olímpicos de combate. Sin embargo, aún quedan importantes lagunas científicas para el seguimiento de los deportistas de alto rendimiento, una de las cuales es la determinación del metabolismo basal de las deportistas de karate.

Objetivo: contribuir al conocimiento de la aplicabilidad de las ecuaciones predictivas para obtener la tasa metabólica basal de esta población.

Métodos: el estudio se caracteriza por ser transversal con un componente retroanalítico, donde se obtuvieron los datos de siete atletas de la historia clínica de cuidado nutricional del proyecto Karate São Paulo Olímpico (KSPO), referidos a la composición corporal y el examen de calorimetría indirecta, con el propósito de compararlos con las ecuaciones predictivas de la tasa metabólica basal.

Resultados: solo una de las cinco ecuaciones evaluadas no mostró ninguna diferencia estadísticamente significativa con respecto al valor medido mediante calorimetría indirecta de circuito abierto.

Conclusión: sería conveniente, si no existe la posibilidad de obtener un metabolismo basal mediante la metodología de referencia (la calorimetría), utilizar la ecuación predictiva de Cunningham (1980) con el fin de obtener el gasto energético total de las deportistas karatecas de alto rendimiento.

Palabras clave:

Metabolismo basal. Calorimetría. Artes marciales. Metabolismo energético. Ciencias de la nutrición y el deporte.

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INTRODUCTION

Karate is a millennial martial art modified to become a modern sport; its potential to promote health, and physical and psychological well-being is well established (1). Currently, karate has received the classification of Olympic Combat Sport (OCS) for meeting modern Olympic competition practices, which involve aspects and concepts of contest (fair play), as well as performance measurement, scientific approach, result comparisons, and rules and standards coded and institutionalized with the aim of maximizing body performance, competitiveness, and spectacularization of body expression (2).

OCS, which include sports modalities like boxing, judo, taekwondo, and wrestling, represent 20 % to 25 % of the total medals disputed in Olympic Games (3), and this proportion should increase with the insertion of karate in the Olympic Games of 2021, in Japan. In an OCS such as karate athletes compete according to body weight divisions in order to promote sports equity in terms of body mass, and many use rapid weight loss procedures (2-10 % reduction in body mass during the week before the competition) to compete in lighter divisions and against smaller and weaker opponents. Therefore, most athletes train with a body mass greater than their competition division, and after the official weigh-in there is a rapid weight gain to compete, thus generating continuous changes in body mass (4). According to Reale et al. (5) "although some have called for the cessation of AWL altogether (6), another more pragmatic approach is to educate athletes about safer practices around AWL and recovery to reduce the potential health risks and performance decrements".

Resting metabolic rate (RMR) is defined as the minimal energy requirement to keep the vital functions of humans such as cardiovascular and respiratory system function, organic synthesis, cell membrane ion pumps, and body temperature (7). It is influenced by factors like age, sex, body composition, and physiological state (8).

The measurement of RMR is highly precise with direct and/or indirect calorimetry techniques for individuals subjected to a thermoneutral environment soon after waking up, in the postabsorptive state (10-12 h fasting), after a minimal rest of 30 min, during wakefulness, and in dorsal decubitus (9); the major difference between basal metabolic rate (BMR) and RMR is the period of resting and fasting before measurements (10). Since RMR cannot be routinely obtained through more accurate methods, such as calorimetry, the WHO proposed in 1985 the use of prediction equations to obtain this value, considering the importance of this parameter to calculate the daily energy requirements of the population at large. Those equations originated from a modification in the data bank of Schofield (11); however, studies in this area have indicated the presence of overestimated RMR values for different ethnic groups, especially for those living in the tropics (12,13). Such differences between populations were attributed to the large number of Italians in the original database (followed by other Europeans and Americans); individuals from regions of predominantly temperate climate; non-standardized calorimetry testing (pre-test fasting); differentiated body composition characteristics; and narrow age range, besides the presence of diverse Caucasian individuals (14).

Although direct or indirect calorimetry is the best methodology to obtain a RMR, it has limitations such as a high cost, need of pre-test standardization, and long evaluation time. As an alternative method, mathematical prediction equations for the basal metabolic activity of individuals employ data that can be more easily obtained during nutrition counseling, including age, height, sex, body mass, and body composition (lean mass). To estimate RMRs in both men and women, the more commonly used equations are those of Harris-Benedict (15), World Health Organization (9), and Cunningham (16). Although largely used, they were not developed for female athletic populations; for example, that of Harris-Benedict had over 200 participants included in its development but only 18 individuals classified as athletes and no women (8).

The American College of Sports Medicine (17), in its Note on Nutrition and Athletic Performance, encouraged the use of specific regression equations for the athletic population but recommended that a reasonable RMR estimate could be obtained with the equations suggested by Cunningham (16) or Harris-Benedict (15) by adopting an appropriate activity factor to estimate total energy expenditure (TEE). RMR represents 60 % to 80 % of TEE for sedentary individuals but may cover only 38 % to 47 % for endurance athletes (17).

The aim of the present study was to evaluate the difference and the impact of using different RMR metodological approaches, such as open-circuit indirect calorimetry, bioimpedance, and prediction equations, on the assessment of energy expenditure in high-performance female karate athletes, since this parameter is essential to health, weight control, and performance-directed diet prescription in this population.

MATERIAL AND METHODS

STUDY POPULATION AND SAMPLE

Data were collected from the Integrated Health Center of a university in São Paulo, Brazil. This Center has an area of around 2.8 thousand square meters with 47 rooms for medical appointments in 10 different health areas, and 5 of these rooms are separated for nutrition counseling of physically active individuals, from sportsmen to high-performance athletes.

This study is cross-sectional with a retro-analytical component; thus, data were obtained from medical records of athletes participating in the project —Karate São Paulo Olímpico— (São Paulo Olympic Karate) (KSPO), during their nutrition counseling. As inclusion criteria, the selected medical records were of high-performance athletes participating in the KSPO project of the —Federação Paulista de Karate— (Karate Federation of São Paulo State) (FPK), who had an appointment in the area of Nutrition in Sports and Physical Exercises with the aim of improving their performance, were within the age range 19-59 years, declared in the nutritional anamnesis to be phys-

Table I. Data of the anthropometric evaluation of high-performance karate athletes in the project "Karate São Paulo Olímpico" (São Paulo Olympic Karate) (KSPO) of "Federação Paulista de Karate" (Karate Federation of São Paulo State) (FPK)

Variable	Mean	SD	CV	Minimal	Maximal
Age (years)	21.7	3.0	14.0	19.0	27.0
Body mass (kg)	62.1	6.0	9.7	57.0	74.5
Height (m)	1.63	0.04	2.3	1.60	1.70
BMI (kg/m^2)	23.15	1.95	8.4	20.18	25.78
% Fat	23.1	2.7	11.7	20.1	26.8
FFM (kg)	47.8	5.6	11.6	43.8	59.5
FBM (kg)	14.3	1.7	11.8	12.1	16.0

SD: standard deviation; CV: coefficient of variation (standard deviation / mean) x 100; BMI: body mass index; FFM: fat-free mass; FBM: fat body mass.

ically active, and signed the appointment consent form at the Integrated Health Center.

The sample comprised seven high-performance female karate athletes participating in the modalities "kata" (moves) and "kumite" (fighting).

VARIABLES

Collected data included: birth date (years), body mass (kg) as obtained with a Filizola mechanical anthropometric scale (0.1 kg precision and 150 kg capacity), and height obtained with a stadiometer coupled to the aforementioned scale (1 mm precision and 2 m capacity), with athletes wearing minimal clothing and positioned in the Frankfurt plane for evaluation. Body mass index (BMI: kg/m^2) was calculated and nutritional status was classified according to the WHO (18). A bioimpedance test was carried out to obtain fat percentage, fat mass, lean mass, and RMR with a Biodynamics 310E device, at 50 khz, and with athletes positioned in horizontal dorsal decubitus, keeping arms and legs apart.

Open-circuit indirect calorimetry was conducted in a nutrition counseling room with low light, temperature between 24 and 26 ^{o}C, and 70-75 % relative humidity. The RMR of athletes lying in dorsal decubitus was measured with the calorimetry device MetaCheck (Koor®, Medical Technologies, Salt Lake City, Utah, USA). RMR was calculated by the mean of values found during 20-min continuous evaluation and by prediction equations, as shown in table III.

STATISTICAL ANALYSIS

Results were reported as sampling summaries of central tendency and variability. To detect statistical differences between

Table II. Values of resting metabolic rate (RMR) obtained by indirect calorimetry, bioimpedance, and prediction equations for female karate athletes

Variable	Mean	SD	CV	Min-Max	*p*
Resting metabolic rate measured by calorimetry					
kcal/24 h	1689.0	285.5	16.9	1263.0-2146.0	-
Resting metabolic rate measured by bioimpedance					
kcal/24 h	1440.0	173.8	12.1	1282.0-1809.0	0.03125
Resting metabolic rate measured by prediction equations					
FAO/WHO/UNU, 1985 (kcal/24 h)	1409.5	88.5	6.3	1333.9-1591.2	0.03125
Harris & Benedict, 1919 (kcal/24 h)	1448.6	54.4	3.8	1409.1-1555.5	0.04688
Cunninghan, 1980 (kcal/24 h)	1552.2	122.4	7.9	1463.0-1809.6	0.1563
Henry & Rees, 1991 (kcal/24 h)	1325.2	69.1	5.2	1266.2-1467.0	0.03125

Table III. Equations for predicting the resting metabolic rate (RMR) of high-performance female karate athletes

Reference	Equation
FAO/WHO/UNU, 1985 19-30 years	14.82 x body mass in kg + 486.6
Harris; Benedict, 1919	655.1 + (9.6 x body mass in kg) + (1.8 x height in cm) - (4.7 x age in years).
Cunningham, 1980	500 + 22 x (fat-free mass in kg)
Henry; Rees, 1991 18-30 years	[(0.048 x body mass in kg) + 2.562] x 239

BMR values for the different prediction equations a Friedman rank sum test was conducted, which established a significant difference ($p = 9.4 \times 10^{-6}$) among the six methods. After that, we used calorimetric results as our reference, and investigated pairwise differences with the other methods conducting a series of paired Wilcoxon rank sum tests. Except for the Cunningham equation, all the other methods showed significant differences when compared to calorimetric results. Table II gives the corresponding *p*-values. We used R (19) for the statistical analyses.

ETHICS

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Human Research Ethics Committee at a local institution under code number CAAE: 12867319.7.0000.5492.

RESULTS

The high-performance karate athletes of the KSPO project of FPK were, on average, 21.7 (3.0) years old, had a BMI of 23.15 (1.97) kg/m² and a fat percentage of 23.1 (2.7) %; thus, they were classified as eutrophic, according to WHO[15], showing a fat percentage within the average range for physically active individuals. The complementary anthropometric profile of these athletes is shown in table I.

The values shown in table II were obtained by open-circuit indirect calorimetry, bioimpedance, and RMR prediction equations.

The comparisons between the results obtained by indirect calorimetry and by equations are presented in figure 1, and show that only Cunningham's equation had no significant statistical difference ($p < 0.05$), and that RMR was underestimated by the different prediction equations.

DISCUSSION

The high-performance female athletes who took part in the present study had higher body mass values and fat percentages when compared to high-performance karate athletes in the project "São Paulo Olímpico" of FPK. On average, the latter were 21.2 (4.3) years old and had a weight of 56.0 (8.8) kg, height of 160.6 (0.1) mm, BMI of 21.63 (2.58) kg/m², and fat percentage of 18.6 (4.0) % (2). Such divergences can be attributed to differences in the body composition of these female athletes (weight category) or to the use of distinct evaluation methods, i. e., bioimpedance in the present study, compared to anthropometry.

An adequate energy balance must be kept for high-performance athletes to ensure appropriate weight and body composition during training cycles and/or the competition season; in addition, it is essential to optimize adaptations and recovery from training (20). RMR represents a significant fraction of TEE; one of the major components responsible for variation is fat-free mass, which may represent 20-30 % of daily energy expenditure (21), suggesting a difference between females and males, even in athletic populations (20,22).

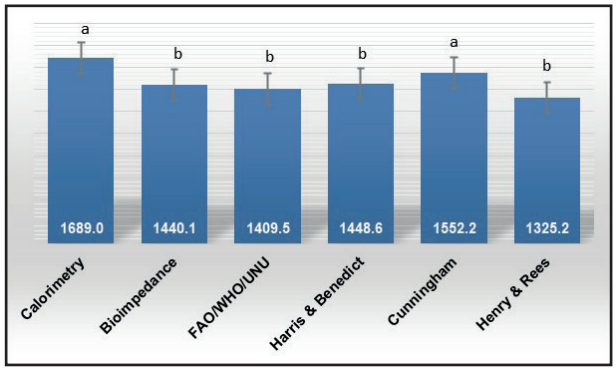

Figure 1.

Results obtained by open-circuit indirect calorimetry and other methodologies (bioimpedance and prediction equations). Statistical meaning: equal letters, without statistical difference ($p > 0.05$); different letters, with statistical difference ($p < 0.05$).

There are few studies in the setting of martial arts and in karate athletes assessing the impact of different prediction equations on RMR, and consequently on TEE. De Lorenzo and collaborators (23) developed seven general equations to calculate BMR, six of which significantly underestimated the values obtained by indirect calorimetry for water polo, judo, and karate athletes. Rossi and Tirapegui (24) investigated the impact of prediction equations on competitive university athletes and found a significant difference between BMR values as obtained with the FAO/WHO/UNU equation (9) and that proposed by Lorenzo et al (23), applicable to martial arts athletes. According to their results, there was a statistically significant difference of ~ 3 % (50.4 kcal), which had a minimal impact on the choice between equations considering applicability to male athletes.

The Harris-Benedict prediction equation (15), recommended by ACSM (17), remains one of the most commonly employed equations in nutritional prescription, although there is a significant amount of conflicting evidence regarding its validity for athletic (11,20,23,25) and female populations (26). On the other hand, Cunninghan's prediction equation (16), which is based on lean mass rather than body mass, has shown good results considering its validity and applicability to athletes (21,25). Cunningham's equation has already shown better accuracy for trained athletes of both sexes (21) and recreational athletes (25). However, Jagim and collaborators (20) demonstrated that this equation led to better RMR predictions for female athletes (several modalities of athletics, swimming, soccer, and tennis) than for male athletes (soccer, athletics, and baseball).

The present study was the first one to evaluate the impact of prediction equations on BMR, compared to open-circuit indirect calorimetry for high-performance female karate athletes. Results proved that although the equation by Cunningham and collaborators underestimates BMR values, it remains as an alternative

applicable to this population for assessing TEE differently from other equations and methods such as bioimpedance. Among the limitations of the study are a small sample size, the division by weight categories, and the limited number of equations available to estimate BMR in an athletic female population, which points to further investigation and studies on this topic.

CONCLUSION

Assessing total energy expenditure in high-performance athletes is important because energy consumption is essential to keep training, especially during intense periods, and reduced energy can lead to loss of physiological function, and increased risk of fatigue, disease and lesion, in addition to unsuccessful adaptation to prescribed training. There is evidence that, for predicting total energy consumption, RMR prediction equations may be inappropriate in athletic populations, but remain highly employed due to the limitations inherent in obtaining direct measures. This was the first study to report RMR evaluation by direct measurement for high-performance female karate athletes in comparison to the prediction equations more commonly employed in sports nutrition. Significant differences were found for the use of different equations, the most appropriate of which was that adopting the lean mass of athletes as a prediction component.

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ARÁN

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Trabajo Original

Otros

Triptófano como suplemento dietético y tratamiento de los sofocos, la astenia y el insomnio en el cáncer

L-tryptophan as dietetic supplement and treatment for hot flashes, astenia, and insomnia in cancer patients

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Resumen

Introducción: tanto en las mujeres con cáncer de mama y cáncer ginecológico como en los hombres con carcinoma prostático, los sofocos, la astenia y el insomnio son síntomas frecuentes y molestos que alteran la calidad de vida.

Objetivo: evaluar la eficacia del aporte de triptófano como tratamiento de los sofocos, la astenia y el insomnio en pacientes con cáncer de próstata, de mama y cervicouterino.

Materiales y métodos: estudio de intervención sin grupo de control en el Servicio de Oncología Radioterápica del HUCA, en el período de julio de 2018 a julio de 2019. Se incluyeron en total 60 pacientes con cáncer de próstata, de mama y cervicouterino que habían recibido tratamiento con radioterapia y hormonoterapia, y que presentaban sofocos, astenia e insomnio. Se administraron 3 g de L-triptófano al día.

Resultados: se reportan un aumento significativo del valor del triptófano sérico al final del estudio ($p < 0,001$) y una disminución significativa de las puntuaciones de los síntomas estudiados; aunque no hemos hallado ninguna significación estadística entre ellos, sí se aprecia una mejoría significativa de cada uno de los síntomas, así como una mejoría de la calidad de vida ($p < 0,001$).

Conclusiones: el estudio actual sugiere que, en los pacientes con cáncer de mama, de próstata o cervicouterino y síntomas de sofocos, astenia e insomnio, el aporte de triptófano como suplemento nutricional se tolera bien, mejora la calidad de vida y puede asociarse a una mejoría de los valores obtenidos en las escalas de los síntomas referidos, aunque no se demuestra ninguna relación estadísticamente significativa con la elevación del triptófano en sangre.

Palabras clave:

Sofocos. Astenia. Insomnio. Calidad de vida.

Abstract

Introduction: in women with breast cancer and gynecologic cancer, as well as in men with prostate carcinoma, hot flashes, asthenia, and insomnia are common and bothersome symptoms that impair quality of life.

Objective: to evaluate the effectiveness of tryptophan intake as a treatment for hot flushes, asthenia, and insomnia in patients with prostate, breast, and uterine cervical cancer.

Materials and methods: intervention study without a control group at the HUCA Radiation Oncology Service, from July 2018 to July 2019. A total of 60 patients with prostate, breast, or uterine cervical cancer who had received treatment with radiotherapy and hormone therapy, and who presented with hot flushes, asthenia, and insomnia were included. L-tryptophan was administered at a dose of 3 g per day.

Results: a significant increase in serum tryptophan levels at the end of the study ($p < 0.001$) and a significant decrease in the scores of the study symptoms were reported. Although statistical significance was not found, a significant improvement in each symptom was observed, as well as an improvement in quality of life ($p < 0.001$).

Conclusions: the study suggests that, in patients with breast, prostate, or uterine cervical cancer, and symptoms such as hot flushes, asthenia, and insomnia, the administration of tryptophan as a nutritional supplement is well tolerated, improves quality of life, and is associated with improvement in the scale scores of the symptoms of interest, although no statistically significant relationship with increased blood tryptophan levels was found.

Keywords:

Hot flushes. Asthenia. Insomnia. Quality of life.

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INTRODUCCIÓN

En los pacientes con patologías oncológicas como el cáncer de mama, el cáncer cervicouterino o el cáncer de próstata, el tratamiento sistémico o local condiciona una alteración hormonal que produce con gran frecuencia efectos secundarios, como sofocos, insomnio y astenia, que alteran de forma significativa la calidad de vida.

Los tratamientos actuales para estos síntomas en los pacientes con cáncer tienen sus limitaciones ya que las terapias farmacológicas están contraindicadas en los cánceres hormonodependientes (1), además de estar asociadas a efectos secundarios bastantes molestos. Por otro lado, las terapias alternativas y el abordaje psicoterapéutico carecen de ensayos clínicos controlados.

El mecanismo fisiológico de los sofocos no está del todo claro, aunque existen pruebas que muestran una reducción de los niveles de serotonina (2); de hecho, los inhibidores selectivos de la recaptación de serotonina son útiles para aliviar los síntomas vasomotores (3,4). También se relacionan con cambios en algunos neuroquímicos, como el estrógeno, la norepinefrina, el péptido relacionado con el gen de la calcitonina y la glucosa (5), y con la participación de alteraciones termorreguladoras.

En los pacientes con cáncer, el insomnio no ha recibido mucha atención a pesar de ser uno de los síntomas más comunes (6), que afecta al 40-60 % de los enfermos según varios autores (7). Savard y Morín afirman que más del 50 % de los pacientes oncológicos presentan problemas de sueño que perduran años después de finalizar el tratamiento (8), siendo este un problema crónico para los pacientes y las familias. Existe evidencia de que en la fisiopatología de diversas afecciones neurológicas que incluyen trastornos del sueño se ven involucradas anomalías en las acciones mediadas por la serotonina, la melatonina y el triptófano (9). Silber y Schmitt, en una revisión, sugieren que el triptófano podría mejorar los trastornos del sueño en los adultos, al aumentar la serotonina cerebral (10). Las pacientes con cáncer de mama son las que se asocian a un mayor nivel de insomnio, con una prevalencia entre el 38 % y el 61 % (11). Los síntomas vasomotores de la menopausia, como los sofocos, referidos por el 40-70 % de las supervivientes del cáncer de mama (12), pueden contribuir a la incidencia del insomnio.

Aunque no encontramos estudios donde se use el triptófano como tratamiento del insomnio en pacientes con cáncer, sí los hay para los trastornos del sueño de pacientes no oncológicos, a los que se han administrado dosis de entre 1 y 5 g al día (13-16), observándose un efecto significativo sobre el sueño en el tratamiento crónico del insomnio severo (13,14).

En los pacientes con cáncer, la astenia es uno de los síntomas con mayor prevalencia, de manera que el 95 % de los pacientes oncológicos que reciben tratamiento presentan astenia en mayor o menor grado (17). Al igual que en el caso de los sofocos, los mecanismos fisiopatológicos implicados en la aparición de la astenia relacionada con el cáncer no están completamente aclarados. Probablemente estén relacionados con una alteración de la regulación de varios sistemas y con la asociación de varios factores contribuyentes. Entre los mecanismos descritos se encuentran las alteraciones de la regulación de la serotonina, la disfunción del eje hipotalámico-hipofisario-adrenal, las alteraciones del ritmo circadiano y la alteración de la regulación de las citoquinas (18).

Como hemos comentado previamente, la vía serotoninérgica está involucrada de alguna manera en la aparición de los tres síntomas mencionados. Los bajos niveles de serotonina se han asociado a problemas del sueño, dolor, ansiedad, depresión, sofocos, estados agresivos y migrañas (19,20).

La serotonina ingerida por vía oral no se incorpora a las vías serotoninérgicas del sistema nervioso central ya que no cruza la barrera hematoencefálica. Sin embargo, el triptófano, que es un aminoácido esencial de la síntesis de proteínas y el precursor del neurotransmisor serotonina y de otros metabolitos, como la melatonina, la quinurenina y la niacina, sí puede cruzar la barrera hematoencefálica. Una vez en el sistema nervioso central (SNC) se convierte en 5-hidroxitriptófano (5-HTP) y luego se descarboxila en serotonina (21). Se ha observado que la reducción de los niveles de triptófano se correlaciona con una reducción de los niveles de serotonina (22).

El triptófano se obtiene de la dieta en cantidades suficientes para la síntesis de la serotonina y otros compuestos (23) y, dado que es un componente natural de la dieta, puede usarse sin complicaciones (24,25), teniendo una toxicidad baja, sin efectos adversos asociados (25-27).

El presente estudio se basa en la suplementación dietética con L-triptófano de pacientes con cáncer de próstata, de mama o cervicouterino con el objeto de mejorar la calidad de vida de los mismos al disminuir la frecuencia de los sofocos, el insomnio y la astenia. Después de una búsqueda bibliográfica exhaustiva por parte de nuestro grupo de trabajo, no se han encontrado estudios donde se analice el efecto del triptófano como tratamiento de los síntomas descritos en pacientes con cáncer.

MATERIALES Y MÉTODOS

Ensayo clínico abierto, sin grupo de control, realizado en el Servicio de Oncología Radioterápica del Hospital Universitario Central de Asturias en el período comprendido desde julio de 2018 hasta julio de 2019. Tanto el proyecto de investigación como la hoja de consentimiento informado fueron aprobados por el Comité de Ética de la Investigación del Principado de Asturias.

Se calculó que el tamaño muestral sería de 60 pacientes, considerando un nivel de confianza del 95 %, una potencia del 80 %, una diferencia de medias a detectar de 8 y una desviación estándar, con respecto a la diferencia obtenida de un estudio piloto previo, de 20 pacientes, el número de pares mínimo, considerando un posible ajuste de las pérdidas del 15 %. Este cálculo se llevó a cabo con el programa Epidat, versión 4.2.

Los sujetos fueron entrevistados por primera vez por el autor, quien determinó si cumplían los criterios de selección. Los participantes del estudio se reclutaron de acuerdo con los siguientes criterios de inclusión:

- Mayores de 18 años.
- Con diagnóstico de cáncer de próstata, de mama o cervicouterino.

- Habiendo recibido tratamiento oncológico con radioterapia y/o hormonoterapia.
- Que presentasen sofocos, astenia e insomnio.
- Valores de triptófano en sangre por debajo de la media del rango de referencia.

Los criterios de exclusión fueron**:**

- Que estuvieran recibiendo tratamiento con antidepresivos que afectaran al metabolismo de la serotonina.
- Que estuviesen tomando algún suplemento o tratamiento para los sofocos, la astenia y el insomnio.
- Que no estuviesen dispuestos a participar y no firmasen el consentimiento informado.
- Que no tuvieran la capacidad de cumplir las pautas.

Como criterios de retirada del estudio se consideraron los valores de triptófano en sangre > 95 ng/ml durante el seguimiento.

Se recogieron los datos de los pacientes (edad, sexo, patología). A todos los sujetos incluidos en el estudio se les administró L-triptófano: 1 sobre de 3 g al día durante 4 meses como mínimo. Debido a que no se han encontrado en la literatura estudios donde se utilice el L-triptófano en pacientes con cáncer, la intervención y su dosis se basaron en los hallazgos de estudios previos acerca de la dosis de triptófano en otros escenarios clínicos, como en el tratamiento de los trastornos del sueño, usando como referencia los estudios con dosis de entre 1 y 5 g/día (14-17). El suplemento fue proporcionado por el laboratorio Nutrición Médica.

Se realizaron las siguientes evaluaciones: analítica de sangre del triptófano libre en el momento basal y, luego, mensualmente durante 3 meses consecutivos. El valor de referencia del triptófano en sangre utilizado fue de 30-95 ng/ml. Las muestras de sangre periférica se obtuvieron mediante técnicas estándar de venopunción, en tubos Vaccutainer que contenían EDTA.K3 como anticoagulante. Después de la centrifugación se desproteinizó una alícuota de 400 µL de las muestras de plasma sanguíneo con ácido sulfosalicílico, después de añadir 100 µL de n-Leu como patrón interno. Se utilizó un analizador de aminoácidos Biochrom (Biochrom Ltd, Cambridge, Reino Unido) en el laboratorio de bioquímica clínica del HUCA para separar los aminoácidos libres presentes en la muestra. El control del plasma ClinCheck para aminoácidos (de Recipe Chemicals + Instruments GmbH, Múnich, Alemania) también se procesó en cada ejecución, como material de control de calidad interno, certificado según la norma ISO 13485, para verificar el rendimiento del análisis.

Se aplicaron cuestionarios para cada síntoma tanto al inicio como al final del estudio. Los sofocos se midieron mediante el cuestionario del estudio ESCAPA. Este cuestionario, que recoge 4 dimensiones —síntomas, temporalidad, estado de ánimo y actividad diaria—analiza además por separado el impacto de los sofocos en la vida diaria (pregunta 19) (28). La astenia se midió mediante el cuestionario Perform, que mide las percepciones de la astenia de los pacientes oncológicos, en su versión adaptada para la población española, que contiene 12 ítems distribuidos en 3 dimensiones: actividades habituales (4 ítems), actitudes y creencias (4 ítems), y limitaciones físicas (4 ítems); en su diseño, las puntuaciones altas conllevan mejores resultados (29). Para el insomnio se empleó el cuestionario ISI 81, que mide el índice de gravedad del insomnio a través de la percepción del propio paciente. Este cuestionario consta de 7 ítems que miden las dificultades para conciliar el sueño, las dificultades para mantener el sueño y despertar por la mañana, la satisfacción con el sueño actual, la interferencia con el funcionamiento diario, la perceptibilidad del deterioro atribuido al problema del sueño y el grado de angustia o cansancio causado por el problema del sueño (30-32). Para evaluar la calidad de vida se aplicó el cuestionario WHOQOL-BREF validado en España, que se centra en la calidad de vida percibida por el paciente y ofrece una puntuación global de la calidad de vida y puntuaciones de las áreas y las facetas que la componen. Consta de 26 ítems que evalúan 4 dimensiones: salud física, salud psicológica, relaciones sociales y ambiente. Las puntuaciones más altas indican una mejor calidad de vida (33-35).

Se evaluaron los posibles efectos adversos haciendo preguntas abiertas a los participantes: por ejemplo, "¿Ha tenido algún problema o efecto secundario desde que toma el suplemento de L-triptófano (como síntomas gastrointestinales o cualquier otro problema)?".

ANÁLISIS ESTADÍSTICO

Se realizó un análisis descriptivo de cada variable recogida, proporcionando medidas de posición y medidas de dispersión para las variables de tipo cuantitativo, y distribuciones de frecuencias absolutas y relativas para las de tipo cualitativo.

Se valoraron los cambios entre el inicio y el final del tratamiento a través del test de la t de Student para muestras relacionadas —previa comprobación de la hipótesis de normalidad— cuando las variables estudiadas eran cuantitativas, y con el test de Madansky cuando eran cualitativas.

Se estudiaron las correlaciones entre variables cuantitativas a través del coeficiente y el test de correlación de Spearman en caso de incumplimiento de la hipótesis de normalidad.

El nivel de significación empleado fue de 0,05.

El análisis estadístico se efectuó mediante el programa R (R DevelopmentCoreTeam), versión 3.4.4 (36).

RESULTADOS

Se incluyen en el estudio 60 pacientes, 37 (61,6 %) hombres y 23 (38,3 %) mujeres. Se obtiene la siguiente distribución de frecuencias por patología: cáncer de próstata 36 (60 %), cáncer de mama 13 (21,6 %), cáncer cervicouterino 11 (18,3 %). La edad media fue en los hombres de 70,8 (8,1) años y en las mujeres de 49,8 (6,8) años.

Se evaluó la elegibilidad de un total de 60 individuos y se excluyeron 3, de los cuales uno abandonó el estudio voluntariamente y 2 presentaron concentraciones de triptófano por encima de los valores normales (> 95 ng/ml) en las analíticas de seguimiento, por lo que fueron retirados del estudio. En total, 57 participantes completaron el estudio.

Al analizar los valores sanguíneos de triptófano observamos que todos los pacientes al inicio del estudio tenían niveles hemá-

Tabla I. Evaluación del cambio de los síntomas en la visita final frente a la basal

Síntomas	Inicio	Final	Valor p
Astenia	39,2 (18,3)	49,1 (10,8)	< 0,001
Insomnio	16,1 (7,4)	7,3 (3,7)	< 0,001
Síntomas	80,1 (16,8)	38,8 (15,4)	< 0,001
Temporalidad	84,3 (15,8)	36,9 (13,7)	< 0,001
Estado de ánimo	66,0 (18,6)	34,2 (11,4)	< 0,001
Actividad diaria	65,4 (17,4)	32,5 (10,1)	< 0,001

Media (DE).

ticos de triptófano bajos o en el límite bajo de la normalidad (valor de referencia: 30-95 ng/ml), produciéndose un aumento significativo de estos niveles durante el estudio, con una media final de 67,0 ± 15,4 en comparación con el valor basal 36,5 ± 11,9 ($p < 0,001$), sin registrarse efectos secundarios asociados a la ingesta de 3 g de L-triptófano.

En relación con los sofocos, en el análisis de las cuatro dimensiones del cuestionario ESCAPA se muestra una mejoría significativa de todas ellas, con una disminución de la media final con respecto a la basal (Tabla I).

Analizando la pregunta 19 del cuestionario se objetiva que el 80 % de los pacientes presentaban al inicio una afectación de la vida diaria moderada o muy alta, disminuyendo dicha percepción al 0 %, con un valor de $p < 0,001$ (Fig. 1).

Con respecto al cuestionario ISI81 para el insomnio, se observó una mejoría clínica de este síntoma, objetivándose que, de 60 pacientes, 40 (66,7 %) presentaban insomnio moderado o grave al inicio del estudio y solo un paciente (1,7 %) presentó insomnio moderado al final del mismo, siendo esta diferencia estadísticamente significativa ($p < 0,001$) (Tabla I).

Del insomnio, en general, se puede decir que la puntuación media disminuyó a 7,3 ± 3,7 con respecto a la media registrada al inicio del estudio (16,1 ± 7,4; $p < 0,001$) (Tabla II).

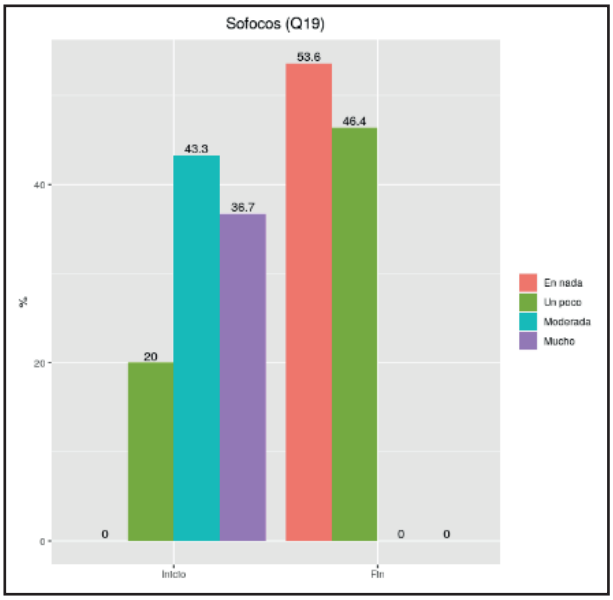

Figura 1.

Comparación de las respuestas del cuestionario de sofocos (Q19). ¿Hasta qué punto cree que los sofocos afectan a su vida diaria?

Para la astenia, al analizar los resultados del cuestionario PERFOM se objetivó una mejoría de este síntoma cuando se compararon los resultados del cuestionario final con los del inicial, con una variación significativa en el aumento de la media final, de 49,1 ± 10,8, con respecto a la inicial, de 39,2 ± 18,3 ($p < 0,001$) (Tabla I).

Se comparó la diferencia de cada síntoma entre el momento basal y el final con la diferencia hallada en los valores de triptófano entre la visita final y la basal, no hallándose diferencias significativas (Tabla III).

Al analizar la influencia del comportamiento de los síntomas estudiados al inicio del estudio en relación con la variable pato-

Tabla II. Comparación de las sumas de todos los ítems del cuestionario de insomnio

Insomnio	Ausencia n (%)	Subclínico n (%)	Moderado n (%)	Grave n (%)	Total n
Inicio	8 (14,04)	9 (15,79)	27 (47,37)	13 (22,81)	57
Final	26 (45,61)	30 (52,63)	1 (1,75)	0 (0,00)	57

Tabla III. Relación del triptófano con los síntomas (astenia, insomnio y sofocos)

Síntomas - Analítica según visitas	R	Valor p
Astenia final *vs.* inicial – Analítica de visita 3 *vs.* basal	0,051	0,707
Insomnio final *vs.* inicial – Analítica de visita 3 *vs.* basal	-0,185	0,168
Síntomas finales *vs.* iniciales – Analítica de visita 3 *vs.* basal	-0,050	0,713
Temporalidad final *vs.* inicial – Analítica de visita3 *vs.* basal	-0,047	0,726
Estado de ánimo final *vs.* inicial – Analítica de visita 3 *vs.* basal	0,062	0,646
Actividad diaria final *vs.* inicial – Analítica de visita 3 *vs.* basal	0,170	0,207

Tabla IV. Relación entre la evolución de los síntomas estudiados (astenia, insomnio y sofocos) y la patología

Variable	Mamaria	Prostática	Cervicouterina	Valor p
Astenia	29,85 (15,38)	43,97 (18,30)	34,91 (17,50)	0,074
Insomnio	19,46 (2,96)	14,29 (8,35)	18,10 (6,98)	0,098
Síntomas	77,40 (12,64)	79,86 (17,94)	84,09 (17,98)	0,469
Temporalidad	87,18 (14,28)	81,71 (16,41)	89,39 (15,41)	0,289
Estado de ánimo	66,92 (18,32)	62,36 (17,95)	76,82 (18,74)	0,077
Actividad diaria	62,82 (18,36)	65,28 (16,18)	69,32 (21,19)	0,352

Tabla V. Comparación entre el inicio y el final del cuestionario de calidad de vida WHOQOL-BREF

Dominios	Inicio	Final	Valor p
Salud física	11,0 (2,2)	15,9 (1,7)	< 0,001
Salud psicológica	8,9 (1,8)	14,5 (2,1)	< 0,001
Relaciones sociales	7,3 (2,2)	13,7 (1,9)	< 0,001
Ambiente	9,8 (1,8)	14,2 (1,1)	< 0,001

Media (DE).

logía, no se obtuvo la significación estadística en ninguno de los casos (Tabla IV).

Las puntuaciones brutas obtenidas en la escala WHOQO-BREF se convirtieron a puntaciones transformadas (rango: 0-20), siguiendo las indicaciones del manual del WHOQOL-BREF, con el objetivo de permitir comparaciones entre las subescalas. Tal y como se refleja en la tabla V, el dominio de la salud física es el que registra un mayor nivel de satisfacción con la vida. Por el contrario, el nivel más bajo se obtuvo en el dominio de las relaciones sociales, resultando estas diferencias estadísticamente significativas ($p < 0,001$).

Respecto a la calidad de vida evaluada con el cuestionario WHOQOL-BREF, esta mejoró durante el desarrollo del estudio, objetivándose que existe una mejoría significativa de la calidad de vida al final del estudio ($p < 0,001$) (Tabla V, Fig. 2). Este hecho se reflejó en la disminución progresiva de las puntuaciones obtenidas en las 4 dimensiones estudiadas (salud física, salud psicológica, relaciones sociales y ambiente).

DISCUSIÓN

En nuestro estudio se pone de manifiesto que la administración de 3 gramos de L-triptófano como suplemento nutricional a pacientes con cáncer de próstata, de mama o cervicouterino, que habían recibido tratamiento con radioterapia y/o hormonoterapia, se asocia a una elevación del nivel de triptófano en sangre y a una mejoría de los valores de las escalas de sofocos, astenia e insomnio. Aunque no hemos hallado ninguna relación estadísticamente significativa entre la elevación de los niveles de triptófano en sangre y el conjunto de los síntomas estudiados, sí se aprecia una mejoría significativa de cada uno de ellos; esto podría estar relacionado con el pequeño tamaño muestral y con otros posibles factores no recogidos en este estudio.

No encontramos estudios científicos con iguales intereses que los propuestos en esta investigación, dirigida a describir el comportamiento de los síntomas asociados a las neoplasias de mama, de próstata y cervicouterinas (sofocos, astenia, insomnio) en relación con la administración de triptófano a dosis de 1 sobre de 3 g al día durante 4 meses mínimo, siendo difícil para los autores establecer diferencias con otras investigaciones médicas similares. Por ello se amplió el abanico de comparación con otros estudios que habían incluido la administración de L- triptófano a pacientes no afectados de cáncer, pero que sí presentaban alguno de los síntomas que se monitorizaron en el actual estudio.

Nosotros observamos que todos los pacientes tenían inicialmente niveles bajos de triptófano libre en la sangre, lo que podría explicarse por un desequilibrio nutricional causado por la enfermedad de base y por los tratamientos oncológicos recibidos, que conllevarían una ingesta deficiente de triptófano, puesto que este aminoácido no puede ser sintetizado directamente por el ser humano. De forma clara y significativa, observamos que el aporte de 3 g/día de L-triptófano produce un aumento de los niveles de este aminoácido en sangre.

En cuanto a los efectos observados, la mayor modificación se aprecia en los sofocos, seguidos del insomnio y la astenia, demostrándose que el uso de 3 g de L-triptófano podría tener la capacidad de disminuir estos síntomas en los pacientes con cáncer.

La mejoría significativa de los sofocos obtenida en nuestra serie podría explicarse por un aumento del nivel de serotonina a nivel cerebral, ya que la concentración de este neurotransmisor es directamente proporcional a la concentración de triptófano en el plasma. Se ha demostrado que el uso de antidepresivos mejora los síntomas de sofocos en las mujeres con cáncer de mama, pero aumenta el riesgo de cáncer de mama (37-39). La suplementación de L-triptófano tendría la capacidad de aumentar la cantidad de serotonina disponible, produciendo un efecto similar a los ISRS sin los posibles inconvenientes asociados. Aunque Freedman (40) no demostró la mejoría de los sofocos en mujeres posmenopáusicas al administrar 150 mg/día de 5-HTP, esto pudo deberse a que dicha dosis está en el extremo inferior del rango terapéutico, además de no recoger ni los niveles basales ni los finales de triptófano en la sangre.

La utilización del triptófano para los desórdenes del sueño se ha estudiado ampliamente. Spinweber observó que la adminis-

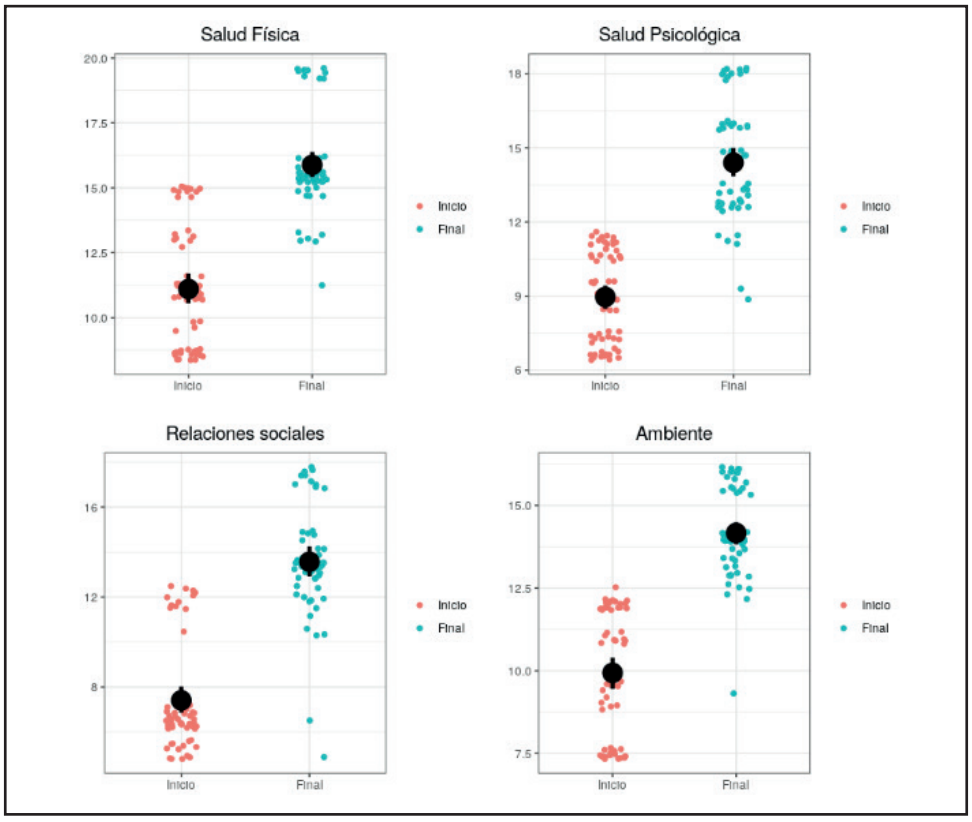

Figura 2.

Comparación entre el inicio y el final del cuestionario de calidad de vida WHOQOL-BREF.

tración de 3 g de L-triptófano había producido un descenso de la latencia de sueño (13). Hajak G., administrando triptófano en un rango de 1-5 g, reportó una acción significativa sobre el sueño al aumentar los niveles de melatonina en el plasma (14). Por su parte, Huether y cols. se cercioraron de que, tras una infusión de L-triptófano, aparece dependencia en relación con los niveles plasmáticos tanto de triptófano como de melatonina (16). Nuestros resultados también demuestran una mejoría del insomnio con el aporte de 3 g de triptófano pero, a diferencia de otros autores, nuestra muestra solo incluye pacientes con cáncer.

En nuestra serie también obtuvimos una mejoría significativa de la astenia, lo cual puede explicarse por el aumento del triptófano en sangre, ya que uno de los posibles mecanismos responsables de la astenia de los pacientes con cáncer es la alteración de los niveles de serotonina a nivel cerebral, debido a la actividad de citoquinas proinflamatorias como la interleuquina 1β (IL-1β), el interferón alfa (IFN-α), el IFN-γ y el TNF-α, producidas por la propia enfermedad y que alteran el metabolismo del 5-HT (18).

En relación con la calidad de vida evaluada con el cuestionario WHOQOL-BREF, se observa una mejoría significativa al final del estudio tanto de la salud física y psicológica como de las relaciones sociales y ambientales, y esto es de gran importancia en los pacientes oncológicos.

Los resultados de este estudio indicaron que administrar triptófano como suplemento nutricional durante 4 meses no produce ningún efecto adverso, por lo que el triptófano parece ser seguro y tolerarse bien.

La presente investigación está claramente limitada al tratarse de un ensayo clínico abierto, sin grupo de control y con un tamaño muestral pequeño, que se agrava por la heterogeneidad de las tres patologías tumorales estudiadas, que condicionan tres submuestras con un "n" muy bajo para alguna de ellas. Además, la muestra corresponde a un único centro y una única región, por lo que no podemos excluir que existan características locales que hayan influido en los resultados. Esto hace necesaria una investigación multicéntrica para confirmar los hallazgos, que por lo tanto deben considerarse de naturaleza preliminar.

CONCLUSIÓN

El estudio actual sugiere que en los pacientes con cáncer de mama, de próstata o cervicouterino, y síntomas de sofocos, astenia e insomnio, el aporte de triptófano como suplemento nutricional se tolera bien, mejora la calidad de vida y puede asociarse a una mejoría de los valores de las escalas de los síntomas referidos, aunque no demuestra que exista una relación estadísticamente significativa con la elevación del triptófano en la sangre. Por ello, este estudio se debe considerar preliminar y se deberán realizar otros ensayos controlados.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Otros

A standardized, integral nutritional intervention and physical activity program reduces body weight in women newly diagnosed with breast cancer

Un programa integral estandarizado de intervención nutricional y actividad física reduce el peso corporal en mujeres recién diagnosticadas de cáncer de mama

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Abstract

Introduction: breast cancer is the most common invasive cancer among women in developed countries. At diagnosis, approximately 70 % of women are overweight, and the additional weight gain that can result from the ensuing treatments has been associated with cancer recurrence and progression.

Objectives: the main objective was to compare the effect of only a nutritional intervention (CG) with a nutrition education program (nutritional intervention, nutrition education, and physical activity) (IG) for 1 year.

Methods: a total of 65 women with breast cancer who had been evaluated at the Clinical Nutrition Department, La Paz University Hospital, Madrid, Spain were recruited into 2 groups: a control group (CG) and an intervention group (IG).

Results: the IG showed a significant reduction in body weight (-1.87 ± 3.41 vs. 1.48 ± 2.01 kg, $p < 0.05$), BMI (-0.61 ± 1.40 vs. 0.65 ± 0.88 kg/m^2, $p < 0.05$), total cholesterol (-32.92 ± 38.45 vs. -3.23 ± 39.73 mg/dl, $p < 0.05$), and low-density lipoprotein cholesterol (-35.29 ± 27.50 vs. 6.33 ± 40.70 mg/dl, $p < 0.05$). Both groups were shown to be more conscious of the importance of physical activity, with increased consumption of grains, fruits, oily fish, and dairy.

Conclusions: dietary interventions and physical activity were shown to be important to achieving several physical and physiological benefits that could reduce some risk factors associated with breast cancer recurrence and progression.

Keywords:

Breast cancer. Nutrition. Physical activity.

Resumen

Introducción: el cáncer de mama es el cáncer invasivo más común entre las mujeres de los países desarrollados. En el momento del diagnóstico, aproximadamente el 70 % de las mujeres tienen sobrepeso, y el aumento de peso adicional que puede resultar de los tratamientos subsiguientes se ha asociado con la recurrencia y progresión de la enfermedad.

Objetivos: el objetivo principal del estudio fue comparar el efecto de solo una intervención nutricional (GC) con un programa integral de educación nutricional (intervención y educación nutricional y actividad física) (IG) durante 1 año.

Métodos: un total de 65 mujeres con cáncer de mama previamente evaluadas en la Unidad de Nutrición Clínica y Dietética del Hospital Universitario La Paz, Madrid, España, fueron reclutadas y divididas en 2 grupos: grupo de control (GC) y grupo de intervención (GI).

Resultados: el GI mostró una reducción significativa del peso corporal (-1,87 ± 3,41 *vs.* 1,48 ± 2,01 kg, p < 0,05), IMC (-0,61 ± 1,40 *vs.* 0,65 ± 0,88 kg/m^2, p < 0,05), colesterol total (-32,92 ± 38,45 *vs.* -3,23 ± 39,73 mg/dl, p < 0,05) y colesterol unido a lipoproteínas de baja densidad (LDL) (-35,29 ± 27,50 *vs.* 6,33 ± 40,70 mg/dl, p < 0,05). Al finalizar el estudio, ambos grupos fueron más conscientes de la importancia de la actividad física y demostraron consumir una cantidad más elevada de cereales, frutas, pescado azul y lácteos.

Conclusiones: las intervenciones dietéticas junto con la práctica de actividad física son importantes para lograr beneficios físicos y fisiológicos que podrían reducir algunos factores de riesgo asociados con la recurrencia y progresión del cáncer de mama.

Palabras clave:

Cáncer de mama. Nutrición. Actividad física.

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INTRODUCTION

Over the last decade, our diet and lifestyle have changed in relation to economic development. In terms of health, nutritional status, eating patterns, and physical activity, this evolution has been negative. As a consequence, there has been a significant increase in chronic noncommunicable diseases and obesity, the prevalence of which has increased and continues to increase at alarming levels in our society (1). According to Keaver et al., overweight and obesity will reach levels of 89 % and 85 % in males and females, respectively, by 2030 (2). In Spain, the most recent data on the prevalence of obesity correspond to the ENPE study, which found an average prevalence of 21.6 % among adults aged 25 to 64 years (22.8 % in men and 20.5 % in women) (3). Obesity substantially increases the risk of diabetes, cardiovascular disease from increased blood pressure and altered blood lipid profile (4,5), certain types of cancer (colorectal, breast, endometrial, renal, esophageal, and pancreatic) (6), and other diseases. Also, as body mass index (BMI) increases (especially when it is ≥ 30 kg/m^2) the relative risk of mortality gradually increases. Obesity has been associated with poorer quality of life, a greater frequency of disability and health services use, and higher economic costs (7).

Breast cancer is the most frequent malignant neoplasm in women worldwide, and is the type of tumor that causes the highest number of deaths in Spain. It accounts for 18.2 % of cancer deaths in women and is the leading cause of death in women between 40 and 55 years. Its incidence is increasing, especially in developed countries, in which 50 % of all cases of breast cancer occur (8). Although the incidence has increased, the mortality rate has remained stable in recent years, a benefit attributed to early detection programs and advances in systemic treatment. One in every 10 women will develop breast cancer at some point in her life. Standardized average survival according to age in Europe is 93 % at 1 year and 73 % at 5 years (9). In Spain, breast cancer has a 5-year survival rate of more than 90 % (10).

Obesity and breast cancer are related: the treatment breast cancer entails is associated with a greater probability of weight gain and the development of overweight and obesity, and the presence of obesity has been associated with poorer breast cancer outcomes. The etiology of weight gain associated with the treatment of breast cancer may be partly explained by a decrease in physical activity resulting from increased feelings of fatigue. This reduction can reach up to 50 % of the usual activity of these women (11). In a study conducted by Lynch et al., patients with breast cancer spent most of the day in sedentary or low-intensity activities (12). However, physical activity has been associated with a protective effect on the development of breast cancer and its recurrence due to its influence on hormone levels, insulin resistance, and hyperinsulinemia (13-15).

Although there are not sufficient data to confirm the role of estrogen metabolites as predictors of breast cancer, a reduction in the circulating levels of primary estrogens may lower the risk of breast cancer in postmenopausal women. During menopause, however, these estrogens are reduced, leading to increased estrogen metabolism from adipose tissue and skin; thus, increased estrogen is directly related to an increase in fatty tissue (16). In addition, various studies have found an association between weight gain and a poorer evolution of breast cancer or its recurrence. This situation could be explained by the inflammatory and hormonal changes that obesity produces, which could favor the growth of tumor-related hormones such as estrogens, androgens, insulin, leptin, etc., as well as the oxidative stress linked to this disease (17,18). Pan et al., in a recent review, found that women with breast cancer and obesity who lost weight after their diagnosis had a reduced risk of recurrence and mortality compared with those who maintained a normal weight, since obesity might be associated with altered hormonal profiles that stimulate tumor development (19). Recent studies have observed that women with overweight or obesity at the time of diagnosis had a 50 % increase in their probabilities of developing a second, more aggressive tumor when compared with those with normal weight (20-22). Finally, women with obesity 1 year before breast cancer diagnosis could have an increased risk of weight gain and mortality as compared with those with normal body weight (23).

Few studies have evaluated the importance of developing multidisciplinary follow-up programs including the prevention and management of obesity (23). Kwiatkowski et al. proposed using nutritional intervention, nutrition education, physiotherapy, psychological support, and physical activity programs for women with breast cancer in the post-chemotherapy phase for 1 year to achieve weight loss. At the end of their study, a significant reduction in weight, as well as in waist circumference, were observed (23). Moreover, significant reductions in body weight had been observed in women who had survived breast cancer after undergoing a nutritional and physical activity intervention, in comparison with a control group (24). In a recent study conducted with overweight and obese women with breast cancer, Cheryl L. Rock et al. concluded that a nutritional intervention resulting in weight loss can significantly reduce cancer recurrence.

However, once the literature is reviewed, we hypothesize that not only a nutritional intervention, but also the effects of nutritional education along with physical activity (the intervention group [IG]), compared with following a nutritional intervention program alone, without nutritional counseling or physical activity (the control group [CG]), in women with breast cancer after a 6-month supervised intervention period and at 1 year of follow-up, might result in an improvement in body weight and in lipid profile, and could provide benefits in terms of breast cancer recurrence and survival.

MATERIALS AND METHODS

STUDY PARTICIPANTS

For the present study, the Medical Oncology and Gynecology Department recruited the participants, who had been evaluated at the Clinical Nutrition Department, La Paz University Hospital (HULP), Madrid, Spain. The criteria to be met to be eligible for the study were as follows: age older than 18 years; female sex; newly diagnosed breast cancer; having a suitable understanding of the

clinical trial; agreeing to voluntarily participate in the study; and signing the informed consent. Exclusion criteria were as follows: patients with disseminated disease; receiving drug treatment for weight loss; suffering from an eating disorder; with mental illness; with low cognitive ability; or with problems complying with the general dietary and physical activity recommendations. Withdrawal criteria from the study included: death or lack of attendance to more than 2 treatment sessions.

All participants gave their informed consent to take part in the study, which was approved by the Scientific Research and Ethics Committee of HULP (Code 3114) in accordance with the ethical standards of the Declaration of Helsinki (25).

STUDY DESIGN

The study took the form of a randomized, prospective, controlled clinical trial lasting 24 weeks, and included 1 year of follow-up. The participants (n = 65) were randomly assigned to 1 of 2 treatment groups: CG or IG. Patients in the CG received a nutritional intervention consisting of an individualized diet; patients in the IG received the same nutritional intervention and also nutritional education and individual physical activity sessions.

NUTRITIONAL INTERVENTION

All participants received an individualized diet according to baseline energy expenditure, as measured with a bioelectrical impedance analyzer (BIA), and the corresponding recommendations for physical activity according to the World Health Organization (WHO) (26). Dietitians at the Clinical Nutrition Unit, HULP, used a food exchange list as a tool for dietary modification, and prepared menu samples in accordance with the healthy eating recommendations issued by the Spanish Society of Community Nutrition (27). This tool helps to develop customized meals, facilitating adherence to a diet. Family and work aspects, as well as mealtimes, were also taken into account.

In cases where weight reduction was required, the main goal was to promote a reduction in energy intake relative to expenditure, aiming for a 200-400 kcal/day deficit. Participants were reminded of the menu monthly, at each visit, and reinforced monthly at each visit throughout the 24 weeks of intervention. A participant's menu was assessed at the beginning, during, and at the end of the intervention period with a 72-hour dietary recall and a validated food intake frequency questionnaire to assess dietary compliance.

NUTRITIONAL EDUCATION

Once a month, a dietitian at the Clinical Nutrition Department, HULP, presented nutritional education sessions, 5 in total, of 1 hour each. The topics covered were as follows:

1. Generalities on obesity: definitions and diagnosis of obesity; complications and treatment of obesity.
2. Principles of nutrition: energy, macronutrients, and micronutrients; food groups, recommended distribution, and nutritional pyramid.
3. Situations of daily life: how to shop for food and cook healthily; how to eat outside the home.
4. Special situations: food myths and beliefs, miracle diets; learning to manage anxious moments and avoid temptations.
5. Physical activity: the importance of physical activity in breast cancer.

PHYSICAL ACTIVITY

The women in the IG attended 4 sessions per week: once a week, they performed a supervised session by the Rehabilitation and Physiotherapy Service, HULP, for 24 sessions in total, to perform aerobic and anaerobic exercises. Physical activity information for each attendant was collected through the International Physical Activity Questionnaire (IPAQ) (28) at the beginning of the intervention, at the end, and after 36 weeks. The supervised workouts were divided into two groups:

- *Aerobic training:* cardiovascular work with big muscle groups. These exercises were performed with a cycle ergometer at < 75 % of the maximum heart rate determined by an initial test. During the exercises, they made progressive increments with a goal of 45 minutes during 4 days, followed by cooling and stretching movements.
- *Anaerobic training:* after two weeks of aerobic training, they started to strengthen smaller muscle groups (biceps, triceps, deltoids, etc.) with weights according to a 40-60 % of their maximum repetition technique. They made three sets of ten repetitions for each muscle groups twice a week.

In addition, they also performed three physical activity sessions per week at home: study participants recorded information on their home training sessions including date, duration, heart rate before, during, and after each session, effort assessment according to the Borg scale, and incidents, and reported it to the Rehabilitation and Physiotherapy Service at HULP.

ANTHROPOMETRIC VARIABLES

Anthropometric measurements were taken at the beginning and at the end of each intervention period using standard techniques, and adhering to the international guidelines set out by the WHO (29). All measurements were made by trained personnel in the morning, with the participant barefoot and wearing only underwear. Body composition was determined using a BIA, the ElectroFluidGraph analyzer (Akern s.r.l., Florence, Italy). Height and waist circumference were measured and recorded adhering to the international norms set out by the WHO. BMI was calculated using the following formula: weight (kg) / height $(m)^2$.

HEALTH VARIABLES

Information was collected on medical conditions and medications taken. Blood pressure and heart rate were measured on

the right arm using a Spot Vital Signs 420 automatic monitor (Welch Allyn, Madrid, Spain) (accuracy: ± 5 mm Hg). Three measurements were taken at 5-min intervals, and the means were calculated. The populations were classified according to whether the participants exhibited prehypertension or high blood pressure that had remained undiagnosed and was not being treated pharmacologically.

BIOCHEMICAL VARIABLES

Blood samples for general biochemistry testing were collected early in the morning at the HULP Extractions Department at the beginning of the intervention, at the end of the 24 weeks of treatment, and after 36 weeks. Samples were kept at 4 °C to 6 °C until they were analyzed, which was always performed within 48 h. Biochemical serum lipid profile (e.g., total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], triglycerides), glucose, and protein levels were measured by an enzymatic spectrophotometric assay using an Olympus AU 5400 apparatus (Izasa; CA, USA).

STATISTICAL ANALYSIS

Data were analyzed using repeated measures (group x time) for within-group and between-group changes. Primary outcomes were body weight; body composition parameters; BMI; waist circumference; bicipital, tricipital, subscapular, and suprailiac folds; and heart rate. Secondary endpoints were physical function (includes aerobic and anaerobic sessions of physical activity) collected through the IPAQ questionnaire; food frequency; and lipid profile serum biomarkers: glucose, TC, HDL-C, LDL-C triglycerides and proteins. The statistical power was determined through a calculation based on the precision of the estimate of the standard deviation and by the treatment effect size.

Compliance and adherence were measured during the study using a specific questionnaire evaluated in the Clinical Nutrition Department, and a subject was considered in the analyses when she verified more than 70 % of compliance verification (nutritional intervention).

The Physiotherapy Service at HULP verified the activity carried out through questionnaires to verify compliance with and adherence to physical activity. Once the adherence was verified, investigators of the Clinical Nutrition Department carried out the statistical analysis of the IPAQ questionnaire to evaluate the physical activity of the subjects.

Changes from baseline to week 48 (1 year) were defined by the difference in the value of a parameter at week 48 minus the value at baseline. Sensitivity analyses were conducted around the assumption of missing data. A p value of < 0.05 was determined to indicate significance. Descriptive statistics were calculated (the mean and standard deviation for quantitative variables, and percentages for qualitative variables). All analyses were performed using SPSS v.26.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

RECRUITMENT AND STUDY POPULATION

The study was performed between February and June 2013. A total of 65 women (50 ± 9.43 years old) with breast cancer were eligible for inclusion. Some 18 participants were lost at 6 months (12 in the CG and 6 in the IG) due to personal reasons (n = 15) and failure to follow treatment instructions (n = 2). Thus, 47 participants completed the 24-week study. During the 1-year follow-up, 12 women were lost to personal causes (n = 6 in each group). Therefore, 35 women ultimately completed the follow-up, and only their results were included in the subsequent analyses (Fig. 1). The baseline characteristics of the 35 women who completed the study were found to be comparable between the two groups. The protocol compliance (nutrition intervention and physical activity) was high and no differences were observed between groups. Also, no significant baseline differences in baseline diet were noted between the groups.

HEART RATE, BODY WEIGHT, AND BODY COMPOSITION OF PARTICIPANTS BY TREATMENT, AND GROUP

Table I shows the results of heart rate, body weight, and body composition. Blood pressure and heart rate remained within

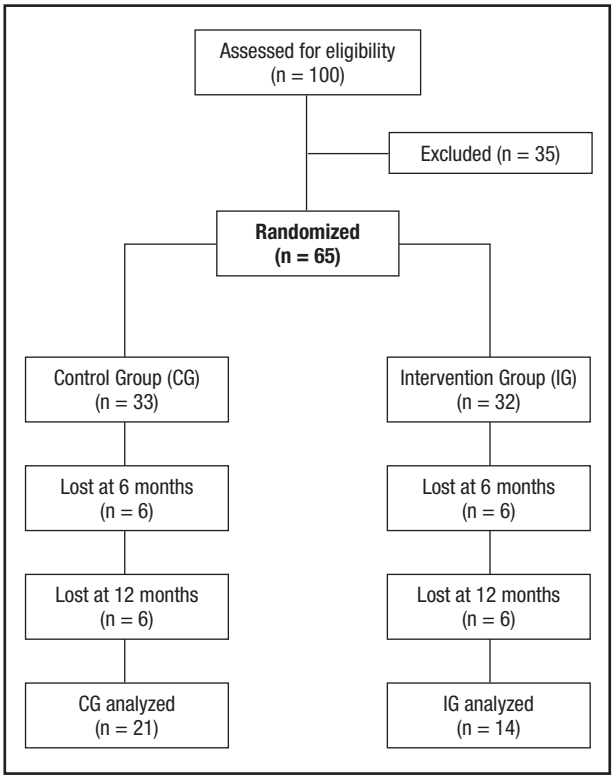

Figure 1.

Flow chart describing the present trial.

Table I. Change in measurements per participant (X ± SD)

	Control Group (CG)				Intervention Group (IG)				p
Heart rate (rate per minute)									
Baseline	77.85 ± 10.78	M6-M0	0.08 ± 8.34		73.57 ± 13.17	M6-M0	-		
Post-intervention	77.92 ± 11.69	M12-M0	-3.54 ± 10.92		79.07 ± 8.16	M12-M0	-3.59 ± 10.22		
1-year follow-up	74.31 ± 8.56	M12-M6	-3.62 ± 11.99		69.98 ± 8.53	M12-M6	-9.09 ± 9.57		
Weight (kg)									
Baseline	67.91 ± 12.72	M6-M0	0.76 ± 4.2		66.24 ± 10.34	M6-M0	0.27 ± 7.57		
Post-intervention	68.67 ± 11.93	M12-M0	2.24 ± 4.26		66.51 ± 10.44	M12-M0	-1.6 ± 7.28		*(p = 0.005)
1-year follow-up	70.15 ± 12.95	M12-M6	1.48 ± 2.01		64.64 ± 10.5	M12-M6	-1.87 ± 3.41		
BMI									
Baseline	26.91 ± 4.51	M6-M0	0.32 ± 1.59		25.53 ± 4.18	M6-M0	0.06 ± 2.97		
Post-intervention	27.23 ± 4.3	M12-M0	0.96 ± 1.71		25.58 ± 3.84	M12-M0	-0.55 ± 3.08	a (p = 0.085)	*(p = 0.011)
1-year follow-up	27.87 ± 4.72	M12-M6	0.65 ± 0.88	a	24.98 ± 3.64	M12-M6	-0.61 ± 1.4		
Waist circumference (cm)									
Baseline	86.88 ± 10.23	M6-M0	-1.05 ± 4.17		84.38 ± 11.37	M6-M0	-1.68 ± 5.95		
Post-intervention	85.82 ± 9.23	M12-M0	-4.22 ± 17.42		82.7 ± 10.13	M12-M0	-4.36 ± 9.51		
1-year follow-up	82.66 ± 17.34	M12-M6	-3.16 ± 16.67		80.01 ± 10.61	M12-M6	-2.69 ± 6.81		
Tricipital fold (cm)									
Baseline	29.63 ± 7.17	M6-M0	1.85 ± 5.29		27.16 ± 8.11	M6-M0	0.8 ± 7.63		
Post-intervention	30.62 ± 7.24	M12-M0	3.07 ± 5.87		27.65 ± 5.99	M12-M0	-1.71 ± 7.61		
1-year follow-up	28.48 ± 6.49	M12-M6	1.28 ± 4.73		26.96 ± 7.96	M12-M6	-1.18 ± 7.26		
Bicipital fold (cm)									
Baseline	20.93 ± 9.72	M6-M0	0.93 ± 5.58		17.86 ± 8.22	M6-M0	1.02 ± 6.93		
Post-intervention	20.4 ± 8.98	M12-M0	-1.77 ± 6.03		19.75 ± 8	M12-M0	-2.8 ± 9.41		
1-year follow-up	13.6 ± 4.33	M12-M6	-0.9 ± 2.38		17.36 ± 5.56	M12-M6	-3.04 ± 6.39		
Suprascapular fold (cm)									
Baseline	27.65 ± 9.26	M6-M0	2.55 ± 4.01		22.54 ± 7.44	M6-M0	2.65 ± 6.88		
Post-intervention	29.63 ± 9.9	M12-M0	9.02 ± 4.89		25.7 ± 7.5	M12-M0	4.46 ± 7		
1-year follow-up	29.35 ± 8.94	M12-M6	5.25 ± 4.44		28.99 ± 9.08	M12-M6	1.97 ± 3.56		
Suprailiac fold (cm)									
Baseline	25.75 ± 10.46	M6-M0	6.97 ± 7.46		22.11 ± 6.6	M6-M0	4.73 ± 11.58		
Post-intervention	31.88 ± 8.87	M12-M0	16.95 ± 4.27		26.65 ± 7.92	M12-M0	9.84 ± 10.14		
1-year follow-up	34.45 ± 8.44	M12-M6	4.88 ± 5.18		32.28 ± 10.17	M12-M6	6.64 ± 8.51		
FFM %									
Baseline	67.2 ± 5.22	M6-M0	-1.2 ± 3.46		69.7 ± 9.59	M6-M0	-1.44 ± 4.88		
Post-intervention	66.15 ± 8.17	M12-M0	0.1 ± 7.17		69.85 ± 7.09	M12-M0	-2.51 ± 6.91		
1-year follow-up	67.38 ± 8.84	M12-M6	1.23 ± 6.56		69.95 ± 9.12	M12-M6	0.7 ± 4.34		
LM %									
Baseline	43.33 ± 4.27	M6-M0	-0.22 ± 4.06		46.22 ± 7.34	M6-M0	-1.11 ± 3.48		
Post-intervention	44.15 ± 7.16	M12-M0	3.22 ± 13.82		47.75 ± 9.55	M12-M0	-1.94 ± 4.16		
1-year follow-up	46.15 ± 12.34	M12-M6	2 ± 11.99		45.96 ± 6.77	M12-M6	-2.14 ± 9.23		
FM %									
Baseline	32.8 ± 5.22	M6-M0	1.2 ± 3.46		30.4 ± 9.54	M6-M0	1.33 ± 4.69		
Post-intervention	33.85 ± 8.17	M12-M0	-0.1 ± 7.17		30.15 ± 7.09	M12-M0	2.39 ± 6.77		
1-year follow-up	32.62 ± 8.84	M12-M6	-1.23 ± 6.56		30.04 ± 9.11	M12-M6	-0.71 ± 4.34		

*Data are expressed as mean ± SD. BMI: body mass index; FFM: fat-free mass; LM: lean mass; FM: fat mass; M0: month 0; M6: month 6; M12: month 12; a: differences after the intervention period between the groups. Significant differences between the start and the end of the intervention periods (*p < 0.05).*

normal values for the general population (120/80 mm Hg) and did not differ between groups neither at baseline, nor after the intervention or after 1 year of follow-up ($p > 0.05$) (Table I). In contrast, there were significant changes in body weight and BMI in the IG at the end of the study ($p > 0.05$) (Table I). There were no significant differences between groups in waist circumference or in tricipital, bicipital, suprascapular, or suprailiac folds, nor any changes in any of the parameters from baseline to any time point, which allowed to obtain accurate values in the variation of body composition (% of fat-free mass, % of lean mass, and % of fat mass) ($p > 0.05$) (Table I).

BIOCHEMICAL VARIABLES

The effects of the interventions on blood lipids, glucose, and protein levels between groups are shown in table II. Despite randomization, there was an imbalance between groups at baseline in TC and protein concentrations, with higher baseline values in the IG. This imbalance was corrected, however, and a significant reduction in LDL-C in the IG occurred between the intervention period and baseline (M6-M0) (-7.33 ± 41.96 vs. 12.80 ± 25.32). There was also a significant difference in TC levels between groups in the same period (2.58 ± 50.55 vs. 9.31 ± 34.37). Although there was no significant reduction in TC at the end of the study (M12), the TC reduction between groups was relevant (-29.29 ± 39 in the IG vs. 6.08 ± 51.87 in the CG) (Table II). In addition, there was a significant difference in triglyceride levels between groups between the 6-month intervention period and the 1-year follow-up (M12-M6) in favor of the IG. On the other hand, the interventions did not significantly affect glucose, HDL-C, or protein values in any group.

DIETARY INTAKE

The mean dietary intake values are outlined in table III. Although no significant differences were observed between the CG and IG

Table II. Blood lipids, glucose, and protein levels at baseline, postintervention, and at 1 year of follow-up

	Control Group (CG)				Intervention Group (IG)				p
Glucose (mg/dl)									
Baseline	109.38 ± 63.83	M6-M0	0.54 ± 6.96		100.64 ± 10.4	M6-M0	-3.43 ± 16.17		
Post-intervention	109.92 ± 66.85	M12-M0	-26.85 ± 71.51		97.21 ± 13.17	M12-M0	-9.64 ± 11.27		
1-year follow-up	82.54 ± 10.78	M12-M6	-27.38 ± 74.57		91 ± 8.56	M12-M6	-6.21 ± 10.66		
TC (mg/dl)									
Baseline	204.77 ± 39.69	M6-M0	9.31 ± 34.37	a	228.71 ± 36.61	M6-M0	2.58 ± 50.55	a (p = 0.055)	
Post-intervention	214.08 ± 20.53	M12-M0	6.08 ± 51.87	c	228.58 ± 47.61	M12-M0	-29.29 ± 39	c (p = 0.002)	*(p = 0.005)
1-year follow-up	210.85 ± 37.47	M12-M6	-3.23 ± 39.73		199.43 ± 29.64	M12-M6	-32.92 ± 38.45		
HDL-Cholesterol (mg/dl)									
Baseline	51.7 ± 15.86	M6-M0	8.2 ± 12.24		60.73 ± 13.42	M6-M0	-6.5 ± 10.61		
Post-intervention	59.29 ± 9.39	M12-M0	6 ± 12.84		57 ± 18.65	M12-M0	-7.14 ± 15.21		
1-year follow-up	60 ± 18.75	M12-M6	5.8 ± 10.16		53.29 ± 12.31	M12-M6	8.5 ± 6.36		
LDL-Cholesterol (mg/dl)									
Baseline	118.6 ± 27.41	M6-M0	12.8 ± 25.32		149.08 ± 27.06	M6-M0	-7.33 ± 41.96		
Post-intervention	128.57 ± 24.78	M12-M0	6.33 ± 40.7	c	137.25 ± 33.06	M12-M0	-35.29 ± 27.5		*(p = 0.003)
1-year follow-up	126.64 ± 29.41	M12-M6	18.4 ± 19.32		114 ± 25.5	M12-M6	-12.5 ± 38.89		
Triglycerides (mg/dl)									
Baseline	141.3 ± 58.61	M6-M0	-16.2 ± 64.28		110.55 ± 67.97	M6-M0	-49.5 ± 160.51		
Post-intervention	115 ± 29.92	M12-M0	-13 ± 60.37		99.25 ± 42.83	M12-M0	-13.29 ± 86.27		
1-year follow-up	121.64 ± 68.19	M12-M6	-2.8 ± 53.83		110.29 ± 68.91	M12-M6	-3.5 ± 42.43		
Proteins (g/dl)									
Baseline	6.72 ± 0.38	M6-M0	-0.08 ± 0.51	a	7.02 ± 0.52	M6-M0	-0.46 ± 0.28	a (p = 0.045)	
Post-intervention	6.64 ± 0.47	M12-M0	0.14 ± 0.56		6.66 ± 0.48	M12-M0	-0.17 ± 0.53		
1-year follow-up	6.86 ± 0.57	M12-M6	0.22 ± 0.27		6.85 ± 0.59	M12-M6	0.25 ± 0.56		

*Data are expressed as mean ± SD. M0: month 0; M6: month 6; M12: month 12; TC: total cholesterol; a: differences after the intervention period between the groups; c: differences after the follow-up period between the groups. Significant differences between the start and the end of the intervention periods (*p < 0.05).*

at the end of the intervention period, both groups increased their daily intake of grains, fruits, oily fish, dairy products, and oils.

Both groups had reduced their consumption of red meat and sweets at the end of the intervention period; however, no significant differences were observed between them (Table III). These data were useful for examining group differences, although this approach will not permit an exact characterization of the dietary intake of any given individual due to day-to-day variations in intake.

PHYSICAL ACTIVITY

The main results of the physical activity questionnaire are shown in table IV. No significant differences were detected in any type of physical activity variable between the CG and IG at the end of the intervention (M6-M0), between the follow-up period and the intervention period (M12-M6), or at the 1-year follow-up (M12-M0).

However, it was observed that the IG was less sedentary at the end of the 1-year follow-up, spending fewer hours a day sitting,

Table III. Results of the food frequency questionnaire during the study period

		Control Group (CG)			Intervention Group (IG)			p
Meals/day	Baseline	3 ± 2.18	M6-M0	0.23 ± 3.23	4 ± 1.49	M6-M0	0.32 ± 3.51	--
	Post-intervention	4 ± 1.06			5 ± 0.82			
Grains/day	Baseline	3 ± 2.54	M6-M0	0.67 ± 2.44	3 ± 2.34	M6-M0	0.58 ± 3.47	--
	Post-intervention	4 ± 2.38			4 ± 1.55			
Fruits/day	Baseline	2 ± 1.29	M6-M0	0.45 ± 3.98	3 ± 1.64	M6-M0	0.32 ± 2.89	--
	Post-intervention	3 ± 1.23			3 ± 0.86			
Red meat/week	Baseline	1 ± 1.15	M6-M0	-0.24 ± 1.38	1 ± 0.90	M6-M0	-0.12 ± 1.54	--
	Post-intervention	1 ± 1.10			1 ± 0.82			
Blue fish/week	Baseline	1 ± 0.93	M6-M0	0.21 ± 1.41	1 ± 1.07	M6-M0	0.14 ± 1.43	--
	Post-intervention	2 ± 0.51			2 ± 0.80			
Dairy/day	Baseline	1 ± 1.58	M6-M0	0.25 ± 2.21	2 ± 1.54	M6-M0	0.41 ± 2.34	--
	Post-intervention	2 ± 1.13			3 ± 0.90			
Oils/day	Baseline	3 ± 1.35	M6-M0	-0.42 ± 2.13	2 ± 0.82	M6-M0	0.48 ± 1.74	--
	Post-intervention	2 ± 0.91			2 ± 0.71			
Sweets/day	Baseline	3 ± 2.68	M6-M0	-0.25 ± 3.03	2 ± 2.05	M6-M0	-0.37 ± 1.79	--
	Post-intervention	2 ± 2.91			1 ± 0.88			
Water/day	Baseline	6 ± 2.20	M6-M0	-0.31 ± 5.51	7 ± 3.27	M6-M0	-0.57 ± 6.19	--
	Post-intervention	6 ± 2.35			6 ± 3.25			

Data are expressed as mean ± SD. There were no significant differences between the start and the end of the intervention periods or in the change recorded between the intervention periods.

Table IV. Results of the physical activity questionnaire during the intervention and follow-up

Type of Physical Activity		Control Group (CG)				Intervention Group (IG)				p
Sitting hours/day	Baseline	6.03 ± 3.25	M6-M0	-2.90 ± 3.78		6.08 ± 2.61	M6-M0	0.86 ± 5.99		
	Post-intervention	3.30 ± 1.49	M12-M0	-0.85 ± 4.98	c	7.75 ± 4.18	M12-M0	-3.55 ± 3.75	c (p = 0.04)	
	1-year follow-up	5.18 ± 2.40	M12-M6	1.17 ± 3.19	b	3.50 ± 1.72	M12-M6	-2.64 ± 4.10	b (p = 0.035)	
Total IPAQ	Baseline	1030.67 ± 911.46	M6-M0	374.98 ± 1232.22	a	1544.55 ± 837.71	M6-M0	-132.45 ± 1232.22	a (p = 0.030)	
	Post-intervention	1494.25 ± 1588.58	M12-M0	301.40 ± 1551.65		1470.25 ± 1125.22	M12-M0	301.40 ± 1551.65		
	1-year follow-up	1458.54 ± 1600.55	M12-M6	–51.85 ± 1177.41		1771.95 ± 1203.98	M12-M6	234.33 ± 1177.41		

Data are expressed as mean ± SD. M0: month 0; M6: month 6; M12: month 12; a: differences after the intervention period between the groups; c: differences after the follow-up period between the groups; b: differences after the follow-up period.

but without statistical significance. Similarly, both groups showed increased physical activity at the 1-year follow-up visit, with no differences between groups (Table IV).

DISCUSSION

The aim of this study was to determine the effect of a 24-week nutrition education program, including nutritional intervention, nutrition education, and physical activity sessions in women with breast cancer. The nutritional intervention comprised a balanced diet adjusted to the energy requirements of each volunteer in both groups. In addition, the IG participated in 5 nutritional education sessions. According to public health policies, the prevention and/or management of chronic diseases involves following a healthy diet, maintaining adequate levels of body mass, reducing sedentary lifestyles, and increasing physical activity (30).

The women in our IG lost, on average, 1.87 ± 3.41 kg of body weight after the 1-year follow-up period. The difference in body weight and consequently in BMI was significant between groups at the end of the study ($p > 0.05$) (Table I). This reduced body weight in the IG group was similar to that resulting from other studies with a similar design, which could be related to the effectiveness of the nutrition education program. Also, physical activity might help to control body weight in patients with breast cancer (31). Lastly, the slight and nonsignificant decrease in heart rate observed at the end of the intervention period could be a consequence of weight loss and the effect of training (Table I).

Some body composition parameters (% of fat free, lean, and fat mass) revealed no differences between groups at the end of the study (Table I). Recent studies have shown that the method of assessing body composition is not precise enough to measure small changes in body fat over time (32). Nutritional education for women with breast cancer had a beneficial effect on their dietary pattern, which in turn could have had a beneficial effect on body weight and BMI.

In this study, both groups made consistent changes in their diet. Based on the food frequency questionnaire, they increased their consumption of grains, fruits, blue fish, dairy, and oils, and reduced their consumption of red meat and sweets. These results could be associated with a better quality of life. In a recent study, Hebert et al. had concluded that a nutrition education program improved the dietary pattern of women with breast cancer, and that they continued to maintain this pattern after the intervention period, resulting in a significant reduction in body weight (32). Similarly, Anderson et al. had found that physical activity and a 6-month nutrition education program in women with breast cancer produced a significant loss of body weight, a significant reduction in saturated fat consumption (-4.2 % vs. -1.2 %; $p = 0.013$), and a significant increase in fruit and fiber consumption (0.5 servings vs. 0.0 servings; $p = 0.006$; 4.8 g per 1000 kcal vs. 1.3 g per 1000 kcal; $p = 0.007$, respectively) (33) compared with a control group (34). Therefore, a dietary intervention and a physical activity program could improve the dietary pattern of women with breast cancer, achieving a healthier eating profile and leading to reduced body weight and better quality of life.

Physical activity is well known to improve strength and daily activity in clinical populations. Our IG reported a reduction in the number of sitting hours compared with the CG (-3.55 ± 3.75 vs. -0.85 ± 4.98). Although no significant differences were observed, the IG group slightly decreased their physical activity level after the intervention period during six months (total IPAQ: -132.45 ± 1232.22), and then they increased it after a year (total IPAQ: 234.33 ± 1177.41). These results are in accordance with other studies, and may be due to complications arising from cancer treatments. Subsequently, patients gained sufficient skills, confidence, and knowledge to focus on long-term physical activity, and to achieve a greater adherence to exercise as participants felt that physical activity represented a way to feel better. In contrast, the women who were in the CG did not receive physical activity recommendations and consequently did not improve their physical activity after the one-year follow-up period. These results are in accordance with recent studies, such as that by Carayol et al. These researchers found that a comprehensive physical activity therapy with aerobic and endurance exercises, as well as dietary counseling, compared with a control group, reduced levels of fat mass and BMI, and increased muscle endurance in women with breast cancer (35).

Our results, showing significant reductions in TC and LDL-C in the IG, are in agreement with the literature investigating the prevention of cardiovascular disease. The literature suggests that increased physical activity and nutritional education can influence lipid profiles in patients with cancer, increasing their survival rates (36). Our results are in line with a recent study that demonstrated the effect of physical activity in patients with breast cancer using recommendations for exercises that could be performed at home, compared with a control group without recommendations. At the end of the intervention period, both BMI (-6 kg/m^2; $p = 0.02$), TC (-38 mmol/L; $p = 0.001$), and LDL-C (-3 mmol/L; $p = 0.023$) were significantly lower as compared with the control group (37). We might not have found reductions in glucose, HDL-C, and protein concentrations due to an insufficient sample size to detect differences between groups. Lahart et al. had concluded in a recent study that patients with invasive breast cancer who performed physical activity with recommendations for exercises that could be performed at home could reduce their TC and LDL-C concentrations when compared with a control group. Similarly, another study conducted by Swisher et al. had shown that the combination of aerobic exercise therapy and dietary counseling reduced BMI (2.4 % vs. 0.4 %, $p < 0.05$), suggesting that exercise and healthy eating can be effective in breast cancer survivors as compared with a control group (38).

The strengths of this study involve a randomized design, a long follow-up period for 1 year in total for each analyzed patient, a wide range of outcomes including both subjective and objective measurements, and an intention-to-treat approach. Limitations include the final sample size after one year of follow-up. This factor should be taken into account for future studies. It will be necessary to take losses into account, which may be due to the

consequences of breast cancer treatment (tiredness, treatment, discomfort, medications, and other diseases). Moreover, self-reported measurements such as the food frequency questionnaire and IPAQ require participants to recall past activity, and represent a subjective means of estimating individual physical activity and dietary pattern levels. Further studies are warranted and should be required to establish physical activity programs and dietary advice as part of any institutional action protocols for women with breast cancer.

CONCLUSIONS

We found that a nutrition education program (including nutritional intervention, nutritional education, and physical activity) resulted in significant favorable effects on body weight, BMI, TC, and LDL-C in women with breast cancer compared with a control group, who received only a nutritional intervention. Reductions in body weight were correlated with improvements in lipid profile. Therefore, dietary interventions and physical activity in patients with breast cancer provide positive effects and could be important therapy components to reduce breast cancer recurrence and increase breast cancer survival. Further studies should examine the long term effects of a lifestyle program in patients with breast cancer.

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Trabajo Original

Otros

Composición corporal, metabolismo mineral y función endocrina del tejido adiposo: influencia de un suplemento nutricional de propóleo

Body composition, mineral metabolism, and endocrine function of adipose tissue: influence of a nutritional supplement of propolis

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Resumen

Introducción: el propóleo y sus componentes influyen en el metabolismo lipídico; sin embargo, se desconoce su efecto sobre la composición corporal y el metabolismo mineral.

Objetivos: determinar el efecto de la suplementación de la dieta con propóleo natural sobre la composición corporal, el metabolismo basal y mineral, y la función endocrina del tejido adiposo.

Material y métodos: veinte ratas albinas Wistar macho (8 semanas) se dividieron en dos grupos de 10 animales cada uno. Las ratas fueron alimentadas con dos tipos diferentes de dietas durante 90 días: una dieta estándar para el grupo de control (grupo C) y la misma dieta estándar + un 2 % de propóleo (grupo P). Se determinaron las hormonas tiroideas, la grelina, la leptina, la adiponectina y la insulina, los ácidos grasos no esterificados (AGNE) en el plasma, la composición corporal (masa magra, masa grasa y agua corporal) y el depósito de minerales en órganos diana (bazo, cerebro, corazón, pulmones, testículos, riñones y fémur).

Resultados: los niveles plasmáticos de hormona estimulante del tiroides (TSH), triyodotironina (T_3) y tiroxina (T_4) no mostraron diferencias tras la ingesta del suplemento de propóleo, mientras que los de grelina y adiponectina disminuyeron ($p < 0,01$ y $p < 0,05$, respectivamente) y los de insulina ($p < 0,01$), leptina ($p < 0,05$) y AGNE ($p < 0,05$) aumentaron cuando la dieta se suplementó con propóleo al 2 %. Se redujeron el peso y la grasa corporal ($p < 0,05$), incrementándose la masa magra. Por último, el suplemento de propóleo mejoró el depósito de calcio en el bazo, los pulmones, los testículos y el fémur ($p < 0,05$).

Conclusión: el suplemento de propóleo al 2 % de la dieta produjo una disminución de la secreción de grelina y adiponectina, incrementando la concentración de AGNE y aumentando la tasa de secreción de insulina. Además, el suplemento de propóleo indujo una mejora del depósito de calcio en los órganos diana sin afectar al resto de minerales, lo que en conjunto mejora la composición corporal al inducir una reducción del peso y del tejido adiposo visceral, mejorando la masa magra.

Palabras clave:

Propóleo. Peso corporal. Composición corporal. Tejido adiposo. Masa magra. Metabolismo mineral.

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Abstract

Introduction: propolis and its components influence lipid metabolism; however, its effect on body composition and mineral metabolism remains unknown.

Objectives: to determine the effect of natural propolis supplementation on body composition, mineral metabolism, and the endocrine function of adipose tissue.

Material and methods: twenty albino male Wistar rats (8 weeks old) were divided into two groups of 10 animals each. The rats were fed two different types of diet for 90 days: a standard diet for the control group (group C) and the same standard diet + 2 % propolis (group P). Thyroid hormones, ghrelin, leptin, adiponectin and insulin, non-esterified fatty acids (NEFA) in plasma, body composition (lean mass, fat mass and body water), and mineral deposition in target organs (spleen, brain, heart, lungs, testicles, kidneys and femur) were assessed.

Results: thyroid stimulating hormone (TSH), triiodothyronine (T_3) and thyroxine (T_4) did not show any differences after supplementation with propolis, while ghrelin and adiponectin decreased ($p < 0.01$ and $p < 0.05$, respectively) and insulin ($p < 0.01$), leptin ($p < 0.05$) and NEFA ($p < 0.05$) increased when 2 % propolis was supplied, while weight and body fat were reduced ($p < 0.05$) and lean mass increased. Lastly, the propolis supplement improves calcium deposition in the spleen, lungs, testes, and femur ($p < 0.05$).

Conclusion: propolis supplementation of the diet (2 %) causes a decrease in the secretion of ghrelin and adiponectin, increasing the release of non-esterified fatty acids and the rate of insulin secretion. In addition, propolis supplementation induces an improvement in calcium deposition in target organs without affecting the rest of minerals, which improves body composition by inducing a reduction in weight and visceral adipose tissue, and improvement in lean mass.

Keywords:

Propolis. Body weight. Body composition. Adipose tissue. Lean mass. Mineral metabolism.

INTRODUCCIÓN

La obesidad es un problema global que ha aumentado en los últimos años en proporción dramática tanto en niños como en adultos. Está bien establecido en la comunidad científica que la obesidad está asociada a una serie de comorbilidades, y que el sobrepeso y la obesidad se han relacionado con un mayor riesgo de mortalidad. Las personas obesas son más susceptibles de sufrir infecciones y de desarrollar más complicaciones graves (1). La dieta juega un papel clave en la composición corporal pero todavía existe información limitada sobre la influencia de determinados alimentos en este sentido.

Durante muchas décadas, el tejido adiposo se consideró un órgano pasivo que participaba exclusivamente en el almacenamiento de lípidos en condiciones de ingesta de energía excesiva, y que proporcionaba sustratos ricos en energía cuando otros órganos la necesitaban. Actualmente existe una nueva visión fisiológica del tejido adiposo como órgano endocrino, gracias al descubrimiento de su papel central en la interacción con otros órganos o tejidos (2).

En los sujetos obesos se ha encontrado una alteración de la homeostasis mineral (que se relaciona con el índice de masa corporal y la distribución de grasa) que podría ser de importancia clínica, ya que se ha encontrado que la masa esquelética está alterada en los sujetos obesos, y los niveles bajos de calcio ionizado en plasma se han asociado con complicaciones vasculares en los sujetos hipertensos, en quienes la obesidad se encuentra con frecuencia (3).

El propóleo es un producto de apicultura, producido en las colmenas, que consiste en una mezcla de saliva de las abejas, extractos de semillas y hojas, y exudados de flora vegetal. Hasta ahora se han aislado más de 500 compuestos químicos presentes en el propóleo (4). Dado que los principales ingredientes del propóleo derivan de los vegetales, su composición química es dependiente de su origen geográfico.

El propóleo se ha utilizado en la medicina tradicional popular y en terapias complementarias para tratar una amplia variedad de enfermedades. El propóleo y sus componentes químicos tienen efectos terapéuticos destacados sobre las enfermedades infecciosas, la inflamación y el cáncer (5). Además, el propóleo también tiene efectos beneficiosos sobre ciertos trastornos metabólicos (6). Concretamente, algunos polifenoles presentes en el propóleo, como la genisteína (sioflavona) y la naringenina (flavona), pueden inducir lipólisis en el tejido adiposo (7), y se ha demostrado que estos componentes derivados de las plantas disminuyen la acumulación de lípidos en los adipocitos (8).

Teniendo en cuenta todo lo descrito, el presente estudio se diseñó para evaluar el efecto de la suplementación oral con propóleo natural al 2 % sobre la función endocrina del tejido adiposo, la composición corporal y el depósito de minerales en órganos diana.

MATERIAL Y MÉTODOS

ANIMALES, DISEÑO EXPERIMENTAL Y DIETAS

Para este estudio se utilizaron veinte ratas albinas Wistar macho (8 semanas) con un peso medio de 215 ± 10 g, suministradas por el Servicio de Animales de Laboratorio de la Universidad de Granada. Los procedimientos de cuidado animal y los protocolos experimentales fueron aprobados por el Comité de Ética de la Universidad de Granada de acuerdo con las directrices de la Comunidad Europea. Se realizó un análisis de potencia para estimar el número de ratas necesarias para obtener un 80 % de potencia con un nivel de confianza del 95 %. Se requerirían ocho animales para obtener una diferencia del 8 % en los parámetros hematológicos entre ambas dietas. De forma similar, se requerirían 7 animales por grupo para obtener una diferencia del 10 % en los parámetros bioquímicos entre las dos dietas. Para garantizar el cálculo de la potencia se usaron 10 ratas por grupo.

Las ratas se dividieron en dos grupos de 10 animales cada uno y fueron alimentadas durante 90 días con dos tipos diferentes de dietas: una dieta estándar AIN-93M (9) para el grupo de control (grupo C) y la dieta AIN-93M + 2 % de propóleo (que contiene

Tabla I. Dietas ensayadas

Componente	Cantidad (g/kg)
Dieta C y Pa	
Proteína (caseína)	140
Grasa (aceite de oliva virgen)	40
Fibra (celulosa micronizada)	50
Suplemento mineral[b]	35
Suplemento vitamínico[c]	10
Cloruro de colina	2,5
Almidón de maíz	621
Sacarosa	100
L-Cistina	1,8

[a]A la dieta del grupo P se le agregó un 2 % de propóleo (que contenía 168,7 ± 3,9 mg de equivalentes de ácido gálico/100 g como compuestos fenólicos totales, y 31,7 ± 1,1 mg de equivalentes de catequina/100 g como flavonoides totales). [b]El suplemento mineral se preparó de acuerdo con las recomendaciones del Instituto Americano de Nutrición (9). [c]El suplemento vitamínico se preparó según las recomendaciones del Instituto Americano de Nutrición (9).

aproximadamente un 50 % de resina y bálsamo vegetal, un 30 % de cera, un 10 % de aceites esenciales y aromáticos, un 5 % de polen y un 5 % de otros compuestos) (4) para el grupo del propóleo (grupo P). La tabla I muestra la composición de las dos dietas experimentales. Los animales se colocaron en jaulas metabólicas individuales en una habitación ambientalmente controlada con una temperatura constante de 22 ± 1 °C, un ciclo de luz-oscuridad de 12 h y un 55 ± 10 % de humedad. Se controló la ingesta de la dieta (*pair feed*) y los animales ingirieron agua bidestilada *ad libitum*. En el día 90, todos los animales fueron sometidos a un periodo de ayuno durante la noche y se determinó la composición corporal mediante resonancia magnética. Posteriormente, las ratas fueron anestesiadas mediante inyección intraperitoneal de 5 mg de pentobarbital sódico/100 g de peso corporal (St Louis, MO, EUA). Se extrajo completamente la sangre mediante canulación de la aorta y se centrifugó con EDTA como anticoagulante (1500 x g, 4 °C, 15 min) para la obtención de plasma y el posterior análisis de hormonas tiroideas, grelina, leptina, adiponectina, insulina y ácidos grasos no esterificados (AGNE). Después se procedió a la extracción y congelación de los distintos órganos objeto del estudio: bazo, cerebro, corazón, pulmones, testículos, riñones y fémur, en los que se determinó el contenido de Ca, P, Mg, Cu y Zn tras el adecuado procesamiento de la muestra.

EVALUACIÓN DE LA COMPOSICIÓN CORPORAL

La composición corporal de los animales se determinó usando un sistema de resonancia magnética cuantitativa Echo MRI Analyzer de Echo Medical Systems (Houston, Texas, EE. UU.). Todas las mediciones de composición corporal se realizaron durante la misma franja horaria (08:00 a.m. a 03:00 p.m.). Los animales se colocaron en un cilindro de plástico durante un breve periodo de tiempo para limitar sus movimientos y se sometieron a un campo electromagnético de baja intensidad para medir la grasa, la masa magra, el agua libre y el agua corporal total.

HORMONAS TIROIDEAS, GRELINA, LEPTINA, ADIPONECTINA E INSULINA

Las hormonas tiroideas, la grelina, la leptina, la adiponectina y la insulina se determinaron mediante Luminex utilizando la tecnología X-Map. Para la determinación de la hormona estimulante del tiroides (TSH), la triyodotironina (T_3) y la tiroxina (T_4) se utilizó el panel RYYMAG-30K Milliplex MAP Rat. La forma activa de la grelina, la leptina y la insulina se determinaron usando el Panel Milliplex MAP de RMHMAG-84K. Los niveles de adiponectina se midieron usando el panel Milliplex MAP RADPCMAG-82K (Millipore Corporation, Missouri, EE. UU.). La tecnología X-Map se basa en inmunoensayos en la superficie de microesferas magnéticas fluorescentes, siguiendo las especificaciones del fabricante (50 eventos por medida, 50 µL de muestra, configuración de ensayo: 8000-15000, 60 segundos). La placa se leyó en el analizador LABScan 100 (Luminex Corporation, Texas, EE. UU.), utilizando el software xPONENT para adquisición de datos. Los valores promedio de cada conjunto de muestras o estándares duplicados se encontraban dentro del 10 % de la media. Las concentraciones de hormona tiroidea, grelina, leptina, adiponectina e insulina en las muestras de plasma se determinaron comparando la media de las muestras duplicadas con la curva estándar para cada ensayo.

ÁCIDOS GRASOS NO ESTERIFICADOS (AGNE)

Los AGNE son liberados por los triglicéridos gracias a la acción de la lipasa, proporcionando una gran parte de la energía metabólica. Los AGNE se midieron usando un kit comercial (Randox Laboratories Ltd., Crumlin, Reino Unido). Para ello se emplearon 50 µl de solución estándar o muestras de plasma. A continuación se añadió 1 ml de la solución R1 a todos los tubos. Las mezclas se sometieron a agitación durante 5-10 segundos y se incubaron a 37 °C durante 10 minutos. Inmediatamente después se añadieron 2 ml de solución R2 y el tubo se mezcló y se incubó a 37 °C. Tras 10 minutos de incubación se determinó la absorbancia de la mezcla a 550 nm en un espectrofotómetro (Bio-tek, Vermont, EE. UU.). Además, todos los estándares, muestras de plasma y controles se analizaron por duplicado. El cálculo de la concentración de AGNE se ajustó usando la siguiente ecuación: AGNE mmol/L = (Absorbancia de la muestra / Absorbancia del estándar) x concentración del estándar.

MINERALES TOTALES

Los minerales totales se determinaron por mineralización total de la muestra por vía húmeda de los órganos. La muestra se

coloca en un vaso de precipitado, se añaden 10-12 mL de ácido nítrico concentrado (riqueza del 69 %) y se tapa el vaso con un vidrio de reloj. Se coloca en un baño de arena SELECTA (Selecta, Barcelona, España) a una temperatura de 70-80 °C y se espera la aparición de vapores rojizos/anaranjados de óxido nítrico. Se añaden 2 mL de nítrico a la muestra, tantas veces como se necesario hasta la aparición de vapores blanquecinos. En ese momento se comienza a añadir 10 mL de mezcla nítrico/perclórico (4:1, v/v) en alícuotas de 2 mL cada vez hasta completar la mineralización. Una vez finalizada la mineralización, se deja enfriar, se filtra en papel Whatman del nº 41 (libre de cenizas) y se enrasa hasta un volumen final de 25 mL en un matraz aforado. Como resultado final obtenemos una solución transparente que emplearemos en la posterior determinación de minerales. Las concentraciones de Ca, Mg, Cu y Zn en los órganos se determinaron por espectrofotometría de absorción atómica (Perkin Elmer 1100B, Norwalk, EUA) a partir de una muestra adecuada, previamente mineralizada por vía húmeda y diluida convenientemente, comparándose frente a una serie de patrones de concentración conocida. En la espectroscopía atómica se consigue que los átomos individuales de una especie interactúen con la radiación electromagnética. La concentración de P se analizó por espectrofotometría visible mediante un kit comercial (Spinreact, Barcelona, España).

ANÁLISIS ESTADÍSTICO

Los datos se muestran como medias ± error estándar de la media (SEM). Los análisis estadísticos se realizaron con el programa informático SPSS (versión 25.0, 2013, SPSS Inc., Chicago, Illinois, EUA). Las diferencias entre los grupos alimentados con dietas de control (C) o suplementadas con propóleo (P) se evaluaron con la prueba de la t de Student. Se estableció el nivel de significación con el valor de $p < 0,05$.

RESULTADOS

Los reguladores endocrinos del metabolismo basal después de la ingesta de la dieta C o P se muestran en la tabla II. La hormona estimulante del tiroides (TSH), la triyodotironina (T_3) y la tiroxina (T_4) no fueron diferentes tras la ingesta de las dos dietas, mientras que la grelina y la adiponectina disminuyeron ($p < 0,01$ y $p < 0,05$, respectivamente) y la insulina ($p < 0,01$), la leptina ($p < 0,05$) y los AGNE ($p < 0,05$) aumentaron cuando se suministró propóleo al 2 % en la dieta.

Al finalizar el tratamiento con la dieta P, el peso y la grasa corporal fueron menores ($p < 0,05$), mientras que la masa magra se incrementó ($p < 0,05$) (Tabla III).

La ingesta de la dieta suplementada con propóleo incrementó el depósito de calcio en bazo, pulmones, testículos y fémur ($p < 0,05$), mientras que no modificó el resto de los minerales determinados en ninguno de los órganos analizados (Tabla IV).

Tabla II. Concentración plasmática de las hormonas que influyen en el metabolismo basal y los AGNE en las ratas alimentadas con la dieta de control o con la suplementada con propóleo

	Grupo C (n = 10)	Grupo P (n = 10)
TSH (pg/mL)	32,25 ± 2,27	32,05 ± 2,11
T_3 (pg/mL)	13312 ± 395,47	13798 ± 311,15
T_4 (pg/mL)	1335 ± 77,44	1336 ± 91,22
Grelina (pg/mL)	21,49 ± 1,43	16,63 ± 0,97†
Insulina (pg/mL)	645,14 ± 33,87	739,12 ± 37,01†
Adiponectina (ng/mL)	1335 ± 121,25	1114 ± 110,67*
Leptina (pg/mL)	1603 ± 101,12	1975 ± 112,94*
AGNE (mmol/L)	0,51 ± 0,08	0,64 ± 0,09*

*TSH: hormona estimulante del tiroides; T_3: triyodotironina; T_4: tiroxina; AGNE: ácidos grasos no esterificados; *Diferencias estadísticamente significativas con respecto al grupo de control (p < 0,05, test de la t de Student); †Diferencias estadísticamente significativas con respecto al grupo de control (p < 0,01, test de la t de Student).*

Tabla III. Composición corporal de las ratas alimentadas con la dieta de control o con la suplementada con propóleo

	Grupo C (n = 10)	Grupo P (n = 10)
Peso corporal (g)	373,22 ± 8,85	308,24 ± 7,31*
Grasa (%)	8,15 ± 0,70	7,51 ± 0,82*
Masa magra (%)	87,11 ± 1,72	91,52 ± 1,80*
Agua libre (%)	0,35 ± 0,03	0,41 ± 0,07
Agua total (%)	74,57 ± 0,51	75,32 ± 0,79

**Diferencias estadísticamente significativas con respecto al grupo de control (p < 0,05, test de la t de Student).*

DISCUSIÓN

En el presente estudio hemos encontrado que el suplemento de propóleo al 2 % aumentó la capacidad lipolítica del tejido adiposo y disminuyó la síntesis de lípidos, reduciendo la adiponectina y la grelina secretadas, hecho que puede explicar la mejora de la composición corporal, la disminución de la adiposidad y el aumento de la tasa de secreción de insulina, ya que esta hormona actúa sobre el sistema melanocortinérgico hipotalámico. La grelina actúa sobre la pituitaria anterior, los islotes pancreáticos, la glándula tiroides, el corazón y varias regiones del cerebro. Estimula el apetito, posiblemente a través de la activación de circuitos nerviosos orexigénicos, de forma coherente con los

Tabla IV. Concentración de minerales en los órganos de las ratas alimentadas con la dieta de control o con la suplementada con propóleo

	Grupo C (n = 10)	Grupo P (n = 10)
Bazo		
Ca (µg/g)	208,15 ± 10,35	252,51 ± 26,09*
P (mg/g)	12,82 ± 0,61	12,91 ± 0,64
Mg (mg/g)	1,51 ± 0,11	1,62 ± 0,12
Cu (µg/g)	16,21 ± 0,57	16,35 ± 0,92
Zn (µg/g)	87,41 ± 3,33	85,16 ± 3,61
Cerebro		
Ca (µg/g)	592,95 ± 38,30	639,24 ± 48,36
P (mg/g)	10,24 ± 0,10	10,27 ± 0,70
Mg (mg/g)	1,29 ± 0,02	1,28 ± 0,04
Cu (µg/g)	15,56 ± 0,22	16,11 ± 0,78
Zn (µg/g)	48,65 ± 0,36	48,84 ± 0,51
Corazón		
Ca (µg/g)	388,35 ± 21,50	398,52 ± 21,37
P (mg/g)	5,50 ± 0,22	5,89 ± 0,19
Mg (mg/g)	1,94 ± 0,02	2,00 ± 0,09
Cu (µg/g)	19,13 ± 0,47	18,68 ± 0,62
Zn (µg/g)	60,22 ± 1,10	61,36 ± 1,50
Pulmones		
Ca (µg/g)	0,41 ± 0,05	0,55 ± 0,03*
P (mg/g)	6,03 ± 0,72	6,14 ± 0,28
Mg (mg/g)	1,32 ± 0,06	1,21 ± 0,06
Cu (µg/g)	10,42 ± 0,91	11,12 ± 0,84
Zn (µg/g)	61,42 ± 2,80	62,49 ± 2,59
Testículos		
Ca (µg/g)	259,60 ± 5,24	293,33 ± 5,10*
P (mg/g)	7,64 ± 0,29	7,70 ± 0,23
Mg (mg/g)	1,01 ± 0,10	1,07 ± 0,08
Cu (µg/g)	17,68 ± 0,80	17,70 ± 0,96
Zn (µg/g)	145,69 ± 2,17	143,18 ± 2,30
Riñones		
Ca (µg/g)	0,65 ± 0,13	0,67 ± 0,08
P (mg/g)	5,91 ± 0,08	6,10 ± 0,10
Mg (mg/g)	1,66 ± 0,04	1,55 ± 0,03
Cu (µg/g)	25,32 ± 1,58	25,22 ± 2,17
Zn (µg/g)	88,97 ± 1,95	86,21 ± 1,98
Fémur		
Ca (µg/g)	168,4 ± 3,23	182,8 ± 3,11*
P (mg/g)	122,7 ± 2,51	125,1 ± 2,91
Mg (mg/g)	4,32 ± 0,21	4,12 ± 0,14
Cu (µg/g)	81,12 ± 2,01	85,31 ± 2,66
Zn (µg/g)	227,37 ± 2,61	228,45 ± 2,82

**Diferencias estadísticamente significativas con respecto al grupo de control (p < 0,05, test de la t de Student).*

efectos observados en los niveles plasmáticos de grelina y otros péptidos neuroactivos, y estimula la lipólisis con independencia de la ingesta de alimentos, ya que se controló esta ingesta mediante *pair feed*, lo que, en conjunto, conduce a un aumento del peso corporal y la adiposidad. Más allá de la regulación del apetito y la secreción de hormona del crecimiento (GH), los efectos de la grelina incluyen la regulación de la motilidad intestinal, el ritmo del ciclo sueño-vigilia, la sensación del sabor, el comportamiento de búsqueda de recompensas y la regulación del metabolismo de la glucosa, mejorando la resistencia a la insulina y la diabetes mellitus de tipo II (10). El suplemento de propóleo en la dieta también produjo una disminución de la adiponectina, una adipoquina que desempeña un papel importante en la homeostasis energética y la sensibilidad a la insulina, y que se correlaciona inversamente con el grado de adiposidad (11), explicando la reducción de la masa grasa encontrada, ya que la adiponectina es producida por el tejido adiposo y su producción es proporcional a la cantidad del mismo. La disminución de los niveles de grelina y adiponectina es opuesta al aumento de las concentraciones plasmáticas de leptina tras la suplementación con propóleo; por lo tanto, induciría una disminución del apetito. Además, en concordancia con otros estudios (2), existe una asociación inversa entre la adiponectina circulante y las concentraciones de AGNE en el plasma, indicando un incremento de la capacidad lipolítica inducido por el suplemento de propóleo en los depósitos adiposos, lo cual influye en la composición corporal, disminuyendo la masa grasa y, por lo tanto, la secreción de adiponectina y grelina (12).

La grelina provoca una inhibición de la secreción de insulina (13,14), mejorando así la sensibilidad a la insulina en los tejidos periféricos (15). Las ratas que portan una mutación de pérdida de función en el inhibidor de la quinasa dependiente de ciclina p27 presentan un número elevado de células ε productoras de grelina, que coincide con una mayor ingesta de alimentos, una mayor masa grasa y una menor estimulación de la secreción de insulina por la glucosa (16). Más allá de su papel como regulador negativo de la secreción de insulina, la grelina también parece tener efectos protectores sobre las células β en presencia de la diabetes de tipo I (17).

El propóleo también aumentó la tasa de secreción de insulina por otros mecanismos independietes de la grelina. Varios estudios han evaluado los efectos del propóleo sobre el nivel sérico de insulina en modelos animales de diabetes inducida por estreptozocina. Dado que la estreptozocina destruye las células β pancreáticas, los niveles de insulina en sangre disminuyen notablemente. En este sentido, extractos etanólicos de propóleo (300 mg/kg/día) protegieron parcialmente la deficiencia de insulina inducida por estreptozocina, mejorando la sensibilidad a la insulina y la función de las células β pancreáticas (18). El propóleo es capaz de prevenir la destrucción de las células β pancreáticas por varios mecanismos. Los flavonoides son capaces de neutralizar y eliminar las especies reactivas del oxígeno (ERO), y la quercetina protege las células β del daño oxidativo (19). De hecho, se ha descrito que la quercetina (15 mg/kg/día durante 4 semanas) recuperó parcialmente la deficiencia de insulina inducida por estreptozocina en ratas (20).

Junto con la eliminación de las ERO en el páncreas, el propóleo tiene un efecto directo sobre el mecanismo de secreción de la insulina. Las células β pancreáticas promueven la secreción de insulina en respuesta a la arginina. La arginina interactúa con su complejo diana para estimular la secreción de insulina en el retículo endoplásmico de las células β. El propóleo fue capaz de mimetizar los efectos de la arginina en líneas celulares β pancreáticas NIT-1. El propóleo (0,01 %) mostró un efecto más prominente que el de la arginina sobre la secreción de insulina, lo que sugiere que ejerce otros efectos estimulantes adicionales, que no han sido descritos, sobre la secreción de insulina (21). Los mismos autores también demostraron que la administración de propóleo produjo un aumento de la concentración de insulina circulante en ratones no diabéticos, junto con una disminución de la glucosa en sangre (21). Varios compuestos químicos presentes en el propóleo mejoran de forma independiente la tasa de secreción de insulina. El ácido cafeico (15-30 mg/kg durante 5 semanas) mejoró significativamente el nivel de insulina en ayunas y la tolerancia a la glucosa en ratones tratados con estreptozocina (22). La crisina (100 mg/kg/día durante 30 días) también mejoró la señalización de la insulina (23). Además, otros compuestos, como la galangina (10-80 M) y la pinocembrina (1-4 M), mejoraron la resistencia a la insulina y potenciaron la acumulación de glucógeno inducida por insulina en células HepG2 resistentes a la insulina (24).

El suplemento de propóleo en la dieta causó una reducción del peso y del tejido adiposo visceral, mejorando la masa magra. Se sabe que el incremento de los lípidos plasmáticos causa obesidad y resistencia a la insulina, y que el perfil lipídico se ve afectado por la dieta y los órganos reguladores, como el hígado, el tejido adiposo y el músculo. Estudios previos (25) han informado de que el propóleo reduce significativamente la actividad de la enzima ácido graso-sintasa en los grupos tratados con extracto de propóleo, sugiriendo que uno de los mecanismos responsables del efecto inhibitorio sobre la acumulación de tejido adiposo visceral es la disminución de la síntesis de ácidos grasos. Diversos estudios han demostrado un papel crucial de las células inmunes del tejido adiposo en la inflamación crónica y en el desarrollo del síndrome metabólico. Se ha demostrado que las células inmunes T CD4+, las células T CD8+, las células T reguladoras y los eosinófilos contribuyen a la diferenciación de los macrófagos inflamatorios y, en este sentido, Kitamura y cols. (26) propusieron que el propóleo mejoraría los niveles de glucosa en sangre y el colesterol plasmático a través de su efecto sobre las células inmunes del tejido adiposo. Sakai y cols. (27) mostraron que la reducción de la infiltración de las células inmunes en el tejido adiposo provoca una reducción de la acumulación de grasa y/o una atenuación de la ganancia de peso corporal durante el tratamiento con propóleo en ratones. En este estudio, el peso y el contenido de grasa de las heces de los ratones tratados con propóleo se incrementó con respecto a los valores hallados en las heces de los ratones que no recibían este compuesto. El propóleo contiene una variedad de compuestos químicos que pueden explicar la disminución de la adiposidad encontrada. Se ha demostrado que el ácido ferúlico promueve la pérdida de peso en las ratas y mejora la glucemia en los ratones alimentados con una dieta alta en grasas (28,29). El kaempferol mejora la hiperglucemia, la hiperinsulinemia y el perfil lipídico (30). Además el ácido p-cumárico incrementa la expresión de carnitina, mejorando el metabolismo lipídico hepático (31).

A pesar de que el propóleo tiene un alto contenido de resinas (4) y estos compuestos poseen la capacidad de inhibir la absorción de minerales de la dieta por su efecto quelante, no se han observado efectos adversos sobre los niveles plasmáticos o el metabolismo de los minerales estudiados. De hecho, en el presente estudio se ha encontrado una mejora del depósito de calcio en los órganos diana. El aumento del depósito de calcio en bazo, pulmones, testículos y fémur puede deberse a la mayor digestibilidad del calcio en los animales alimentados con el suplemento de propóleo, que, como se ha publicado previamente (32), contiene aminoácidos libres, como la lisina, el aspartato, el glutamato y la ornitina, que favorecen la absorción del calcio. Otro mecanismo que explica el mejor depósito de calcio en los órganos diana es su contenido en ácido 4-hidroxibenzoico, que favorece la solubilidad del calcio de la dieta, aumentando así la absorción de este mineral (33).

Por último, la mejora de la composición corporal también puede atribuirse a la mejora de la homeostasis del calcio que se ha encontrado con el propóleo. Se ha demostrado que en los sujetos obesos existe un aumento de la unión del calcio a las proteínas plasmáticas, en lugar de a las proteínas transportadoras de calcio. El calcio intracelular ionizado desempeña un papel clave en la regulación del metabolismo de los adipocitos al modular las reservas de triglicéridos. Debido a que las hormonas calciotrópicas regulan el calcio intracelular, la supresión de estas hormonas cuando aumenta la biodisponibilidad del calcio redirige la energía de la dieta desde el tejido adiposo hacia la masa magra corporal y la termogénesis (34,35); también el calcio de la dieta en el tracto gastrointestinal conduce a la precipitación de jabones insolubles de ácidos grasos que hacen que la grasa esté menos disponible para su absorción (35). Además, varios estudios (36-38) han demostrado que la suplementación de calcio en la dieta produce efectos beneficiosos sobre la reducción del peso, la grasa corporal y la homeostasis de la glucosa en ratones y seres humanos.

CONCLUSIÓN

En el presente estudio hemos encontrado que el suplemento de propóleo al 2 % de la dieta produjo una disminución de la secreción de grelina y adiponectina, incrementando la concentración de AGNE y la tasa de secreción de insulina. Además, el suplemento de propóleo indujo una mejora del depósito de calcio en los órganos diana sin afectar al resto de los minerales, lo que en conjunto mejoró la composición corporal al inducir una reducción del peso y del tejido adiposo visceral, mejorando la masa magra.

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Revisión

Morphofunctional assessment of patient´s nutritional status: a global approach

Evaluación morfofuncional del estado nutricional de los pacientes: un nuevo enfoque

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Abstract

Disease-related malnutrition represents an imbalance between the intake and the requirements of energy and nutrients. It produces a series of metabolic and functional changes in the body. There are multiple limitations in the classic parameters for nutrition assessment including body mass index, weight loss, food intake, or standard laboratory parameters such as albumin or lymphocytes. We can establish some points of interest in this new approach to nutrition focused on the assessment of nutritional status by evaluating changes in composition and function using parameters such as PhA and other electrical measurements of bioimpedance, dynamometry, functional tests, muscle ultrasound, or laboratory parameters such as CRP/prealbumin.

Each of these parameters has a number of uses and limitations that should be understood when evaluating its ability to diagnose malnutrition as related to disease, its concordance with other tests, and its prognostic value. Emerging nutritional parameters for future use should be sensitive, specific, and interrelated to allow a better understanding of each patient's status at different time points during their disease.

Keywords:

Disease-related malnutrition. Body composition. Phase angle. Muscle strength. Ultrasonography. Functional tests.

Resumen

La malnutrición relacionada con la enfermedad representa un disbalance entre el aporte y los requerimientos de energía y nutrientes, que produce una serie de cambios metabólicos y funcionales a nivel corporal. Existen múltiples limitaciones de los parámetros clásicos de valoración nutricional, como el índice de masa corporal, la pérdida de peso, la ingesta o los parámetros analíticos clásicos, como es el caso de la albúmina o los linfocitos. Sugerimos un nuevo enfoque de la nutrición clínica centrado en la valoración del estado nutricional del paciente evaluando los cambios de composición y función con nuevos parámetros como el ángulo de fase y otras medidas eléctricas de la bioimpedanciometría, la ecografía nutricional©, los nuevos parámetros analíticos como el cociente PCR/prealbúmina, la dinamometría o los test funcionales.

Cada uno de estos parámetros tiene una serie de utilidades y limitaciones que es importante conocer a la hora de evaluar su capacidad de diagnosticar la desnutrición relacionada con la enfermedad, la concordancia con otros tests y su valor pronóstico. La nueva visión global de la nutrición clínica debería integrar diferentes aspectos de composición y función del organismo para poder establecer un diagnóstico más preciso de la situación nutricional y un plan terapéutico individualizado. Los parámetros nutricionales emergentes deben ser sensibles y específicos, y estar relacionados entre sí, de forma que permitan un mejor conocimiento de la situación particular de cada paciente en los diferentes momentos evolutivos de su proceso patológico.

Palabras clave:

Malnutrición relacionada con la enfermedad. Composición corporal. Ángulo de fase. Fuerza muscular. Ultrasonografía. Test funcionales.

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INTRODUCTION

Disease-related malnutrition (DRM) represents an imbalance between energy and nutrient intake, and energy and nutrient requirements, leading to metabolic and functional changes that usually are hardly noticeable in early stages but can be assessed as changes in nutritional status and body composition (BC) markers during the course of disease (1). The Global Leadership Initiative on Malnutrition (GLIM) was convened in order to respond to the needs of the clinical nutrition and medical communities, with global reach, to focus on standardizing the clinical practice of DRM diagnosis. It is a two-step model. The assessment for diagnosis and DRM severity grading was based on five top-ranked criteria, including three phenotypic criteria (non-volitional weight loss, low body mass index, and reduced muscle mass) and two etiologic criteria (reduced food intake or assimilation, and inflammation or disease burden) (2).

These phenotypic and etiologic criteria can be useful in clinical practice to diagnose complex clinical situations such as cachexia and sarcopenia, and to support the management of these pathologies. As a result of the development of these criteria, the American Society for Parenteral and Enteral Nutrition (ASPEN) conducted a systematic review to validate BC methods (3). Morphological and functional criteria need to be evaluated within this classification for a better understanding of their clinical utility. There are other reference methods for BC assessment such as dual-photon X-ray absorptiometry (DXA) (4), but the technique is expensive and difficult. These limitations reduce its use in clinical practice.

Classic bioelectrical impedance analysis (BIA) estimates BC indirectly based on predictive equations, which limit its clinical use. Multi-frequency spectroscopic and segmental BIA devices open up a range of possibilities for other measurements such as monitoring body fluids. Vectorial BIA provides raw electrical values: impedance (Z), resistance (Rz), reactance (X_C), and phase angle (PhA). Its direct application or vector representation have proven useful to assess BC changes in the short term, and act as a specific nutritional status marker, nutritional prognostic indicator, and morbidity and mortality risk indicator (5-7). In this sense, PhA provides a measurement for energy (electrical) changes, which is related to cell function and the composition of the internal environment, not from a molecular point of view but from a bioelectric one. Changes in cellular and tissue bioenergy are sensitive to nutritional and metabolic changes, and therefore provide comprehensive information about tissue composition and functionality.

The use of ultrasound for the morphological and structural study of muscle mass is to determine muscle architecture parameters such as muscle thickness, fascicle lengths, and pennation angles (8). Ultrasound has the advantage of being relatively affordable, is portable, and produces no ionizing radiation. More clinical research is needed to help establish evaluation patterns for ultrasound results that correlate with morbidity and mortality outcomes and other health indicators. We need to classify adipose tissue to complete BC assessment as the second component of fat mass (FM). In this sense, publications have been referenced with subcutaneous adipose tissue (SAT) at the level of the femoral area with muscle studies, and in the abdominal area with the possibility of evaluation of subcutaneous and visceral fat (9).

Classic laboratory data need to be adapted to more specific biomolecular markers that assess nutrition, inflammation (CRP/prealbumin), metabolic changes, etc. Functional assessment is always necessary not only for nutritional diagnosis but also to assess functional changes (10). Nowadays, estimated muscle strength using handgrip dynamometry should complement nutritional status assessments. Global assessments of body function remain to be systematized. Functional tests such as the Timed Up and Go (TUG) test, Gait Speed, or the Barthel Index (BI) should be included in nutritional assessments as they complement BC data (11).

It would be important, in this regard, to consider the incorporation of parameters for nutritional assessment that should be practical, sensitive, and specific, as well as reproducible in patient follow-up. In addition, these parameters should be convergent with other diagnostic tools for malnutrition, as well as capable of predicting clinical prognosis. We must provide a global view of all these techniques rather than the contribution of each one, that is, a morphofunctional assessment of DRM as a whole. The fundamental value of these techniques is their incorporation into routine clinical practice.

The most commonly used parameters of nutritional interest in clinical practice and their evolution are described in the figure below (Fig. 1). Some of them have been clearly established, classic nutritional parameters such as weight loss, BMI, skinfolds, circumference measurements, albumin, lymphocytes, cholesterol, and food intake, while other novel parameters for clinical nutrition are now emerging, and their introduction into clinical practice is generating an increasing amount of interest, such as BIA and PhA measurements, nutritional ultrasound, CRP/prealbumin, dynamometry, and functional tests.

Many of the classical parameters have a different diagnostic value in DRM. These parameters are included in most DRM screening tools and assessment tools (MUST, MNA, NRS-2002, SGA, etc.). For example, albumin is a global marker of morbidity and mortality that correlates with disease severity but loses specificity when considered of purely nutritional value. On the other hand, intake assessment with sensitive techniques applicable to clinical practice is a fundamental factor in the detection of DRM,

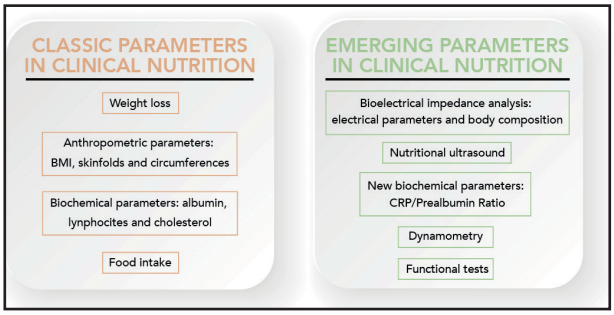

Figure 1.

Evolution of parameters for nutritional assessment. Source: own elaboration.

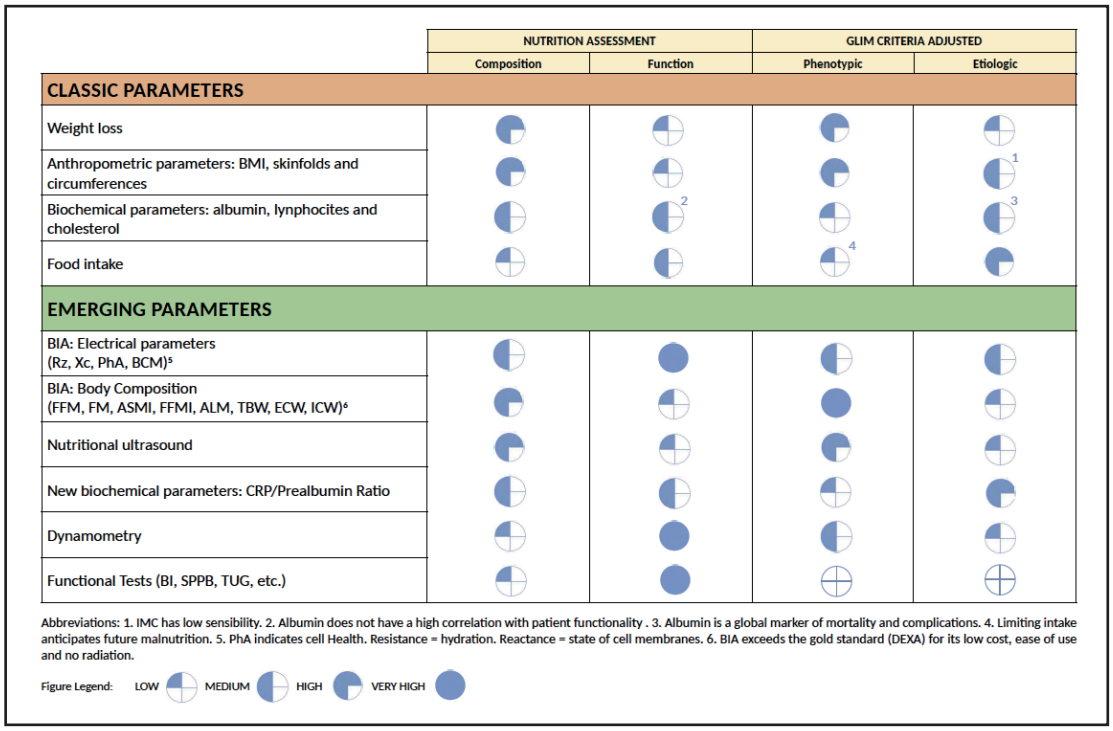

Figure 2.

Morphofunctional parameters in the diagnosis of DRM and their possible application, adapted to the recent GLIM criteria. Source: own elaboration.

and must be understood as an essential part of the diagnostic criteria (GLIM CRITERIA) (2).

The aim of this publication is a narrative review of all the potentially useful parameters for nutritional assessment, with a practical contextualization of commonly used tools in clinical practice, and an assessment of present and future application options.

MORPHOFUNCTIONAL PARAMETERS IN CLINICAL NUTRITION

The definition, usefulness, and limitations of the most commonly used parameters of nutritional interest in clinical practice are described throughout the article.

These morphofunctional parameters in the diagnosis of DRM could be applied to the recent GLIM criteria, contributing to measure some different etiologic and phenotypic criteria as described in figure 2.

CLASSIC PARAMETERS IN CLINICAL NUTRITION

WEIGHT LOSS

Weight is the simplest method, and is important, to assess nutritional status but is not sensitive enough for the early detection of DRM (12). The clinical use of weight loss is important when screening patients for risk of DRM, as well as for DRM diagnosis and to estimate nutritional requirements (13). According to the GLIM criteria, losing more than 5 % of body weight within 6 months, or more than 10 % beyond 6 months (2), is one of the phenotypic criteria used to diagnose DRM.

There are several potential limitations such as: lack of information about usual weight, presence of oedemas, or other alterations in hydration status (12,14). Involuntary weight loss is a key parameter for nutritional assessment as it indicates a negative energy balance (15). It should be a required value in a patient's medical record.

ANTHROPOMETRIC PARAMETERS: BODY MASS INDEX, SKINFOLDS, AND CIRCUMFERENCES

Body mass index (BMI) (16) is calculated by taking a patient's weight in kilograms and dividing it by their height squared in meters (BMI = weight [kg] / height [m^2]).

BMI is an anthropometric measure used for defining DRM cut-off points, using BMI values < 20 kg/m^2 for people under 70 and < 22 kg/m^2 for patients over 70 years of age (17). Based on the GLIM criteria, severe DRM corresponds to BMI values < 18.5 kg/m^2 in people under 70 and < 20 kg/m^2 in patients over 70 years of age (2).

BMI has low sensitivity for the early detection of DRM (21 % sensitivity and 95 % specificity) (12). Furthermore, it has been observed that catabolic patients may lose more than 10 % of their weight over 3-6 months and have BMI values above the normal range (17). It is a required parameter in nutritional assessment, but it is not an exclusion criterion for diagnosing DRM (18).

Skinfolds and muscular circumferences are useful at the individual level but are limited due to the difficulties inherent in extrapolating a clinical result and its variability during short-term follow-up. They provide a measure of the depletion or excess of adipose tissue and the muscular protein compartment, but indirectly and always in relation to BMI (12,19).

BIOCHEMICAL PARAMETERS: ALBUMIN, LYMPHOCYTES, AND CHOLESTEROL

Biochemical parameters such as albumin, lymphocytes, and cholesterol are general health markers that provide indirect information about nutritional status due to their correlation with whole-body protein, energy status, or nutrient balance. Albumin, the main visceral protein, is the most established marker because of its high correlation with morbidity and mortality in different clinical situations (20,21). These biomarkers are exposed to many interferences from inflammatory processes since many of them behave like acute phase reactants in them (21).

Total lymphocyte count and low cholesterol levels, which are usually included in automated screening methods, show an indirect correlation with energy restriction and are included in different DRM diagnostic and coding systems (22,23). However, they are not included in the GLIM criteria for the diagnosis of DRM (2).

FOOD INTAKE

An insufficient nutrient intake is an etiologic factor for DRM during illness due to different factors, as reported in the GLIM criteria (2). Food intake is determined with the use of categories to measure the amount of food eaten by patients during a period of time. Quartiles of intake is the most frequent semi-quantitative method used in different diagnostic test approaches, and is useful when setting therapeutic guidelines for the nutritional support required (24,25). Food intake assessment methods require collaboration by patients.

Lack of intake is the presumption of future DRM. Anorexia is one of the main symptoms associated with disease. This factor and increased requirements due to the inflammatory process cause intake restriction, which can lead to DRM.

EMERGING PARAMETERS IN CLINICAL NUTRITION

There are emerging techniques that provide information in the analysis of BC and functionality such as BIA and PhA measurements, nutritional ultrasound, CRP/ prealbumin, dynamometry, and functional tests. These techniques are accessible to routine clinical practice. On the other hand, there are other standardized techniques to measure BC that are focused on research studies such as DXA and Computed Tomography (CT). These emerging techniques are exploration techniques that can be applied as many times as needed to assess nutritional status, are not invasive, and do not pose any risks to patients from ionizing radiation, which does not imply that we can use DXA and CT techniques whenever they are available. The difference is that these emerging techniques cannot be planned prospectively for the clinical course of patients in clinical nutrition.

BIOELECTRICAL IMPEDANCE ANALYSIS

BIA is a classic BC technique. However, for years the direct bioelectric data that avoid the bias and errors introduced by formulas and equations have not been studied in depth. In recent years, the analysis of bioelectric data has been re-emerging due to its correlation with prognostic factors and its non-dependence on predictive formulas.

BIA results can be divided into BC electrical parameters and laboratory indices. Each one of these areas focuses on different aspects of BC and function. Bioelectric parameters are raw measures obtained with the direct measurement without interference of anthropometric factors such as weight or age. BC parameters are based on the application of predictive equations for the calculation of the different fat free mass (FFM) and FM compartments, adjusted for clinical variables. This point is important due to the possibility of error and inaccuracies derived from the use of predictive formulas or their application in a specific clinical area.

The global and muscular indices obtained by recalculation of bioelectrical and clinical parameters contribute more information to the clinical course of specific aspects such as muscle structure and function, or the degree of hydration or nutrition of the body. Different formulas determine varying results between measurements, with a possible interference of anthropometric and clinical factors.

This emerging technique has a number of limitations that are inherent in the measurement technique and the characteristics of the different devices with their bioelectric measurement plates. The most important biases also affect measurement protocols with the possibility of intra- and inter-observer bias. They are not widely used techniques in nutrition units due to the limited number of normal population references (percentile tables by age and sex) and of individualized cut-off points for each pathology in order to enable clinical decision-making (3).

BIA electrical parameters

BIA is an indirect method to measure BC, based on the human body's ability to conduct electricity. The current is transmitted through liquids and electrolytes, while fat and bone are not really

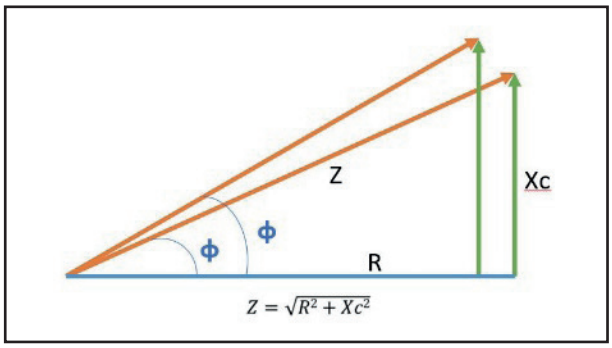

Figure 3.

Graphical representation of impedance components: Xc: reactance; Z: impedance; Rz: resistance; ϕ: phase angle. Source: own elaboration.

conductors (26,27). Through raw impedance parameters, such as Rz and Xc, the PhA can be obtained (PhA = arc tangent (Xc / R) x 180 ° / π). By definition, PhA is positively associated with tissue reactance (associated with cell mass, integrity, function, and composition) and negatively associated with resistance, which depends mainly on the degree of tissue hydration (26,27) (Fig. 3).

At present, BIA is probably the most widely used method to study BC in different contexts, mainly because of its low cost, because it is easy to use and transport, and because inter-observer variability is lower than with other techniques (6,25). PhA is considered a good indicator of cell integrity and has been proposed as a nutritional status marker for adults and children after having been studied in the setting of numerous pathologies. It has also been proposed as a useful prognostic marker for several clinical conditions. Several authors also suggest that it may be a useful tool to evaluate the progression of disease. In general, lower levels of PhA suggest a worse prognosis and greater morbidity and mortality (28,29).

In healthy populations, PhA varies physiologically depending on sex, age, BMI, and race. Several authors have studied the reference values for PhA according to variables in healthy populations, and they are between 5.5 and 9 ° (30). At present, the absence of reference values for the Spanish healthy population and for different pathologies limit its use in everyday clinical practice. It is important to follow the protocol for measuring and positioning the patient.

BIA and body composition

There are different aspects in the analysis of BC by BIA. There is the analysis of water and BC and, on the other hand, the measurements and muscle indexes that are of great interest in the GLIM criteria (2).

BIA BC data provide information about the different body compartments (FFM and FM) and also about hydration: total body water (TBW), extracellular water (ECW), and intracellular water (ICW). We can also obtain direct muscle data such as Appendicular Skeletal Muscle Index (ASMI), Fat Free Mass Index (FFMI), and Appendicular Lean Mass (ALM). All of these parameters have are high-value because they focus on the distribution of body compartments with great relevance in nutritional assessment. GLIM recommended cut-off values for muscle mass reductions from the European Working Group on Sarcopenia in Older People (EWGSOP), and from The Foundation of National Institute of Health (FNIH) initiative and the Asian Working Group on Sarcopenia (AWGS) (2).

The global indices provide information about different aspects as adapted to clinical practice.

NUTRITIONAL ULTRASOUND

The use of ultrasound is an emerging technique that is based on the application of ultrasound to determine the surface of muscle tissue. Particularly, ultrasound analysis allows us to measure key muscle architecture parameters such as muscle thickness, fascicle length, and pennation angles (8).

Muscle ultrasound techniques

Most studies focus their attention on the rectus femoris muscle of the quadriceps or on combinations of muscle groups that involve major muscle bundles with an important functional role on the patient's gait or basic activities of daily living (BADLs). Measurement of the rectus femoris muscle of the quadriceps is one of the most widely used approaches because of its correlation with force and functional execution or performance tests (31).

Currently, all definitions of DRM include its effect on muscle mass measurements; however, there is not just one assessment method. Classic imaging techniques such as DXA, computed tomography, and magnetic resonance imaging are considered "gold standards" but their clinical application is difficult under routine conditions (8,32).

Adipose tissue ultrasound techniques

Ultrasound techniques to assess adipose tissue (FM compartment) in clinical nutrition evaluate subcutaneous (superficial and deep-layer) and visceral adipose tissues (Hamagawa's technique) (9). Figure 4 describes the available nutritional ultrasound techniques.

The clinical utility of this technique is to assess fat distribution and correlate this with clinical variables. Each type of adipose tissue may be related to different functions. The superficial subcutaneous fat layer is related to energy reserve. The deep subcutaneous fat layer may play a role in neuroendocrine regulation via the secretion of adipokines (adiponectin). The preperitoneal visceral adipose tissue is a visceral ectopic tissue, the equivalent of hepatic steatosis and other pathological adipose tissues. The clinical value of visceral deposits is related to metabolic manifestations such as diabetes or atherosclerosis.

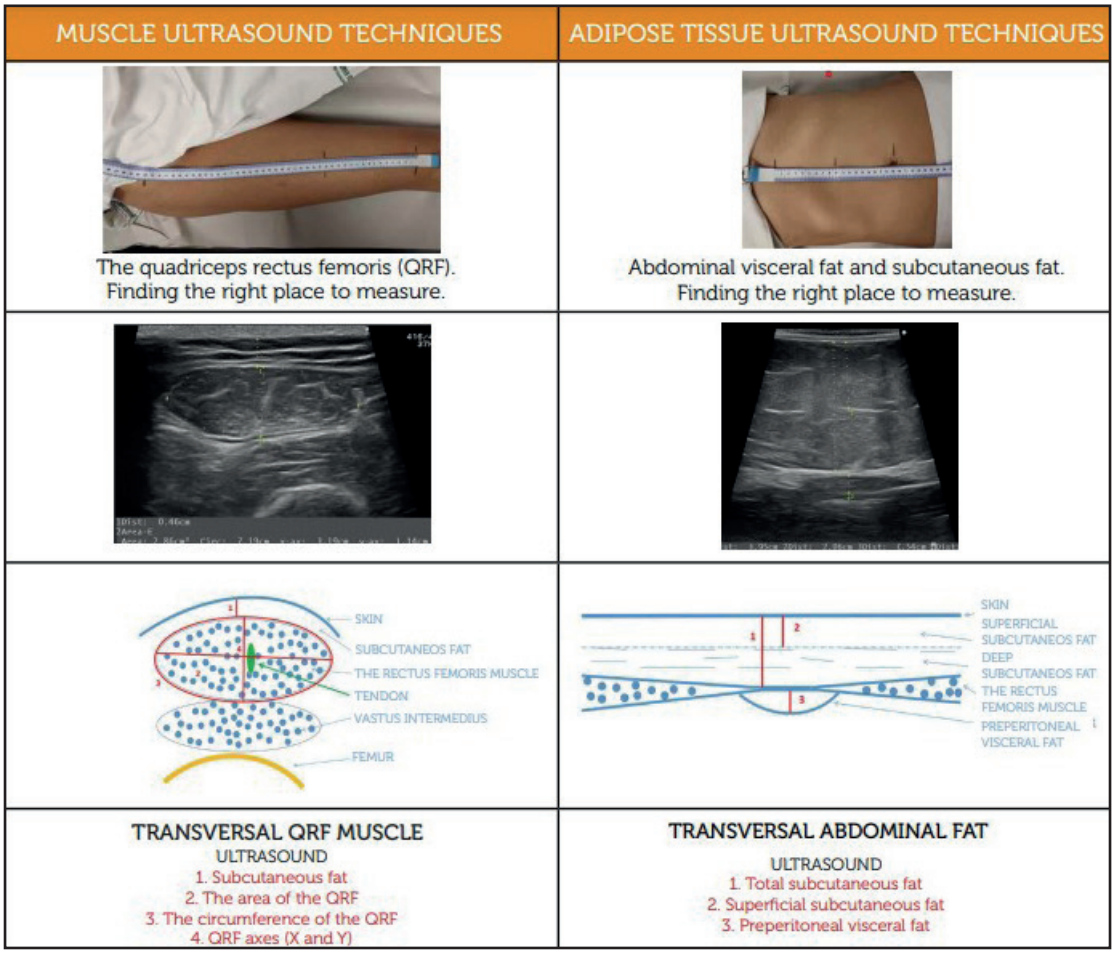

Figure 4.

The techniques of nutritional ultrasound. Source: own elaboration.

Ultrasound has the advantage of being relatively affordable and portable, and produces no ionizing radiation. Several studies have confirmed the reliability of this technique to measure the size of the quadriceps muscle in a healthy population. Studies have been published on the reliability of rectus femoris ultrasound measurements with an intraclass correlation coefficient (ICC) of 0.97 (95 % CI: 0.92-0.99) for test-retest reliability of this technique (33). A femur muscle area below 5.2 is associated with frailty, which involves a worse survival prognosis (34). There are also studies on the application of ultrasound measurements in clinical practice for the nutritional assessment of different pathologies, for example in critical patients (35) and the elderly (36).

The main limitation is the uniform application of this measurement in clinical practice, or the recommendations for evaluating nutritional status. More clinical research is needed to help establish evaluation patterns for ultrasound results that correlate with morbidity and mortality outcomes and other health indicators.

There are other morphofunctional techniques such as CT, magnetic resonance imaging, and DXA that have been shown in multiple studies to have high precision and reliability (37), and provide diagnostic values for the evaluation of muscle mass and sarcopenia with an association with morbidity and mortality (38), especially in cancer patients, since they provide images that are used for the planning of radiotherapy treatment (39); however, they have the limitation of poor applicability in clinical practice because of limitations such as exposure to ionizing radiation, and need for specific skills and knowledge of anatomy to interpret results, in addition to limited availability and high cost. The objective of this narrative review is to analyze DRM screening and diagnostic techniques that can be implemented in routine clinical practice.

BIOCHEMICAL PARAMETERS: CRP/PREALBUMIN RATIO

Prealbumin, a protein that transports thyroxine, is much more sensitive to any changes in whole-body protein status than albumin and transferrin, because it has a very short half-life (2-3 days). Unlike albumin, hydration status does not affect prealbumin (40).

Its association with ultra-sensitive C-reactive protein (CRP) levels, a pure marker for inflammation in the body, may increase its interest as a predictor of morbidity and mortality, and of nutritional/inflammatory changes (21,41).

Prealbumin is considered by some scientific societies the best laboratory protein parameter to monitor nutritional status and its therapeutic changes (13). As with the rest of plasma proteins, infections and other acute inflammation processes can interfere with its results (42). In critical patients a cut-off point of > 0.24 for the CRP/prealbumin ratio (CRP mg/dL / prealbumin mg/dL) has been found to be a predictor of mortality and of hospital stay extension (43,44).

More prospective studies are needed to provide cut-off points, involving therapeutic approaches with clinical benefits for patients.

DYNAMOMETRY

Dynamometry is a functional method to assess muscle strength that measures handgrip strength. It is easy and quick to carry out. It has good reproducibility and a high sensitivity and specificity for the prediction of post-surgical complications, stay in hospital, higher rate of readmissions, and a decline in physical condition (12,45,46).

Dynamometry has become a general marker for nutritional status and is being used as a variable result in nutritional interventional studies (46). This parameter is very sensitive to re-nutrition changes, which is why it is very useful when monitoring the effects of nutritional therapy even in the short or medium term (12).

Jamar® dynamometers are most widely used in international studies, and have several handle positions. Measurements obtained must be compared with population average values according to age and sex in tables. Sánchez et al. have published, in their epidemiological study "Pizarra", the reference values for dominant hand muscle strength for this type of dynamometer in a Spanish population to assess DRM. Apart from this, they concluded that hand grip dynamometry is associated with lean mass (LM), which confirms its usefulness in nutritional assessment (47).

It should be noted that hand grip strength measurements are an indicator of upper limb strength and, even if they have predictive potential, they should not replace the evaluation of activities of daily living (ADLs), the strength of lower limbs, or gait speed in fragile populations such as the elderly or patients suffering from neuromuscular disorders (46).

There are some limitations related to hand grip measurements; for example, there are no measurement protocols. Another limitation is that they require the collaboration of the patient (45). However, key application scenarios are still to be defined for nutritional screenings as a diagnostic measurement or for monitoring nutritional recovery.

FUNCTIONAL TESTS

Functionality can be measured through self-reported scales or rating scales based on the reports of others, or through objective performance or execution tests. Basic activities of daily living (BADLs) include self-care, mobility, and transfer activities, which are mainly necessary to maintain independence at home (48).

The BI (also known as The Maryland Disability Index) is one of the best scales to assess BADLs (49). Studies have shown that patients at risk of DRM or with DRM show a decline in ability to perform BADLs, resulting in greater functional dependence (50). BI provides measurements that are easy to apply and interpret with a high degree of reliability and validity. In addition, it can be adapted to different cultural environments, and is useful to monitor the progress of patient functionality (49).

TUG test measures the time a patient takes to rise from a chair, walk 3 meters, turn, walk back, and sit down again (51). This is a quick test, easily included in clinical practice, that requires no special training for the staff in charge, provides good inter-observer and intra-observer reliability, has adequate validity, and can predict fall risks with a sensitivity and specificity higher than 80 % (48).

A functional diagnosis of patients is important for DRM. This should include evaluating their activity and monitoring any clinical changes over time in order to implement therapies to improve balance, stability, and gait to reduce dependence and/or disability. In the end, the ultimate purpose is the patient's functional recovery, with positive changes in weight, FM, FFM, and functionality.

CONCLUSIONS AND FUTURE LINES OF RESEARCH IN THE FIELD OF CLINICAL NUTRITION

In clinical nutrition, due to the absence of universally accepted criteria to define DRM based on standard parameters that may be applied to clinical practice, it has become essential to establish lines of research to provide results that help implement a clinically accurate approach, based on final health outcomes. The loss of LM affects the clinical outcome of both acute and chronic illnesses, and as such, its assessment is of particular interest in clinical nutrition. The application of emerging techniques such as BIA and nutritional ultrasound is becoming increasingly important for nutritional status assessment.

Regarding BIA, despite its being an indirect method and having limitations in obese patients with BMI > 35 kg/m^2 and other populations, evolution towards multifrequency devices, the introduction of specific software, and most particularly the assessment of raw parameters such as PhA allow a direct approach to cell function and health status measured as body cell mass (BCM) and both intracellular and extracellular hydration status (52). Considering PhA, there are at least 19 clinical trials in subjects with different pathologies: cancer patients, critically-ill patients, elderly patients, patients with amyloidosis, etc., which explore the future application of this parameter for studying and monitoring patients in clinical practice (see at https://clinicaltrials.gov/; condition or disease: phase angle).

It is necessary to perform a standardization of imaging techniques such as nutritional ultrasound and CT to establish refer-

ence values and critical points for decision-making. On the other hand, more prospective studies are needed to assess its prognostic value in the field of nutritional intervention for DRM in order to evaluate response times and to describe the minimum clinically significant change in all these parameters. These techniques must be correlated with other classical parameters of nutritional assessment already established that provide nutritional prognostic value (e.g., subjective global assessment, SGA).

Functional changes in clinical nutrition must be studied in depth as they are closely related to health outcomes. Some studies are being conducted regarding hand dynamometry, TUG testing. and other functional tests to evaluate the role nutritional intervention plays in a patient's functional recovery.

In the future, specific biochemical markers for muscle proteins, adipose tissue, and different metabolic pathways that provide information on DRM and inflammation status shall be equally validated. It is necessary to develop an expert positioning on the applicability of these techniques and their incorporation into routine clinical practice.

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ARÁN

Nutrición Hospitalaria

Revisión

Inmunonutrición del paciente quirúrgico en los procedimientos *fast-track:* revisión de la evidencia y algoritmo adaptado

Immunonutrition in fast-track surgical patients — Evidence review and adapted algorithm

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Resumen

El estrés quirúrgico predispone a los pacientes a la disfunción inmune y a un mayor riesgo de infección. Los pacientes quirúrgicos desnutridos presentan una mayor morbimortalidad posoperatoria, mayores tasas de reingreso y costes hospitalarios más elevados. En las guías de la ESPEN se asocia el uso de una fórmula inmunomoduladora a una reducción significativa de los problemas de la cicatrización de heridas, de los fallos de la sutura y de las complicaciones infecciosas y globales. Varios autores han sugerido que, dado que la mayoría de los ensayos clínicos que evalúan la eficacia de la inmunonutrición se han realizado en un entorno perioperatorio tradicional, sería interesante investigar su eficacia en un entorno más controlado, como en el protocolo ERAS (*Enhanced Recovery after Surgery*). El objetivo de este trabajo es: a) definir el papel que debe jugar la inmunonutrición en los protocolos ERAS sobre la base de la mejor evidencia científica; b) analizar las dificultades que siguen existiendo en la práctica clínica real para realizar el cribado del riesgo nutricional del paciente; c) proponer unos algoritmos adaptados a las características de nuestro entorno sobre el cribado, la valoración y el tratamiento nutricional del paciente quirúrgico en modalidad *fast-track.*

Palabras clave:

Nutrición enteral. Inmunonutrición. Inmunomodulación. Protocolo ERAS. Cirugía.

Abstract

Surgical stress predisposes patients to have immune dysfunction and an increased risk of infection. Malnourished surgical patients have higher postoperative morbidity and mortality rates, higher readmission rates, and higher hospital costs. The use of an immunomodulatory formula is associated in the ESPEN guidelines with a reduction in wound healing problems, suture failure, and infectious and global complications. Several authors have suggested that, since most clinical trials evaluating the efficacy of immunonutrition have been carried out in a traditional perioperative setting, it would be interesting to investigate its efficacy in a more controlled setting, such as in the ERAS (Enhanced Recovery after Surgery) protocol. The objective of this work was: a) to define the role that immunonutrition should play in ERAS protocols based on the best scientific evidence available; b) to analyze the difficulties that continue to exist in real-life clinical practice to screen the nutritional risk of patients; c) to make a proposal of algorithms adapted to the characteristics of our environment regarding the screening, assessment, and nutritional treatment of surgical patients in fast-track surgery.

Keywords:

Enteral nutrition. Immunonutrition. Inmmunomodulation. Enhanced Recovery After Surgery protocol. Surgery.

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INTRODUCCIÓN

El estrés quirúrgico predispone a los pacientes a la disfunción inmune y a un mayor riesgo de infección. Este riesgo es aun mayor cuando el paciente está desnutrido antes de la agresión quirúrgica (1-2). Un estado nutricional subóptimo predice, de manera independiente, peores resultados posquirúrgicos, y los pacientes quirúrgicos desnutridos presentan una mayor morbimortalidad posoperatoria, mayores tasas de reingreso y costes hospitalarios más elevados (3).

A lo largo de las últimas décadas se han estudiado diversas estrategias nutricionales con la finalidad de paliar los efectos de la desnutrición sobre la función inmunitaria y prevenir la aparición de complicaciones en el paciente quirúrgico. Una de estas aproximaciones es la inmunonutrición.

La inmunonutrición se define como "la administración de nutrientes que tienen efectos tanto nutritivos como farmacológicos, con la finalidad de contrarrestar la desnutrición y la disfunción inmune" (4). Cuando esos nutrientes se administran en cantidades superiores a las fisiológicas con el objetivo de inducir efectos farmacológicos, pasan a ser denominados inmunonutrientes (4). Los inmunonutrientes que se han estudiado con mayor profundidad aparecen en la tabla I.

Sin embargo, es importante tener presente, además de los inmunonutrientes y para asegurar el beneficio clínico, otros factores como el momento de la administración (pre-peri-posoperatorio) o la duración del tratamiento, que también van a influir en la eficacia de la intervención (3). Al mismo tiempo, los inmunonutrientes administrados de manera aislada no han logrado el mismo nivel de eficacia clínica que los estudios que combinan varios inmunonutrientes en una concentración determinada, sugiriendo: a) que se produce una acción sinérgica entre ellos (3,5) y b) que algunas formulaciones son más eficaces que otras en la prevención de complicaciones posteriores a la cirugía.

Toda esta complejidad inherente a la inmunonutrición se suma a la ya existente para mantener al paciente adecuadamente nutrido en el entorno perioperatorio; por ejemplo, en sus dos primeras semanas de estancia en la UCI, el paciente crítico quirúrgico recibe tan solo el 50 % de las calorías pautadas por su médico (6).

Se ha demostrado que una terapia nutricional perioperatoria adecuada mejora específicamente los resultados de la cirugía gastrointestinal oncológica, donde se dan las tasas más elevadas de desnutrición basal (aparece hasta en un 65 % de los casos). Las guías ESPEN recomiendan la administración perioperatoria, o al menos posoperatoria, de fórmulas específicas enriquecidas con inmunonutrientes (arginina, ácidos grasos omega-3 y ribonucleótidos) a los pacientes desnutridos sometidos a una cirugía mayor oncológica. Y el uso de una fórmula inmunomoduladora se asocia a una reducción significativa de los problemas de cicatrización de las heridas, de los fallos de las suturas y de las complicaciones infecciosas y globales (7).

Las intervenciones nutricionales (pre y posoperatorias) tienen un papel clave en todos los pacientes quirúrgicos en general, y pueden mejorar los propios resultados quirúrgicos, así como reducir la morbilidad infecciosa y la mortalidad (8), y mejorar la cicatrización de la herida quirúrgica (9). También se ha identificado la ingesta oral precoz como determinante independiente de la recuperación temprana después de numerosos tipos de cirugía mayor abdominal (3).

Varios autores han sugerido que, dado que la mayoría de los ensayos clínicos que evalúan la eficacia de la inmunonutrición se han realizado en un entorno perioperatorio tradicional, sería interesante investigar su eficacia en un entorno más controlado, como es el caso del protocolo ERAS (*Enhanced Recovery after Surgery*).

En nuestro país, en el año 2007 se creó el grupo multidisciplinar español de rehabilitación multimodal (GERM), cuyo principal propósito ha sido la realización de una guía de práctica clínica perioperatoria amparada en la medicina basada en la evidencia científica, y que ha desarrollado la vía clínica de la recuperación intensificada en cirugía abdominal (RICA), al amparo del Ministerio de Sanidad (10).

Según las recomendaciones emitidas recientemente por las guías de cuidados perioperatorios en cirugía colónica electiva, según el protocolo ERAS, publicadas en la revista *World Journal of Surgery* en 2019, hay numerosos aspectos del protocolo que tienen que ver con la valoración e intervención nutricional, como el cribado y la valoración, y el soporte preoperatorio si se precisa, el ayuno preoperatorio y la sobrecarga de carbohidratos, el inicio precoz de la ingesta oral y el soporte posoperatorio y al alta, si es necesario (11).

Tabla I. Inmunonutrientes más estudiados en la bibliografía y su principal mecanismo de acción. Adaptada de Grimble y cols., 2005 (4)

Inmunonutriente	Principales mecanismos de acción
Ácidos grasos omega-3	Efecto antiinflamatorio al suprimir la producción de citocinas proinflamatorias; revierten la inmunosupresión
Aminoácidos azufrados (metionina, cisteína y derivados)	Mejoran las defensas antioxidantes a través de la síntesis de glutatión o la "protección" del glutatión disponible a través de la provisión de otros grupos sulfhidrilo para interactuar con las moléculas oxidantes
Glutamina	Nutriente esencial para las células inmunes; mejora la función de barrera intestinal y es un precursor no-sulfhidrílico del glutatión
Arginina	Precursor del óxido nítrico; mejora la función y el número de linfocitos T y estimula la producción de hormona del crecimiento
Nucleótidos	Precursores de ADN y ARN; mejoran la función linfocitaria

El objetivo del trabajo de este grupo multidisciplinar compuesto por cirujanos, anestesistas y endocrinólogos expertos en nutrición, todos ellos con conocimiento y experiencia previa en los protocolos ERAS o *fast-track*, es triple:

1. Definir el papel que debe jugar la inmunonutrición en los protocolos ERAS sobre la base de la mejor evidencia científica.
2. Analizar las dificultades que siguen existiendo en la práctica clínica real para realizar el cribado del riesgo nutricional del paciente.
3. Proponer unos algoritmos adaptados a las características de nuestro entorno para el cribado, la valoración y el tratamiento nutricional del paciente quirúrgico en modalidad *fast-track*.

MATERIAL Y MÉTODOS

El presente trabajo ha sido realizado por un equipo multidisciplinar de 8 miembros, especialistas en anestesiología y reanimación, en cirugía general y en endocrinología y nutrición. A continuación se detallan las fases que se han seguido a fin de conseguir los objetivos propuestos.

ESTRATEGIA DE BÚSQUEDA BIBLIOGRÁFICA

Se realizó una búsqueda en la base de datos PubMed® con el objetivo de identificar aquellos artículos relevantes publicados en los 10 años anteriores al momento de la búsqueda (periodo: julio de 2009 a julio de 2019). La búsqueda incluía los términos "*immunonutrition*", "*ERAS"*, "*enhanced recovery*" y "*fast track*" como palabras clave, así como *Medical Subject Headings* (MeSH), resultando en 161 resultados. Se incluyeron también en el análisis 13 guías de práctica clínica relevantes de las principales sociedades científicas implicadas.

SELECCIÓN DE ESTUDIOS

Se realizó un cribado de los resultados a partir de los títulos y resúmenes, excluyendo aquellos resultados duplicados o correspondientes a publicaciones fuera del alcance de la revisión, resultando en 86 publicaciones. Los criterios de inclusión y exclusión de estudios fueron los especificados en la tabla II.

Se obtuvo el texto completo de todas las publicaciones y se eliminaron 2 por corresponder a análisis retrospectivos, incluyéndose finalmente en el análisis 84 publicaciones. El esquema correspondiente al flujo de selección y exclusión de publicaciones se muestra en la figura 1.

Los ensayos clínicos aleatorizados incluidos en la revisión pueden consultarse en el anexo I.

ANÁLISIS Y EVALUACIÓN DE LA BIBLIOGRAFÍA

Se examinaron, revisaron y calificaron las publicaciones resultantes, tabulando la información y las características de todos los candidatos mediante un formulario de extracción de datos que contenía: características básicas de cada estudio (primer autor, año de publicación, tamaño de la muestra, edad de los participantes), diseño del estudio (aleatorización, control, cegamiento, brazos del ensayo), intervención (elementos incluidos en la fórmula de inmunonutrición, duración del soporte nutricional, momento pre, peri o posoperatorio), resultados de interés (resultados clínicos, indicadores inmunológicos y bioquímicos, etc.) y, finalmente, sesgos y limitaciones del estudio. La calidad metodológica de los ensayos clínicos se evaluó cuantitativamente según

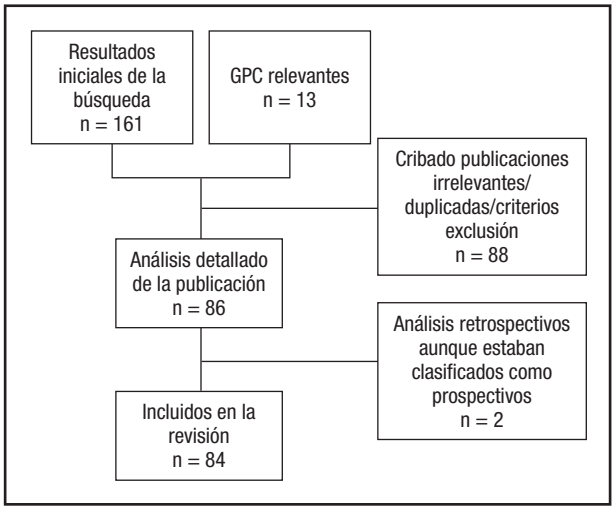

Figura 1.

Esquema resumen de la selección y exclusión de los resultados bibliográficos de la revisión.

Tabla II. Criterios de inclusión y exclusión de publicaciones en la revisión

Criterios de inclusión	Criterios de exclusión
– Trabajos prospectivos o metaanálisis – Publicados en español o inglés – Cirugía de cabeza y cuello, gastrointestinal, urológica y ginecológica – Estudios con fórmulas enriquecidas con inmunonutrientes	– Estudios en los que los inmunonutrientes se administraban de manera aislada (fuera de una fórmula) o fuera de la práctica clínica habitual – Estudios en pacientes oncológicos que, además de cirugía, incluían radioterapia y/o quimioterapia concomitante – Vía parenteral

el sistema de puntuación de calidad Jadad-Oxford (12). Para la evaluación cualitativa de las recomendaciones se siguieron las pautas de adaptación del sistema de calificación de recomendaciones, evaluación, desarrollo y evaluación (GRADE) formuladas por la ASPEN (13).

REFLEXIÓN EN EL CONTEXTO SANITARIO Y CREACIÓN DEL ALGORITMO

El análisis de las dificultades que siguen existiendo en la práctica clínica real para realizar el cribado del riesgo nutricional del paciente y la propuesta de algoritmos adaptados se llevaron a cabo usando la metodología *Design Thinking*, que ya se ha utilizado anteriormente en el diseño y optimización de intervenciones y flujos clínicos (14). En concreto, se utilizó la técnica del *Journey Mapping* para identificar los puntos de mejora en el viaje que realiza el paciente y los puntos de encuentro (y desencuentro) con los profesionales médicos, y se empleó el *Concept Development* para diseñar un algoritmo (15) que permitiera conseguir una valoración/intervención nutricional del paciente quirúrgico desde el mismo momento en que se decide la intervención, y continuar el proceso en la estrategia del protocolo *fast-track*.

METODOLOGÍA DE CONSENSO

La búsqueda de consenso entre los autores se sistematizó según una metodología Delphi mixta (16), exigiendo un porcentaje de consenso mínimo del 85 %.

RESULTADOS

RESULTADOS EN EL USO DE INMUNONUTRIENTES EN LA FASE PREOPERATORIA

Resultados obtenidos

Parámetros analíticos

Los parámetros analíticos en los que se mostraron beneficios se relacionaban con la inflamación y la respuesta inmune. Acerca de la inmunidad celular, se describió un menor descenso posoperatorio de los linfocitos CD4 (17) y una mayor proliferación estimulada de linfocitos y de diferenciación Th1/Th2 (18), sin evidencia de beneficios para la inmunidad humoral. En cuanto a la inflamación en los distintos momentos del posoperatorio, se han reportado niveles menores de PCR (19), prostaglandina E2 e interleuquinas en algunos, aunque no en todos los estudios (20). También se observaron mayores niveles de resolvina E1, mediador derivado de los omega-3 con efecto antiinflamatorio (21).

En el estudio con inmunonutrición asociada a polifenoles se evaluaba la capacidad antioxidante *in vitro*, objetivándose una mejoría en el grupo tratado (22).

Cuando se evaluó el perfil sérico de ácidos grasos, se demostró un mayor nivel de ácido eicosapentaenoico (EPA) y de la ratio EPA/ácido araquidónico (AA) (18,21) asociado a la inmunonutrición.

Otros beneficios observados aisladamente fueron unos niveles posoperatorios de transferrina mayores (22) y de transaminasas menores (19).

Parámetros clínicos

a) *Infección*
En cinco de los trabajos se ha mostrado algún beneficio estadísticamente significativo en cuanto a la reducción de las complicaciones infecciosas (7 *vs.* 28 %, p = 0,034 (17); 13,6 *vs.* 50 %, p = 0,028 (23); 40 *vs.* 75 %, p = 0,025 (21); 28 *vs*. 60 %, p = 0,023 (18); riesgo relativo (RR) = 0,5; intervalo de confianza: 0,31-0,93; p = 0,031 (24)), contemplándose dentro del total la infección del sitio quirúrgico y también los focos respiratorios y de cavidad abdominal y, solo en un caso, flebitis, infección urinaria o bacteriemia (23). Dentro de estos, en el trabajo de Fujitani y cols. (24), este beneficio significativo solo era aplicable a la infección de la herida quirúrgica y al subgrupo de pacientes con pérdida de peso superior al 5 % en 3 meses. En el estudio de Manzanares y cols. (23), la significación solo se alcanzó para las complicaciones menores y los pacientes con cirugía rectal. Además de estos resultados, se observó una tendencia no significativa hacia una menor necesidad de antibióticos para la infección de la herida quirúrgica en el estudio de Barker y cols. (25).
En los trabajos de Ruiz Tovar y cols. (19) y de Nagata y cols. (22), en cirugía bariátrica y donantes de hígado, respectivamente, no se produjeron complicaciones infecciosas en ninguno de los grupos. En el estudio de Hübner hubo una mayor tasa de infecciones en el grupo de inmunonutrición (20), sin significación estadística, y en los restantes dos estudios (26,27) no hubo diferencias significativas.
En cuanto a la duración del SIRS (*Systemic Inflammatory Response Syndrome*), solo el estudio de Okamoto y cols. (17) en el ámbito de la gastrectomía mostró beneficios del uso de las fórmulas (0,77 ± 0,90 días *vs.* 1,34 ± 1,45, p = 0,04). En los otros tres estudios que analizaron este dato en los ámbitos de la cirugía gastrointestinal, la gastrectomía y la duodenopancreatectomía (18,20,24), no se encontraron diferencias significativas.

b) *Complicaciones posquirúrgicas*
En ninguno de los estudios se demostró una reducción significativa de las complicaciones no infecciosas (17,18,21,25-27) o totales asociada a la inmunonutrición, incluyendo la fuga anastomótica. Sin embargo, en el estudio de Uno y cols. (21) se objetivó un beneficio en cuanto a la gravedad de las complicaciones totales según la clasificación de Clavien-Dindo (28).

c) *Estancia hospitalaria*
La estancia hospitalaria fue un parámetro evaluado en todos los estudios revisados. Únicamente en el estudio de

Uno y cols. (21), en el campo de la cirugía hepatobiliar, se mostró una reducción significativa de la estancia para el grupo de inmunonutrición frente al grupo no suplementado (36,9 ± 3,3 días *vs.* 53,9 ± 5, p = 0,006). En los restantes no se demostraron diferencias estadísticamente significativas.

d) *Morbimortalidad y supervivencia*
Los estudios describieron la mortalidad posoperatoria (no a largo plazo) y no se mostraron diferencias significativas en relación al tratamiento con inmunonutrición. Cabe mencionar que solo en cuatro de los trabajos se produjo alguna muerte (20,25-27), estando el dato más elevado en la cirugía pancreática, con 6 de 16 pacientes en el grupo de control y ninguno en el grupo de inmunonutrición, sin significación estadística.

e) *Costes*
Dos trabajos han evaluado los costes (23,25), sin encontrar diferencias significativas.

Resultados en relación con el estado nutricional

El estado nutricional de los pacientes analizados varió entre estudios y se reportó de manera desigual.

Entre aquellos que han mostrado beneficios clínicos o analíticos, la información es variable. En el trabajo de Okamoto y cols. (17) no se describía el estado nutricional, si bien el estudio recogía a pacientes con carcinoma gástrico, en los que el riesgo de desnutrición es elevado. En el de Fujitani y cols. (24), también en el campo de la gastrectomía por carcinoma gástrico, los beneficios se demostraron solo en el subgrupo de pacientes con pérdida de peso reciente mayor del 5 %. En el de Aida y cols., el índice de masa corporal (IMC) medio fue cercano a 22 kg/m^2, y 4 de 50 pacientes habían perdido más del 10 % de su peso; además, no presentaban alteraciones significativas de los valores medios de albúmina, prealbúmina, transferrina o *retinol binding protein* (RBP). En el estudio de Manzanares y cols. (23), el 64,3 % de la muestra se encontraba en riesgo nutricional según el *Nutritional Risk Screening 2002* (NRS-2002), y la prevalencia de la alteración de las proteínas viscerales y de los datos interpretados como desnutrición calórica fue del 31 y 60,7 %, respectivamente. Sin embargo, en el estudio de Nagata y cols. (22), el perfil de la población (donantes de hígado) no era *a priori* susceptible de alteraciones nutricionales y en ellos sí se demostraron beneficios analíticos. Lo mismo sucede con los datos favorables obtenidos en pacientes obesos sometidos a cirugía bariátrica (19). En el estudio de Uno y cols. (21) no se reflejaron datos antropométricos y la albúmina media basal fue de 3,6 a 3,7 g/dL.

En uno de los cuatro estudios en los que no se observaron beneficios se incluyó una mayoría de pacientes normonutridos según la Valoración Global Subjetiva (VGS), con una clasificación A en el 76 % y el 81,6 % en los grupos de tratamiento y control, respectivamente (25). En otro se incluyó por protocolo solo a pacientes normonutridos (26). En el estudio de Gade y cols. (27) hubo un 40 % de pacientes clasificados como "en riesgo nutricional" según el NRS 2002. En el estudio de Hubner y cols. (20), los pacientes incluidos tenían desnutrición grave conforme al un cribado NRS-2002 mayor o igual que 3. No obstante, este fue el estudio en el que la adherencia a la suplementación fue más baja.

En definitiva, no se puede deducir una estratificación de los beneficios según el estado nutricional, si bien es cierto que, en los pacientes normonutridos, no se ha logrado demostrar ningún beneficio a nivel clínico, a excepción de la pérdida de peso en la cirugía bariátrica.

Como conclusión, los datos apuntan a posibles beneficios de la inmunonutrición preoperatoria, fundamentalmente en términos de complicaciones infecciosas y de parámetros relacionados con la respuesta inmune y la inflamación. No obstante, la extracción de conclusiones se ve limitada por la heterogeneidad en factores como las patologías evaluadas, los resultados para una misma patología o el estado nutricional de los pacientes, así como la duración de la intervención, el tratamiento de los grupos de control y los resultados evaluados. Cabe reseñar que en cinco de los siete trabajos donde se reflejaba algún beneficio en relación con la administración de suplementos nutricionales orales, la comparación se realizó con la ausencia de suplementación, lo cual dificulta la atribución del efecto a la presencia de inmunonutrientes en la fórmula. Por último, el tamaño muestral de las publicaciones fue generalmente pequeño.

RESULTADOS DEL USO DE INMUNONUTRIENTES EN LAS FASES PERI Y POSOPERATORIA

Numerosos ensayos clínicos se centraron en el uso de inmunonutrientes en el periodo peri (29-41) y posoperatorio (42-45) (Anexo I). Únicamente en el trabajo de Moya y cols. se empleó la inmunonutrición dentro de un protocolo ERAS (34).

Resultados obtenidos

Parámetros analíticos

Muchos de los estudios mostraron datos bioquímicos sugestivos de mejoría de la función inmunitaria, sin que se encontrase ninguna traducción clínica. Los estudios sugerían que la reducción del recuento linfocitario y de las células T ocurre ya desde el momento de la inducción anestésica, y que estas variables disminuyen en los primeros 5 días del posoperatorio. La optimización de estos parámetros podría jugar un papel protector frente a las complicaciones infecciosas, y la reducción de linfocitos se asocia a una mayor morbimortalidad. Hamza y cols. (31), Hamilton y cols. (33) y Klek y cols. (43-45) evidenciaron un aumento del recuento linfocitario: en concreto, de los linfocitos CD4 (30,31). Las cifras de TNF-α e IL-6 fueron menores, pero sin alcanzar la significación estadística (salvo Mudge y cols. [32]). Existe cierta tendencia a mantener o incrementar, sin significación estadística, los niveles de albúmina plasmática, prealbúmina y transferrina

(salvo el aumento de la prealbúmina (29) y el aumento de las proteínas en los pacientes desnutridos con tratamiento prolongado [41]). Adicionalmente, la inmunonutrición podría modificar favorablemente otros parámetros bioquímicos como la concavalina (Con A), la fitohemaglutinina (PHA) y los niveles de EPA y ácido descosahexaenoico (DHA) (36,39,41).

Parámetros clínicos

a) *Infección*
   En general, hay una tendencia hacia la disminución de la tasa de infecciones que alcanza significación estadística (11,7 % *vs.* 31,3 %, p = 0,021 (29); 0-11,5 %, p = 0,006 (34); 28,3 % *vs.* 39,2 %, p = 0,04 (43-45); 23,5 % *vs.* 56,3 %, p = 0,05 (40)). En este apartado se incluye fundamentalmente la infección del sitio quirúrgico, aunque algunos trabajos recogieron una disminución de infecciones pulmonares y urinarias (29).
b) *Complicaciones posquirúrgicas*
   Las publicaciones quedan divididas en resultados favorables (29,30,33,38,42-45) o no significativos (34,36,37,39-41) en cuanto a morbilidad. Factores que podrían influir en el resultado son el estado nutricional y el momento del posoperatorio en que se midió la presencia de complicaciones; dos trabajos encontraron diferencias solo en el posoperatorio tardío (30,33). Por otro lado, el trabajo de Miyauchi y cols. no mostró diferencias en la tasa de complicaciones ni en la gravedad de las mismas analizando el manejo pre o perioperatorio (36). En cuanto a la dehiscencia anastomótica, en general se incluyó en el apartado de las complicaciones posquirúrgicas, aunque en algún caso se englobó dentro de las infecciosas. Dos trabajos mostraron una disminución significativa de la tasa de fugas (29,30), aunque en la mayoría no se hallaron diferencias (34,36,39). Por último, Scislo y cols. objetivaron un menor número de complicaciones por paciente y una menor tasa de complicaciones respiratorias (42).
c) *Estancia hospitalaria*
   Se halló una disminución significativa de la estancia media en 5 de los trabajos (29,30,37,40,44), no así en el resto (32,34,35,39,41). Habría que destacar que los estudios con mayores tamaños muestrales no mostraron diferencias significativas (32,34).
d) *Mortalidad y supervivencia*
   Tres ensayos clínicos hallaron una disminución de la mortalidad posoperatoria (42,44,45). Otros trabajos no encontraron diferencias en la mortalidad precoz (30,32,34) ni a largo plazo (35).

Resultados en relación con el estado nutricional

Los resultados obtenidos varían en función del estado nutricional de los pacientes incluidos. En relación al uso de inmunonutrición en los pacientes normonutridos existe controversia. De hecho, muchos de los estudios en los que la inmunonutrición no mostró efectos clínicos significativos fueron realizados en pacientes bien nutridos, mientras que aquellos estudios realizados en pacientes con desnutrición de moderada a grave mostraron una reducción de las complicaciones (42-45). En el estudio de Klek y cols. de 2014 no hubo diferencias estadísticamente significativas en cuanto a la morbilidad posquirúrgica (44). Sin embargo, el análisis del subgrupo desnutrido reveló el impacto positivo de la inmunonutrición enteral en la reducción de las complicaciones (28,3 *vs.* 39,2 %, respectivamente; p = 0,043) y la estancia hospitalaria.

Algunos autores consideran que, en los pacientes normonutridos, la suplementación a corto plazo en el posoperatorio sería por sí sola inútil pero que, sin embargo, el manejo perioperatorio durante 7 días podría ofrecer ciertas ventajas en términos de disminución de las complicaciones posquirúrgicas. Por otro lado, Hamza y cols. sugieren que el abordaje preoperatorio es preferible en los pacientes normonutridos, mientras que el abordaje perioperatorio sería más adecuado para los pacientes desnutridos, asociando una reducción relativa del 50 % en las complicaciones posoperatorias en comparación con el uso aislado preoperatorio (31).

Como conclusión, parece claro que el estado nutricional influye en los resultados posoperatorios, beneficiándose fundamentalmente los pacientes con desnutrición y no quedando claro cuál es la estrategia óptima (tratamiento pre, peri o posoperatorio, duración y dosis). La opción de que los pacientes normonutridos también puedan beneficiarse de este tipo de soporte nutricional todavía no se ha demostrado de manera convincente.

RESUMEN DE LOS RESULTADOS DE LOS METAANÁLISIS

Se incluyeron en la presente revisión 17 metaanálisis publicados entre los años 2010 y 2018. Los metaanálisis incluidos en la revisión pueden consultarse en el anexo II.

En general, la mayoría de estudios no se realizaron dentro de protocolos *fast-track*. En los dos trabajos que incluían en dicho protocolo la inmunonutrición se observó una reducción de las infecciones de la herida quirúrgica, de modo que sus autores sugieren que dicho soporte nutricional podría ser más efectivo en caso de emplearse en los protocolos *fast-track*.

En todos los estudios revisados, el aporte de la inmunonutrición por vía oral/enteral se comparaba frente al soporte nutricional estándar o la alimentación oral. La composición de la inmunonutrición, en la mayoría de los estudios, era una mezcla de arginina, ácidos omega-3 y nucleótidos en diferentes concentraciones, dependiendo de la fórmula nutricional, aunque en algunos trabajos analizados por los metaanálisis se administraban los inmunonutrientes de forma aislada. No se reflejaba el estado nutricional en todos los estudios incluidos y los criterios de diagnóstico nutricional empleados eran heterogéneos. Respecto al momento de administración del soporte nutricional, este se indicaba preoperatoriamente y/o posoperatoriamente.

Algún trabajo sugería el empleo de la inmunonutrición al menos 3 días antes y preferiblemente 5-7 días antes de la intervención quirúrgica, así como su continuación posoperatoria si fuera posible. El trabajo publicado en 2010 por Marik y cols. (46), y que incluye pacientes malnutridos y con alto riesgo nutricional que se intervienen de cáncer gastrointestinal, de cabeza y cuello, de cirugía abdominal y de cirugía cardíaca, recomiendan el inicio preoperatorio puesto que, tras la intervención quirúrgica, pueden surgir problemas de tolerancia gastrointestinal.

El metaanálisis más relevante respecto al momento de administración es el de Osland de 2014, que incluye 20 estudios en pacientes con neoplasia gastrointestinal y hepática, y concluye que la administración perioperatoria y posoperatoria reduce las complicaciones infecciosas y la estancia hospitalaria (47). No se especifica durante qué intervalo de tiempo debe administrarse la inmunonutrición, si bien las vías de administración son heterogéneas (vía oral, enteral) y los actuales protocolos de *fast track* no incluyen la administración rutinaria de nutrición enteral en el posoperatorio.

En el metaanálisis de 2012 de Casas y colaboradores, de pacientes con cáncer de cabeza y cuello, se observó una disminución significativa del número de fístulas en los pacientes tratados con dosis altas de arginina si se comparaban con los receptores de una nutrición con dosis medias de la misma (48). Uno de los trabajos incluidos en el metaanálisis concluía que la inmunonutrición prolongaba la supervivencia, siendo esta de 34,8 meses para los pacientes suplementados con inmunonutrición frente a 20,7 meses en el grupo de control. El metaanálisis posterior de 2014 de Vidal Casariego (49) y la revisión Cochrane de Howes de 2018 (50) respaldan también la reducción de las fistulas y la estancia hospitalaria en el grupo tratado con inmunonutrientes, aunque no todos los estudios incluidos eran de alta calidad metodológica.

La mayoría de los metaanálisis concluyen que la inmunonutrición reduce la estancia hospitalaria. Los trabajos como el de Song y colaboradores de 2015 (51) y el de Cheng de 2018 (52) muestran mejorías de los parámetros inmunológicos con la inmunonutrición, aunque no mejora la estancia hospitalaria. En ambos, la población incluida era de pacientes con cáncer gástrico.

El cociente de coste-efectividad de la inmunonutrición se analizó en el trabajo de Reis de 2016 (que incluía 6 estudios), encontrándose resultados positivos en cuanto al coste-efectividad y reduciéndose la estancia hospitalaria (53).

El metaanálisis que incluía más estudios es el publicado en 2017 por Probst y cols., que incluía 83 ensayos aleatorizados y controlados, y 7116 pacientes analizados, intervenidos de cirugía mayor abdominal (resección de hígado, páncreas o cirugías que implicaban anastomosis del tracto gastrointestinal). Concluía que la inmunonutrición reduce las complicaciones totales e infecciosas y la estancia hospitalaria con un grado de evidencia moderado-bajo. No demostró efectos sobre la mortalidad con un grado de evidencia alto (54).

El metaanálisis de Cerantola de 2011 incluyó 21 trabajos, 12 de los cuales fueron de alta calidad metodológica; concluyó que, tras excluir los estudios de baja calidad, la inmunonutrición administrada antes y después de la intervención quirúrgica (o únicamente después) había reducido las complicaciones posoperatorias y la estancia hospitalaria (55). Por tanto, los autores recomiendan su uso rutinario.

Como conclusión, tras revisar los 17 metaanálisis, las principales limitaciones encontradas son la falta de registro del estado nutricional de los pacientes y, en los casos en que se ha registrado, el hecho de que se han empleado diferentes métodos de diagnóstico nutricional. Además, no se suele hacer alusión al estadio tumoral del paciente o a la administración de tratamiento neoadyuvante. En los aspectos relacionados con la inmunomodulación, habitualmente se han administrado fórmulas comercializadas con combinaciones de inmunonutrientes por vía oral o enteral, pero en algunos estudios esta se ha administrado de forma aislada. En general, en los estudios se han registrado pocos datos sobre los abandonos y en pocos trabajos se ha reflejado la participación de la industria.

RECOMENDACIONES SEGÚN LAS GUÍAS DE PRÁCTICA CLÍNICA

En relación con la indicación de suplementación con fórmulas inmunomoduladoras en el ámbito de la cirugía, encontramos recomendaciones en distintas guías de práctica clínica (GPC):

ESPEN

La Sociedad Europea de Nutrición Clínica y metabolismo (ESPEN) ha publicado recientemente sus GPC sobre el soporte nutricional en la cirugía (7) y en el paciente con cáncer (56).

Para el paciente quirúrgico en general, la ESPEN recomienda, con el grado B de la escala SIGN (*Scottish Intercollegiate Guidelines Network*), la administración perioperatoria o al menos posoperatoria de fórmulas orales/enterales específicas, enriquecidas en inmunonutrientes (arginina, ácidos grasos omega-3 y ribonucleótidos), en los pacientes desnutridos candidatos a cirugía mayor oncológica (7). En lo que respecta al uso exclusivo en el preoperatorio, añade que no existe una clara evidencia que respalde su uso frente a las fórmulas estándar (grado de recomendación B/O de la escala SIGN (57), 89 % de consenso). Aunque no se presenta como una recomendación al uso, en esta GPC se recoge (dentro de un apartado de "indicaciones especiales") la integración de las fórmulas inmunomoduladoras en los protocolos ERAS sobre la base de un ensayo clínico aleatorizado en pacientes con cáncer colorrectal (34).

En el paciente oncológico, la ESPEN (56) recomienda la administración perioperatoria de fórmulas orales/enterales específicas enriquecidas en inmunonutrientes (arginina, ácidos grasos omega-3 y ribonucleótidos) en el contexto de protocolos quirúrgicos tradicionales del tubo gastrointestinal alto, con un nivel de evidencia alto y un grado de recomendación fuerte. No se hace referencia explícita al estado nutricional del paciente como requisito para la prescripción del tratamiento. Asimismo, se recomienda que el protocolo quirúrgico de elección en el paciente oncológi-

co siga las directrices ERAS (*Enhanced Recovery After Surgery*) (recomendación fuerte, nivel de evidencia alto). Como cuestiones a resolver plantean el papel de los inmunonutrientes en el manejo de los pacientes candidatos a cirugía gastrointestinal alta dentro de los protocolos ERAS.

Sociedad ERAS

En relación a las vías ERAS®, la ESPEN, en colaboración con la Sociedad ERAS, ha publicado GPC de soporte nutricional para la cirugía colónica (58), pélvico-rectal (59), duodeno-pancreática (60) y urológica (cistectomía) (61). La propia sociedad ERAS ha publicado varias GPC, algunas de las cuales se han actualizado recientemente. Así, disponemos de GPC publicadas en los últimos 7 años para las cirugías colónica (11), onco-ginecológica (62), esofágica (63), pulmonar (64), hepática (65), bariátrica (66) y gástrica (67).

En la reciente actualización (11) de la GPC de cirugía colónica ERAS (58) se recomienda ofrecer comida y suplementos nutricionales orales desde el día de la cirugía (recomendación fuerte, nivel de evidencia moderado). La inmunonutrición perioperatoria de los pacientes malnutridos es beneficiosa para los pacientes con cáncer colorrectal (recomendación fuerte, nivel de evidencia bajo). En la guía de cirugía ERAS pélvico-rectal (59) no se recoge una recomendación específica sobre el uso de fórmulas inmunomoduladoras.

En la cirugía duodeno-pancreática, la Sociedad ERAS recomienda (con grado débil y evidencia moderada) que el soporte nutricional con fórmulas inmunomoduladoras durante 5-7 días perioperatorios se considere sobre la base de la reducción de la tasa de complicaciones infecciosas. Si bien añade que no existía en el momento de la publicación de la GPC (2012) ningún estudio que analizara los efectos de la inmunonutrición en el contexto de la cirugía ERAS.

En el caso de la cirugía urológica, la ERAS no hace ninguna recomendación específica sobre la base de la evidencia disponible. Su papel en la reducción de la morbimortalidad de estos pacientes no se conocía cuando se publicó la guía (2013) (61).

En el caso de la cirugía onco-ginecológica (62), en las guías ERAS se hace alusión a la inmunonutrición en el apartado de "nutrición perioperatoria", en su mayoría por extrapolación del estudio sobre el colon, y se cita un único estudio realizado en pacientes con neoplasias ginecológicas (37), con resultados positivos. No se hace recomendación específica sobre el uso de las fórmulas inmunomoduladoras en el contexto de la cirugía ERAS de pacientes con neoplasias ginecológicas. Tampoco se hace recomendación específica en el caso de la cirugía bariátrica (66).

Las GPC para el manejo perioperatorio de la esofaguectomía de la sociedad ERAS (63) afirman que la evidencia en torno al uso de las fórmulas inmunomoduladoras en pacientes candidatos a cirugía oncológica esofágica es conflictiva y su uso rutinario no puede recomendarse en la actualidad (recomendación fuerte, evidencia moderada).

En el caso de la cirugía torácica ERAS (64), el posicionamiento es similar, es decir: no se dispone de suficiente evidencia para recomendar las fórmulas inmunomoduladoras frente a las fórmulas estándar, pero se cree que podrían tener algún papel en el posoperatorio de los pacientes malnutridos (recomendación débil para el posoperatorio, evidencia baja y extrapolada).

En los pacientes candidatos a cirugía hepática ERAS (65), la evidencia sobre el uso de fórmulas inmunomoduladoras es limitada (recomendación débil, evidencia baja). A este respecto se hace referencia al estudio PROPILS (68) (Clinicaltrial.gov: NCT02041871), un estudio prospectivo, aleatorizado, controlado con placebo y doble ciego en fase IV que compara dos tratamientos nutricionales (inmunomodulador y estándar) en pacientes candidatos a cirugía hepática y cuyos resultados no se han publicado aún.

Las GPC de cirugía gástrica ERAS (67) sostienen que no existe suficiente evidencia para recomendar el uso rutinario de fórmulas inmunomoduladoras en los pacientes candidatos a gastrectomía (recomendación débil, evidencia moderada). Añade que el posible efecto beneficioso sobre la tasa de infecciones y de complicaciones de la herida quirúrgica en los pacientes candidatos a cirugía mayor abdominal no se ha reproducido en ensayos de alta calidad metodológica y centrados en la gastrectomía.

Vía RICA

A nivel nacional contamos con la vía clínica de recuperación intensificada en cirugía abdominal (RICA) (10), elaborada en 2015 y posteriormente actualizada en 2018. No se recoge ninguna recomendación específica sobre el uso de fórmulas inmunomoduladoras en este contexto clínico.

En la tabla III se resumen las recomendaciones sobre el uso de la inmunonutrición en las guías de práctica clínica analizadas.

LIMITACIONES Y FUENTES DE HETEROGENEIDAD CLÍNICA Y METODOLÓGICA

Como se ha visto, el análisis y la revisión de la bibliografía (tanto de los metaanálisis como de los ensayos clínicos) realizados ponen de manifiesto que la calidad metodológica de los estudios revisados es con frecuencia baja o muy baja según las escalas de valoración de la calidad. A su vez se constata que, en el análisis de las revisiones sistemáticas, muchas de estas agrupan y comparan estudios heterogéneos clínica y metodológicamente.

Si bien la heterogeneidad estadística se analiza y considera en todos los metaanálisis revisados, las diferencias a nivel clínico y metodológico entre los estudios incluidos no se han tenido suficientemente en cuenta en los resultados de cada trabajo. De un modo parecido, las revisiones metaanalíticas examinadas no detallaban sistemáticamente cuáles eran los fallos metodológicos de los estudios que revisaban, ni ponderaban su posible impacto sobre los resultados. En esta sección se detallan las principales fuentes de heterogeneidad a nivel clínico y metodológico halladas durante el análisis. Se describen a continuación aquellas que están frecuentemente relacionadas con el campo de la inmuno-

nutrición y la nutrición enteral, a fin de que futuras investigaciones puedan tenerlas en cuenta (tanto en el diseño de los ensayos como en la ponderación en las revisiones metaanalíticas). Además de las mencionadas, toda nueva investigación debería considerar aquellos aspectos metodológicos o de diseño del estudio que son comunes a cualquier estudio científico y/o revisión sistemática (p. ej., la *CONSORT checklist* [69]).

Se han clasificado en tres categorías (Tabla IV):

a) Relativas a la intervención nutricional.
b) Relativas al paciente.
c) Relativas a las variables principales del estudio.

ALGORITMOS BASADOS EN LOS RESULTADOS Y EN LA PRÁCTICA CLÍNICA

Considerando toda la revisión realizada de la bibliografía, así como las experiencias clínicas de los autores, se trabajó en consensuar un algoritmo sencillo, compartido por los diferentes especialistas implicados y que fuera viable en la práctica clínica habitual, sin requerir un aumento de los recursos humanos para su puesta en práctica (lo cual lo haría inviable en el contexto actual de escasez de recursos en la sanidad pública). El algoritmo resultante se muestra en las figuras 2 y 3.

Algunas consideraciones previas en relación con el diseño del algoritmo:

1) Teniendo en cuenta las características del paciente se identifican cuatro perfiles principales según la patología de base (oncológica o no oncológica) y según la programación de la cirugía (diferida o urgente).
2) En nuestro entorno, si bien se reconoce el uso esporádico de la escala MUST por parte de algunos de los equipos de cirugía (que puede ser aplicada tanto por el médico como por la enfermería), su uso no está extendido ni es sistemático, y el criterio de derivación a Nutrición no está bien establecido.
3) Desde el colectivo de cirugía y anestesia se comenta que principalmente y de forma voluntaria se utiliza la escala MUST (70) (Fig. 4) para la valoración nutricional en la fase preoperatoria del paciente no hospitalizado candidato a

Tabla III. Resumen de las recomendaciones sobre inmunonutrición de las guías de práctica clínica analizadas

GPC, referencia y año	Posicionamiento	Grado de recomendación	Grado de evidencia
Soporte nutricional en cirugía (2017) (7)	Paciente oncológico malnutrido candidato a cirugía del TGI superior	B de la escala SIGN	2++/2+ escala SIGN
Soporte nutricional en cáncer (2017) (56)	Paciente oncológico candidato a cirugía tradicional del TGI superior	Fuerte	Alto
Cirugía pélvico rectal ERAS (2012) (59)	No incluye recomendación específica sobre la inmunonutrición		
Cirugía duodeno-pancreática ERAS (2012) (60)	Se recomienda considerar su uso en 5-7 días del perioperatorio	Débil	Moderada
Cirugía urológica, cistectomía ERAS (2013) (61)	No incluye recomendación específica sobre la inmunonutrición		
Cirugía colon ERAS (2018) (11) (Actualización de la previa de 2012) (58)	La inmunonutrición perioperatoria en pacientes malnutridos es beneficiosa para los pacientes con cáncer colorrectal	Fuerte	Bajo
Cirugía Onco-ginecológica ERAS (2019) (62)	No incluye recomendación específica sobre la inmunonutrición		
Cirugía esofágica ERAS (2019) (63)	No recomienda su uso rutinario en base a la evidencia disponible	Fuerte	Moderada
Cirugía pulmonar ERAS (2019) (64)	No puede hacerse recomendación para uso rutinario en base a la evidencia La inmunonutrición podría resultar beneficiosa en el posoperatorio de pacientes malnutridos.	Débil	Baja (extrapolada)
Cirugía hepática ERAS (2016) (65)	No puede hacerse recomendación para uso rutinario en base a la evidencia	Débil	Baja
Cirugía bariátrica ERAS (2016) (66)	No incluye recomendación específica sobre la inmunonutrición		
Cirugía gástrica ERAS (2014) (67)	No puede hacerse recomendación para uso rutinario en base a la evidencia	Débil	Moderada
Vía clínica RICA (2018) (10)	No incluye recomendación específica sobre la inmunonutrición		

Tabla IV. Principales limitaciones y fuentes de heterogeneidad clínica en los estudios revisados

Categoría	Ítem	Descripción
Tratamiento nutricional	Composición de la fórmula	La composición de la fórmula debería detallarse y estandarizarse en el estudio
		En el caso de revisiones, es recomendable incluir únicamente estudios que utilicen una composición similar
	Dosis diarias	Es necesario que las dosis diarias que reciben los pacientes en el estudio sean comparables y estén indicadas en la publicación
	Características de la fórmula de control	No es suficiente indicar que el grupo control recibe "nutrición estándar". Para una valoración adecuada del efecto de los inmunonutrientes, debería emplearse una fórmula control isoproteica e isocalórica respecto a la fórmula de estudio, e indicarlo en la publicación
	Nutrición parenteral complementaria	En caso de fórmula enteral, es necesario tener presente si se está usando nutrición parenteral complementaria y detallarlo en la publicación
	Periodo/fase	La evidencia sugiere que el momento de la intervención puede condicionar sus efectos. De este modo, es recomendable definirlo claramente en el protocolo del estudio (preoperatorio/posoperatorio/perioperatorio)
	Vía	Debería indicarse por qué vía se administra la fórmula (oral/enteral/parenteral/combinada) y dónde se ha colocado la sonda (p. ej., yeyunostomía)
	Duración del tratamiento	La duración del tratamiento debería estar determinada en el protocolo o al menos ser comparable entre todos los pacientes a estudio. Debe explicitarse en la publicación
	Cumplimiento	Debería medirse el cumplimiento del tratamiento e indicarse en la publicación (p. ej.: dosis indicada *vs.* dosis recibida por el paciente)
Paciente	Tipo de cirugía	Además de qué tipo de cirugía se trata, deben detallarse y estandarizarse al máximo en el diseño del estudio otros procesos asociados a la intervención quirúrgica (p. ej., preparación colónica) y que puedan influir sobre los resultados
	Estado nutricional	Dado que el estado nutricional previo condiciona el efecto de toda intervención previa, debería tenerse en cuenta en el diseño del estudio y detallarse en la publicación
	Gravedad	La gravedad de los pacientes y/o la estimación de la morbimortalidad perioperatoria debería indicarse mediante algún indicador aceptado (p. ej.: índice de gravedad de Charlson o P-POSSUM)
	Estadio tumoral, presencia de neoadyuvancia	En caso de intervenciones oncológicas, es necesario explicitar los estadios tumorales de los pacientes del estudio, así como la administración de tratamiento neoadyuvante
	Protocolo *fast track*	Si en el estudio se está siguiendo un protocolo *fast-track*, debería indicarse en la publicación
Objetivos	Complicaciones posoperatorias	Se recomienda utilizar definiciones internacionalmente aceptadas de las complicaciones posoperatorias; p. ej.: definiciones EPCO (*European Perioperative Clinical Outcome*) que faciliten la comparación de las publicaciones en futuras revisiones
	Tiempo de estancia en el hospital	La duración de la estancia hospitalaria debería aparecer en los resultados, a ser posible especificando los días de ingreso hasta que el paciente cumple los criterios del alta, independientemente de cuando salga del hospital
	Costes	Un registro estandarizado de los costes facilitará un estudio farmacoeconómico posterior

una cirugía programada, tanto benigna como maligna. Esta escala está enfocada principalmente en valorar la variación del peso en un periodo de tiempo. Pese a no precisar pruebas analíticas y exigir muy poco tiempo para su aplicación en la visita médica, la tasa de cumplimiento por parte del equipo de cirugía y anestesia es en general bajo.

4) También se considera clave la determinación de la albuminemia para disponer de una imagen más fidedigna del estado nutricional de este tipo de paciente y de su riesgo de sufrir complicaciones. Sin embargo, también se reconoce que, generalmente, no se solicita este parámetro de forma rutinaria en la analítica preoperatoria, ni por los cirujanos, ni por los anestesistas.
5) Si bien se reconoce que la responsabilidad original del cribado nutricional debe recaer en los servicios de cirugía, también es importante reconocer que, en este sentido, el

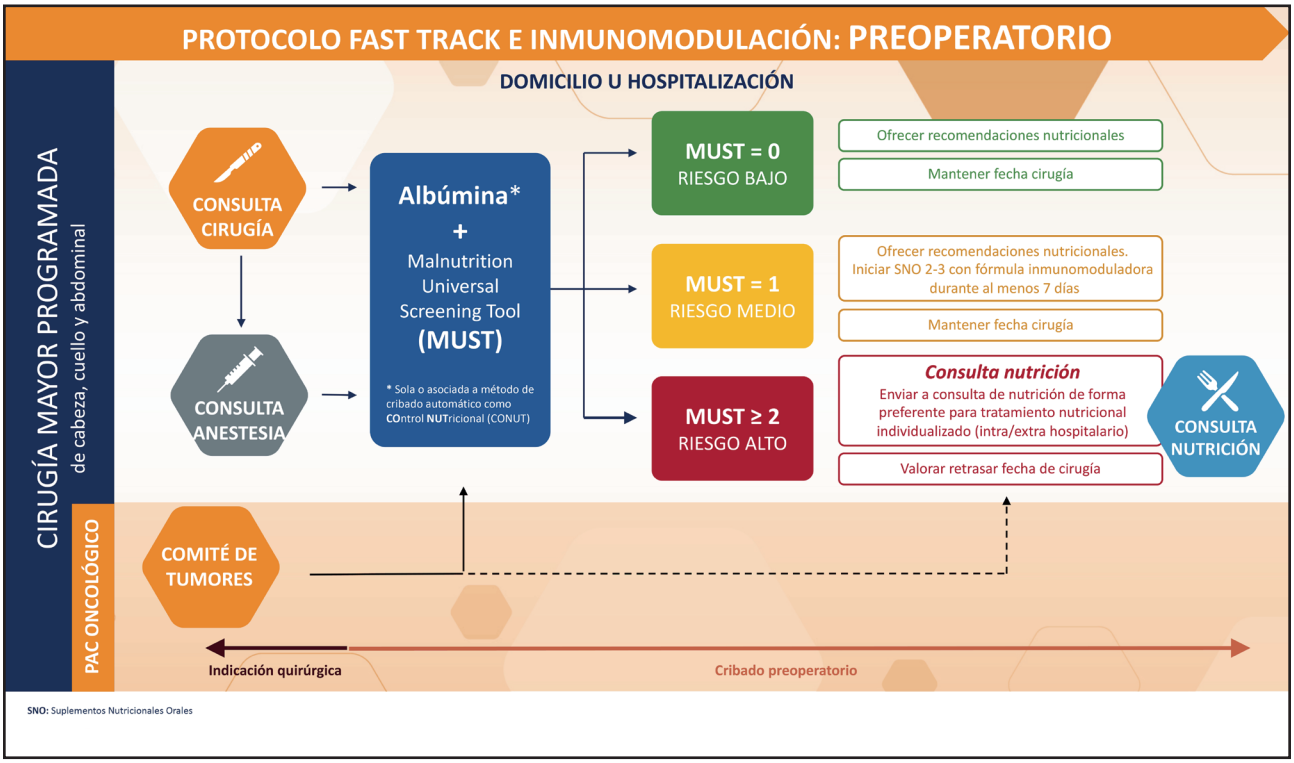

Figura 2.

Algoritmo para el periodo preoperatorio. En el Anexo III se pueden encontrar unas recomendaciones nutricionales adaptadas.

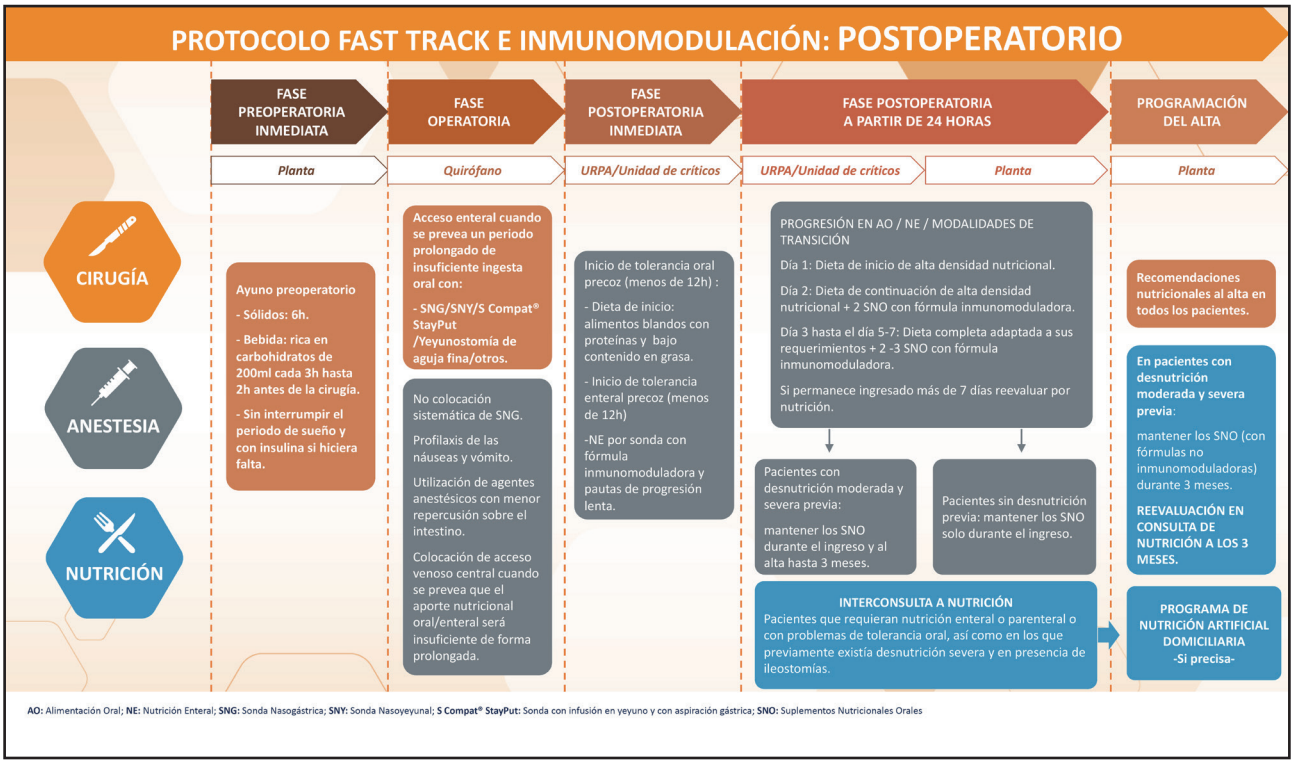

Figura 3.

Algoritmo para el periodo posoperatorio y el alta. En el Anexo III se pueden encontrar unas recomendaciones nutricionales adaptadas.

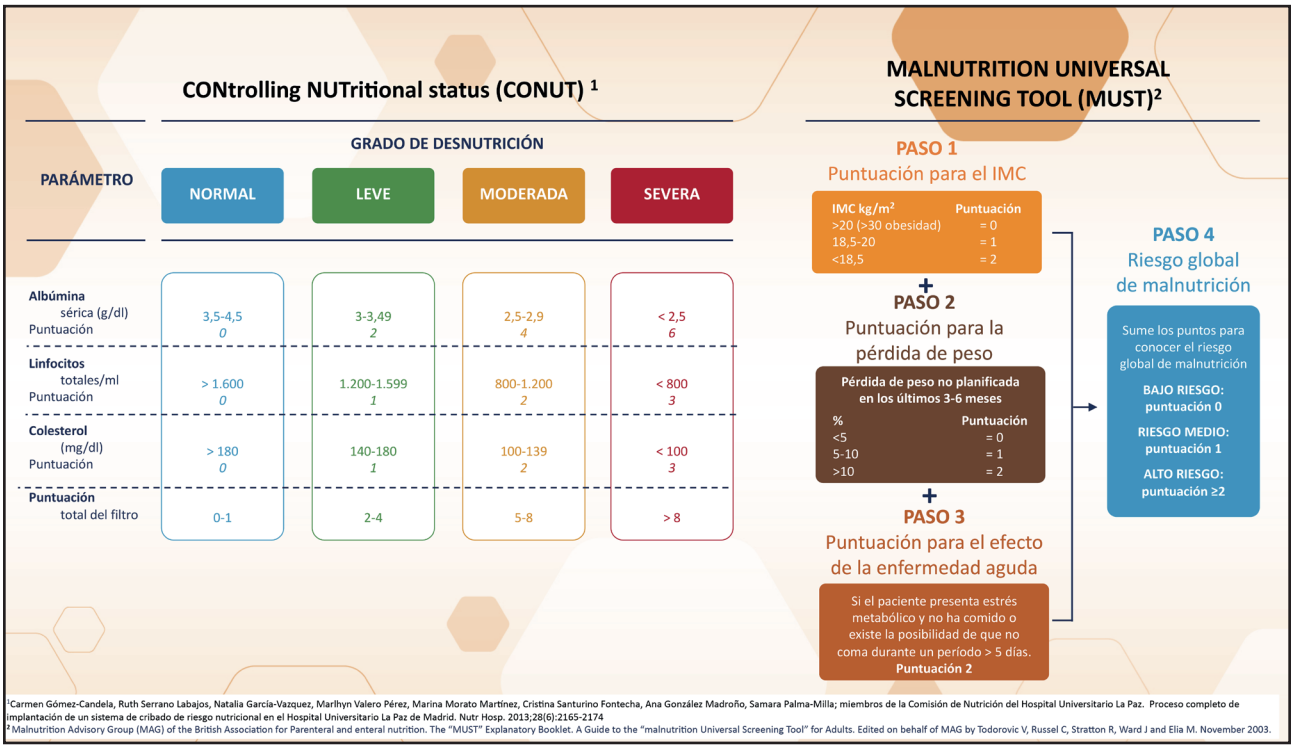

Figura 4.

Método CONUT de cribado del riesgo nutricional y escala MUST de valoración nutricional del paciente.

servicio de anestesia actuaría como un doble filtro y se trataría de una responsabilidad compartida por igual por ambos colectivos.

6) En el caso del paciente hospitalizado con cirugía programada, cada centro debería usar su propio método de cribado del riesgo nutricional (71,72). Los diferentes equipos deberían solicitar una valoración nutricional completa mediante una interconsulta a Nutrición con suficiente antelación cuando sea preciso, de tal forma que se pueda iniciar la re-nutrición del paciente entre 7 y 10 días antes de la cirugía, o retrasar la cirugía en caso de desnutrición grave. Harían falta protocolos consensuados en cada centro hospitalario.
7) En el caso del paciente oncológico que precisa cirugía programada podría ser muy interesante diseñar una estrategia en los numerosos comités de tumores de los centros, para que exigieran una valoración nutricional previa del paciente y la constancia de que, nutricionalmente, el paciente es apto para esa cirugía. Y si no lo fuera o no estuviera valorado, poner en marcha una valoración y un tratamiento nutricional de urgencia para llevarlo a cabo. En todo caso, consideramos y reconocemos que es técnicamente imposible que un representante de Nutrición pueda estar incorporado en todos los comités.

DISCUSIÓN

La inmunonutrición ha demostrado que es capaz de reducir las complicaciones totales, las complicaciones infecciosas y la estancia hospitalaria en los pacientes quirúrgicos.

A fin de poder determinar cuáles serían las condiciones óptimas de la intervención inmunonutricional (duración, momento de inicio, tipo de intervenciones quirúrgicas favorables/desfavorables, efecto de inmunonutrientes específicos, etc.), es necesario tener presente, no obstante, que la extracción de conclusiones generales se ve limitada por la heterogeneidad en factores como las patologías evaluadas, los resultados divergentes para una misma patología, el estado nutricional de los pacientes y los protocolos empleados. En algunos contextos (p. ej., el preoperatorio), estamos limitados para asumir una atribución de los resultados favorables a la presencia de inmunonutrientes en las fórmulas y descartar que se deban a otros factores (p. ej., una suplementación nutricional hiperproteica *per se)*. En cualquier caso, las GPC actualmente recomiendan la administración perioperatoria de fórmulas orales/enterales específicas, enriquecidas con inmunonutrientes, en determinados contextos: p. ej., en los protocolos quirúrgicos tradicionales del tubo gastrointestinal superior (grado de recomendación fuerte) (56) o en los pacientes malnutridos intervenidos por cáncer colorrectal (grado de recomendación fuerte) (62).

Sería necesario llevar a cabo estudios adicionales pero que en su diseño tuvieran en cuenta, además de lo comúnmente exigible a un ensayo clínico (uso de procesos robustos de enmascaramiento y control, tamaños muestrales adecuados, etc.), las peculiaridades y fuentes de heterogeneidad propias del campo de la inmunonutrición (pacientes estratificados según su estatus nutricional, uso de controles isocalóricos e isoproteicos, registro adecuado del cumplimiento de tomas, etc.), cuya omisión ha limitado, en la revisión de la literatura, la determinación de conclusiones y recomendaciones sólidas en varios puntos del proceso que todavía hoy no se han esclarecido.

También es necesario tener presente la barrera que supone el hecho de que los aspectos nutricionales parecen ser secundarios, especialmente en el colectivo de cirujanos o anestesistas. La esfera nutricional dispone de una consideración menor tanto en la fase preoperatoria como en la fase posoperatoria. Se asocia este fenómeno a falta de conocimientos adecuados, de protocolos y de interacciones apropiadas entre estos servicios y el de nutrición. También se considera importante la escasez de personal en los diferentes servicios. Esta situación todavía se agrava más en los procedimientos *fast-track*, de implementación parcial o incompleta en muchos centros, y donde se tiene que vigilar con mayor precisión que la intervención de todos los actores se realice en el tiempo y la forma adecuados. Así, y fruto de la comprensión de la situación actual con respecto al soporte nutricional en el paciente quirúrgico, y especialmente en el modelo *fast-track,* las posibles actuaciones a llevar a cabo pasarían por aumentar el conocimiento específico en esta materia de todos los profesionales implicados, principalmente en las área de cirugía, anestesia y nutrición. En este sentido, en el recientemente publicado documento de recomendaciones de cuidados perioperatorios, el grupo de expertos de la ESPEN afirma que los programas ERAS son apropiados para todos los pacientes, pero que sus beneficios dependen del cumplimiento de las recomendaciones por parte de todo el equipo implicado (73).

Para una óptima validez de los resultados sería necesario que todas las posibles investigaciones futuras en este campo evaluasen a pacientes sometidos a procedimientos quirúrgicos equiparables en cuanto a parámetros clínicos, bioquímicos y analíticos en relación con el estado nutricional; y la morbilidad posoperatoria debería registrarse según clasificaciones previamente definidas en la literatura, como la clasificación Clavien-Dindo (28) (1), las guías del *International Council for Harmonisation Good Clinical Practice* (ICH-GCP) (74) (2), las definiciones de los *Centers for Disease Control* (CDC) (75,76), etc. Y de un modo parecido, deberían incluirse como variables la estancia hospitalaria, los costes y los reingresos.

El cumplimiento de un protocolo estandarizado como el ERAS ayudaría a que estuvieran objetivamente definidos muchos de los otros parámetros no nutricionales que también se tienen que controlar (como una profilaxis antibiótica correcta, la hipotermia, etc.).

Finalmente, es necesario implicar al paciente y trabajar para que tanto él como sus familiares conozcan la importancia que tiene un adecuado estado nutricional en el éxito de la cirugía y en la recuperación tras la misma, para que sean más colaboradores y se hagan más demandantes de medidas de valoración y de soporte nutricional, y por supuesto, para que estén más satisfechos.

ANEXO I.

ENSAYOS CLÍNICOS ALEATORIZADOS INCLUIDOS EN LA REVISIÓN

Autor	n	Cirugía	ERAS (Sí/No)	Fórmula	Jadad	Resultados
Okamoto 2009 (17)	60	Gastrectomía	No	IMPACT®	2	Disminución de la duración del SIRS y de las infecciones, y mejor inmunidad
Çelik 2009 (37)	50	Ginecología	No	IMPACT®	1	Disminución de infecciones, dehiscencias y estancia
Felekis 2010 (38)	40	Carcinoma de cabeza y cuello	No	IMPACT®	4	Disminución de infecciones
Mikagi 2011 (77)	26	Hepatectomía	No	IMPACT®	2	Menor inflamación y mejor función hepática
Klek 2011 (43)	167	Cirugía oncológica	No	STRESSON®	3	Sin diferencias en cuanto a complicaciones
Fujitani 2012 (24)	244	Gastrectomía	No	IMPACT®	3	Disminución de infecciones en pacientes desnutridos
Hubner 2012 (20)	152	Cirugía abdominal mayor	No	IMPACT®	5	Sin diferencias
Barker 2013 (25)	95	Cirugía gastrointestinal	No	IMPACT®	3	Sin diferencias

(Continúa en página siguiente)

ANEXO I (Cont.).

ENSAYOS CLÍNICOS ALEATORIZADOS INCLUIDOS EN LA REVISIÓN

Autor	n	Cirugía	ERAS (Sí/No)	Fórmula	Jadad	Resultados
Giger-Pabst 2013 (26)	108	Cirugía oncológica abdominal	No	IMPACT®	4	Sin diferencias
Nagata 2013 (22)	23	Donantes de hígado	No	ANOM®	3	Diferencias analíticas, no en resultados clínicos
Turnock 2013 (39)	8	Cáncer de cabeza y cuello	No	IMPACT®	3	Diferencias analíticas, no en resultados clínicos
Marano 2013 (30)	109	Gastrectomía	No	IMPACT®	1	Menor incidencia de complicaciones, menor estancia hospitalaria
Aida 2014 (18)	50	Duodenopancreatectomía	No	IMPACT®	1	Disminución de infecciones posoperatorias
Falewee 2014 (40)	312	Cáncer de cabeza y cuello	No	IMPACT®	5	Sin diferencias
Klek 2014 (44)	776	Gastrectomía y pancreatectomía	No	IMPACT®	3	Disminución de estancia hospitalaria, infecciones y mortalidad
Hamza 2015 (31)	37	Duodenopancreatectomía	No	IMPACT®	3	Modula la respuesta inflamatoria e intensifica la respuesta inmunitaria
Plank 2015 (41)	120	Trasplante hepático	No	IMPACT®	5	Sin diferencias en los aspectos nutricionales ni en las complicaciones
Gade 2016 (27)	35	Pancreatectomía	No	IMPACT®	2	Sin diferencias
Uno 2016 (21)	40	Cirugía hepatobiliar	No	IMPACT®	3	Reducción de las complicaciones infecciosas y la estancia hospitalaria
Hamilton-Reeves 2016 (33)	29	Cistectomía	No	IMPACT®	4	Mejoría de la respuesta inmune y disminución de las infecciones
Ruiz-Tóvar 2016 (19)	60	Cirugía bariátrica	No	ATEMPERO®	2	Mayor pérdida de peso preoperatoria, menor PCR, menos dolor
Moya 2016 (34)	122	Cirugía colorrectal	Sí	ATEMPERO®	3	Reducción de las complicaciones
Yildiz 2016 (29)	41	Cirugía esofagogástrica y pancreática	No	ABOUND®	1	Disminución de las complicaciones y la estancia hospitalaria
Martin II 2017 (78)	71	Cáncer de páncreas	No	IMPACT®	0	Reducción de las complicaciones y la estancia
Manzanares-Campillo 2017 (23)	84	Cáncer colorrectal	No	IMPACT®	2	Menor incidencia de complicaciones infecciosas en la cirugía rectal
Klek 2017 (45)	99	Gastrectomía	No	RECONVAN®	5	Mejoría de la supervivencia a corto plazo, no a largo plazo
Palma-Milla 2018 (79)	38	Cáncer de cabeza y cuello	No	ATEMPERO®	5	Disminución de las complicaciones infecciosas y la estancia
Scislo 2018 (42)	98	Gastrectomía	No	RECONVAN®	2	Disminución de las complicaciones respiratorias y la mortalidad precoz
Mudge 2018 (32)	278	Cáncer esofágico	No	IMPACT®	5	Sin diferencias
Shinsuke 2019 (35)	40	Esofaguectomía	No	IMPACT®	2	Disminución de las complicaciones infecciosas
Miyauchi 2019 (36)	60	Pancreatectomía	No	IMPACT®	2	Sin diferencias

ANEXO II.

REVISIONES SISTEMÁTICAS Y METAANÁLISIS INCLUIDOS EN LA REVISIÓN

Autor	n	Tipo de cirugía	ERAS S/N	Fórmula utilizada	Resultados
Cerantola Y 2010 (55)	2370	Cirugía oncológica gastrointestinal	No	Fórmula con arginina, omega-3 y RNA en el pre/pos/perioperatorio	Reducción significativa de las complicaciones posoperatorias e infecciosas y de la estancia hospitalaria
Zhang Y 2012 (80)	2331	Cirugía oncológica gastrointestinal	No	Fórmula con arginina, omega-3 y RNA en el pre/pos/perioperatorio	Reducción significativa de las complicaciones posoperatorias e infecciosas y de la estancia hospitalaria
Osland E 2014 (47)	2005	Cirugía oncológica gastrointestinal	No	Fórmula con arginina, omega-3 y RNA en el pre/pos/perioperatorio. IMPACT® en el 65 % de los casos	Reducción significativa de las complicaciones infecciosas y la estancia hospitalaria en caso de administración peri o posoperatoria. Reducción significativa de las complicaciones no infecciosas en caso de administración posoperatoria. Reducción significativa de la tasa de dehiscencia de suturas en caso de administración perioperatoria
Wong C 2016 (81)	2016	Cirugía gastrointestinal	No	IMPACT® Oxepa®	Reducción significativa de las complicaciones infecciosas y la estancia hospitalaria en caso de administración posoperatoria
Song GM 2017 (82)	840	Cirugía oncológica gástrica	No	Combinaciones variables de inmunonutrientes	La combinación óptima de inmunonutrientes en una fórmula inmunomoduladora para reducir las complicaciones infecciosas y la estancia hospitalaria es: arginina + RNA + omega-3 o arginina + glutamina + omega-3
Howes N 2018 (50)	1099	Cirugía oncológica de tumores de cabeza y cuello	No	Distintas fórmulas inmunomoduladoras. IMPACT® fue la más empleada	No se encontraron diferencias significativas en las complicaciones, infecciosas o no, ni en la estancia hospitalaria, ni en la tolerancia a la fórmula
Marik PE 2010 (46)	1918	Cirugía electiva – 15 estudios de cirugía oncológica gastrointestinal – 2 estudios de cirugía abdominal – 3 estudios de cáncer de cabeza y cuello – 1 estudio de cirugía cardíaca	No	Distintas fórmulas inmunomoduladoras IMPACT® fue la más empleada. En su mayoría, en el posoperatorio	Una inmunonutrición que incluya arginina y omega-3 disminuye significativmaente las complicaciones infecciosas, las complicaciones de la herida quiúrgica y la estancia hospitalaria. Se sugiere su inicio en el preoperatorio si es posible
Casas Rodera P 2012 (48)	836	Cirugía oncológica de tumores de cabeza y cuello	No especificado	Fórmula polimérica enriquecida con arginina u omega-3 o IMPACT® o Nutrison Intensive®. Perioperatorio	La inmunonutrición disminuye la estancia hospitalaria, aunque no está clara la razón. Disminución de la incidencia de fístulas

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ANEXO II (Cont.).

REVISIONES SISTEMÁTICAS Y METAANÁLISIS INCLUIDOS EN LA REVISIÓN

Autor	n	Tipo de cirugía	ERAS S/N	Fórmula utilizada	Resultados
Hegazi RA 2014 (5)	1156	Cirugía oncológica de tumores gastrointestinales y hepáticos	No	Fórmulas inmunomoduladoras no especificadas. Pre y posoperatorio	La inmunutrición frente a la suplementacion isocalórica/ isonitrogenada no reduce la incidencia de las infecciones de la herida quirúrgica, las complicaciones infecciosas y no infecciosas, ni la estancia hospitalaria
Vidal-Casariego A 2014 (49)	397	Cáncer de cavidad oral, faringe y laringe	No	Fórmula enriquecida con arginina. Pre y/o posoperatorio	La inmunonutrición muestra una reducción de la incidencia de fístulas y de la estancia hospitalaria, pero no una disminución de las infecciones de la herida quirúrgica y otras infecciones
Song GM 2015 (51)	785	Cirugía oncológica gástrica	No	Combinaciones variables de inmunonutrientes (arginina, glutamina, omega-3 y RNA). Posoperatorio	La inmunonutrición mejora la situación inmune y reduce la respuesta inflamatoria en los pacientes intervenidos de gastrectomía
Reis AM 2016 (53)	966	Cirugía oncológica gastrointestinal	No	En la mayoría de estudios, dieta suplementada con arginina, omega-3 y RNA	Las fórmulas inmunomoduladoras reducen las complicaciones y la estancia hospitalaria, y todos los estudios fueron positivos en términos de coste-efectividad
Probst P 2017 (54)	7166	Cirugía mayor abdominal (resección de hígado o páncreas, cirugía que implique anastomosis del tracto gastrointestinal). Excluye la cirugía urológica	No	Combinaciones variables de inmunonutrientes o administración aislada (arginina, glutamina, omega-3 y RNA). Pre o posoperatorio	La inmunonutrición reduce las complicaciones totales, las infecciosas y la estancia hospitalaria. Ningún efecto sobre la mortalidad
Cheng Y 2018 (52)	583	Cirugía oncológica de cáncer gástrico	No	Combinaciones variables de inmunonutrientes (arginina, glutamina, omega-3 y RNA). Pre o posoperatorio	– Incremento del nivel de linfocitos $CD4^+$ y $CD4/CD8^+$, y de prealbúmina – Disminución de SRIS y de complicaciones posoperatorias – Sin cambios en cuanto a neumonías y estancia hospitalaria
Xu J 2018 (83)	1004	Cirugía de cáncer colorrectal electiva	2 estudios en protocolo ERAS	Combinaciones variables de inmunonutrientes (arginina, glutamina, omega-3 y RNA) por vía enteral o administración de glutamina u omega-3 por vía parenteral. Pre y posoperatorio	La NE con inmunonutrientes disminuye la estancia hospitalaria, las complicaciones infecciosas y las complicaciones de la herida quirúrgica; la NP con inmunonutrientes disminuye la estancia hospitalaria, los niveles de IL6, CD3, CD4 y CD4/CD8, y CD8 Sugieren que la inmunonutrición podría ser más efectiva dentro de los protocolos ERAS

ANEXO III.

EJEMPLO DE RECOMENDACIONES NUTRICIONALES EN LA CIRUGÍA MAYOR

RECOMENDACIONES NUTRICIONALES EN LA CIRUGÍA MAYOR: ANTES, DURANTE Y DESPUÉS DE LA INTERVENCIÓN

Es fundamental llegar a la cirugía con un óptimo estado nutricional para así poder disminuir las infecciones y otras posibles complicaciones, facilitar la cicatrización de las heridas quirúrgicas y conseguir una recuperación más rápida. Una intervención quirúrgica supone una importante agresión para el organismo y esto condiciona unas elevadas necesidades de energía y numerosos nutrientes, aumentando su demanda de forma muy especial y por encima de lo habitual.

OBJETIVOS

Mejorar y/o mantener un adecuado estado nutricional antes, durante y después de la cirugía para evitar posibles complicaciones y facilitar la recuperación al alta.

RECOMENDACIONES ANTES DE LA CIRUGÍA

Conviene realizar una alimentación saludable que aporte todos los grupos de alimentos en las cantidades y proporciones adecuadas, pero prestando una mayor atención a ciertos alimentos que contienen algunos nutrientes fundamentales para el proceso quirúrgico:

Nutriente	¿Dónde lo encuentro?	¿Por qué es importante?	¿Cuántas veces al día debo consumirlo?
 Proteínas de alto valor biológico	Carnes magras (pollo, pavo, cerdo, jamón, etc.) Pescados y mariscos Huevos Lácteos (leche, yogur, queso, derivados lácteos)	Contienen aminoácidos esenciales que ayudarán a reparar los tejidos dañados y a cicatrizar adecuadamente las heridas	Aumentar su consumo incluyendo proteínas en cada ingesta y, a ser posible, enriqueciendo los platos con estos alimentos
 Antioxidantes	Frutas y verduras de diferentes colores	Alivian y protegen al organismo del estrés oxidativo, además de fortalecer el sistema inmune	Tres frutas al día mínimo (una de ellas cítrica) y dos platos de verdura al día aseguran una adecuada ingesta de estos nutrientes
 Omega-3	Pescado azul Semillas de lino Nueces Alimentos enriquecidos	Es un potente antiinflamatorio que aliviará la agresión de la cirugía	Pescados azules 2-3 veces a la semana. Semillas y/o frutos secos, un puñado diario

Ejemplo de menú

Desayuno	Media mañana	Comida	Merienda	Cena	Recena
Café con leche + leche en polvo Pan integral con tomate, jamón y aceite de oliva + 2 kiwis	Frutos secos Fruta	Espinacas con huevo y jamón Pollo al limón con patatas al horno Fruta Pan	Yogur con fruta	Salmón con pimientos asados Yogur natural Pan	Vaso de leche + leche en polvo

(Continúa en página siguiente)

ANEXO III (Cont.).

EJEMPLO DE RECOMENDACIONES NUTRICIONALES EN LA CIRUGÍA MAYOR

En algunas ocasiones, si el estado nutricional no es el adecuado, el médico le prescribirá suplementos nutricionales ricos en proteínas y otros nutrientes específicos. Por ello, es importante que sea usted quien controle su peso corporal y reflexione sobre las dificultades que tiene para comer, para detectar las pérdidas involuntarias cuanto antes y para que pueda avisar a su médico. Si lo precisa, será atendido por el equipo de nutrición.

RECOMENDACIONES DURANTE LA ESTANCIA HOSPITALARIA

Tras la cirugía, su médico le pautará una dieta para que empiece a comer lo antes posible, siempre teniendo en cuenta el tipo de intervención realizada y las necesidades de su organismo. Normalmente comenzará con una dieta de fácil digestión, incompleta, con alimentos blandos; a continuación se irá progresando lentamente.

En ocasiones puede ser necesario completar la alimentación oral con suplementos nutricionales y/o módulos de algún nutriente específico, pero también puede llegar a requerir una alimentación artificial a través de una sonda (nutrición enteral) y/o a través de las venas (nutrición parenteral).

El objetivo principal de esta etapa es evitar el riesgo de desnutrición, que puede provocar que la recuperación sea más lenta y la estancia hospitalaria más larga, y que aparezcan nuevas complicaciones.

RECOMENDACIONES AL ALTA HOSPITALARIA TRAS UNA CIRUGÍA

Una vez que se encuentre en su domicilio, deberá continuar con una alimentación lo más saludable y equilibrada posible y, al igual que antes de la cirugía, deberá fomentar el consumo de proteínas de diferentes fuentes para recuperar la masa muscular perdida y ayudar a cicatrizar las heridas; frutas y verduras para aportar antioxidantes y fibra; y alimentos ricos en omega-3 para ayudar a modular la inflamación que ha padecido. Además, deberá asegurar un adecuado estado de hidratación, bebiendo suficiente cantidad de agua y líquidos diariamente, para ayudar a reponer los fluidos que perdemos durante la cirugía.

En determinadas cirugías es necesario realizar recomendaciones nutricionales más individualizadas que su médico le aconsejará. Si es su caso, deberá priorizar esas pautas.

Tras algunas cirugías pueden aparecer síntomas que dificulten su alimentación, como pérdida del apetito, dificultad para tragar, saciedad precoz, estreñimiento o diarrea, o simplemente dolor, lo que aumentaría nuevamente el riesgo de desnutrición; por ello es importante conocerlos y avisar a su médico en caso de padecerlos.

Si antes y/o durante el ingreso ha presentado desnutrición, al alta hospitalaria le prescribirán suplementos nutricionales orales y/o módulos de nutrientes durante al menos tres meses. Es importante que cumpla con la pauta prescrita para asegurar una adecuada recuperación, evitar reingresos hospitalarios y mejorar la calidad de vida. En ocasiones podría llegar a precisar nutrición por sonda o por vena, para lo cual recibirá las instrucciones oportunas antes de irse a casa.

Además, le aconsejamos que realice un control del peso corporal, registrándolo regularmente cada 15-20 días. Si tiene pérdida de peso involuntaria, debe avisar a su médico, ya que es posible que no esté cubriendo sus demandas energéticas o que esté perdiendo nutrientes, lo que le llevará a un estado de desnutrición.

Por último, es común que, después de una cirugía, se pierda masa muscular a causa de la inmovilización y la rotura de músculo para conseguir energía, lo que provocará que esté más cansado e incluso que aparezca desnutrición. Es importante que realice ejercicios regularmente y progresando en intensidad. Puede comenzar por estiramientos y caminatas hasta llegar a realizar ejercicios de resistencia y fuerza. Consulte con su médico cuál es el mejor ejercicio para usted.

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ANEXO III (Cont.).

EJEMPLO DE RECOMENDACIONES NUTRICIONALES EN LA CIRUGÍA MAYOR

Pirámide de la Alimentación Saludable de la Sociedad Española de Nutrición Comunitaria (SENC). Guía divulgativa Alimentación saludable para Atención primaria y colectivos ciudadanos. Disponible en: http://www.nutricioncomunitaria.org

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Revisión

Hypothesis regarding the connections between severe COVID-19 in children and nutrition: a narrative review

Hipótesis sobre las conexiones entre COVID-19 severo en niños y nutrición: una revisión narrativa

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Abstract

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2). Compared with adults, children with SARS-CoV-2 infection may have fewer and less severe symptoms. Gastrointestinal symptoms are commonly reported in children, sometimes as the only manifestation of the disease, and most often manifest as anorexia, diarrhea, nausea and vomiting, or abdominal pain. Although most children have asymptomatic or mild disease, 10 % of those infected may experience serious or critical disease, or even death. Multisystem inflammatory syndrome is a rare but serious condition recently reported in children with COVID-19. Studies indicate that children with obesity are at higher risk of developing severe COVID-19, and inflammation associated with obesity could be one of the factors that worsens COVID-19 symptoms due to an increased inflammatory response involving molecules such as interleukin 6, tumor necrosis factor alpha, and monocyte chemoattractant protein. On the other hand, evidence has been reported of a higher protein expression of ACE2 in the visceral adipose tissue of obese and malnourished humans, and this could be associated with complications and severity of COVID-19. Therefore, regulation of the intake of macronutrients or micronutrients could be used as a strategy to reduce the consequences of COVID-19. Diet in general and bioactive compounds could play an important role in the prevention of the inflammatory cascade. The micronutrients with the most evidence suggesting a role in immune support are vitamins C and D, zinc, and polyphenols.

Keywords:

Pediatrics. SARS-CoV-2. Inflammation. Nutrition. Oxidative stress. COVID-19.

Resumen

La enfermedad por coronavirus 2019 (COVID-19) está causada por el virus "síndrome respiratorio agudo severo-coronavirus 2" (SARS-CoV-2). En comparación con los adultos, los niños con infección por SARS-CoV-2 pueden tener menos síntomas y estos pueden ser menos graves. Los síntomas gastrointestinales se informan comúnmente en los niños, a veces como única manifestación de la enfermedad. Los más comunes son anorexia, diarrea, náuseas y vómitos, y dolor abdominal. Aunque la mayoría de los niños tienen un cuadro leve o asintomático, el 10 % de los infectados pueden experimentar un cuadro grave o crítico, e incluso la muerte. El síndrome inflamatorio multisistémico es una afección poco común, pero grave, que se documentó recientemente en niños con COVID-19. Los estudios indican que los niños con obesidad tienen mayor riesgo de desarrollar COVID-19 grave, y la inflamación asociada con la obesidad podría ser uno de los factores que empeoran los síntomas de la COVID-19 debido a una respuesta inflamatoria aumentada en donde se ven involucradas moléculas como la interleucina 6, el factor de necrosis tumoral alfa y la proteína quimioatrayente de monocitos. Por otro lado, se ha encontrado evidencia de una mayor expresión proteica de ACE2 en el tejido adiposo visceral de los seres humanos obesos y desnutridos, y esto podría estar asociado a las complicaciones y la severidad de la COVID-19. Por tanto, la regulación de la ingesta de macronutrientes o micronutrientes podría utilizarse como estrategia para reducir las consecuencias de la enfermedad. La dieta en general y los compuestos bioactivos podrían desempeñar un papel importante en la prevención de la cascada inflamatoria. Los micronutrientes con mayor evidencia indicativa de que desempeñan un papel en el apoyo inmunológico son las vitaminas C y D, el zinc y los polifenoles.

Palabras clave:

Pediatría. SARS-CoV-2. Inflamación. Nutrición. Estrés oxidativo. COVID-19.

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INTRODUCTION

Obesity or excess ectopic fat deposition is associated with the most important risk factors for developing severe coronavirus disease 2019 (COVID-19) as it reduces the protective cardiorespiratory reserves, promotes poor regulation of the immune system, and mediates progression to a critical state with organ failure (1); this remains true in children (2). It is known that obesity also favors the development of thrombosis in patients, which is relevant given the association between severe COVID-19 and disseminated intravascular coagulation and a high rate of venous thromboembolism. In addition to the cardiometabolic and thrombotic consequences, regardless of whether obesity determines lung function in terms of the immune response, there is a clear association between obesity and a state of chronic inflammation. In addition, it has been described that oxidative stress (OS) may contribute to the pathogenesis of COVID-19 by decreasing antioxidant levels and increasing the levels of pro-oxidant substances such as reactive oxygen species (ROS) in the lung parenchyma (3). On the other hand, the characteristic clinical profile of COVID-19 in children has been reported to start with gastrointestinal manifestations that may affect patient nutrient intake and nutritional status. Another way in which COVID-19 affects the nutritional status of children is the severe presentation of the disease, in which patients go through a critical stage secondary to a rapid progression of the complications of the disease. Critical illness induces intestinal dysfunction and dysbiosis, which extends and accentuates the inflammatory response, causing cellular dysfunction. This has recently been associated with the development of multiple organ failure. At the same time, it causes a loss of macronutrients and micronutrients due to the intense hypermetabolic and hypercatabolic response, leading to increased acute malnutrition, sarcopenia, and muscle weakness, and favoring the development of complications, multiple organ dysfunction, sepsis, and eventually death. Therefore, the aim of this review was to analyze the potential explanations for disease severity in children with COVID-19, as well as potential therapeutic and supportive nutritional strategies.

CORONAVIRUS DISEASE 2019 (COVID-19): PATHOPHYSIOLOGY, CLINICAL CHARACTERISTICS, AND SEVERE MANIFESTATIONS IN CHILDREN

SARS-CoV-2 AND CELL ENTRY

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an enveloped, positive-sense, single-stranded RNA virus, approximately 30 kb in length, that is classified as a *Betacoronavirus* in the *Coronavirinae* subfamily. SARS-CoV-2 shares 79 % and 50 % of its genome sequence with SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), respectively (4). The genome encodes 9,860 amino acids and 27 proteins, including the spike (S) protein, a transmembrane trimetric glycoprotein projecting from the viral surface that determines viral tropism. The protein comprises two functional subunits, S1 and S2, which are responsible for viral attachment to the host receptor and viral fusion to the host membrane, respectively. SARS-CoV-2, like other coronaviruses, uses angiotensin-converting enzyme 2 (ACE2) as a functional receptor for cell entry, and has a higher affinity for ACE2 when compared to SARS-CoV (5).

ACE2 is an enzyme in the renin-angiotensin system (RAS), which involves a mosaic of factors that regulates arterial blood pressure and electrolyte balance (6). The presence of a local RAS has been described in several tissues; hence, ACE2 is in the cell membranes of tissues such as the lungs, ileum, colon, stomach, gallbladder, kidney, testes, arteries, heart, and others (7). The main function of ACE2 is to hydrolyze the peptide angiotensin II, which is a potent vasoconstrictor, to generate angiotensin-(1-7), a vasodilator (6). Differential expression of ACE2 may explain the differences in clinical manifestations between children and adults. In this respect, a recent study mentioned that children have higher levels of circulating ACE2 than adults (8), and since the S protein of SARS-CoV-2 has a high affinity for ACE2, the circulating ACE2 may neutralize the virus and prevent viral arrival at the target cells, and the spread of the infection. It is important to study whether the circulating levels of ACE2 are altered in children with severe COVID-19 and if a nutritional approach might improve the levels of ACE2 in the plasma, with the aim of reducing the severity of the infection.

CLINICAL MANIFESTATIONS IN CHILDREN

Pediatric coronavirus disease-19 (COVID-19) infection is relatively mild when compared to adults. As of June 19th, more than 8 million laboratory-confirmed COVID-19 cases and 450,000 deaths have been reported globally (9). Children represent 1-5 % of all patients diagnosed with COVID-19 and less than 3 % of hospital admissions. Compared with adults, children may experience fewer and less severe symptoms of the infection (10). The most common manifestations in symptomatic children are fever (41-56 %), cough (30-54 %), sore throat (6-46 %), and rhinorrhea (7-19 %) (11). Moreover, gastrointestinal symptoms have been commonly reported in this age group, sometimes as the only manifestation prior to the onset of respiratory symptoms (11). The most frequent gastrointestinal symptoms reported are anorexia (35 %), diarrhea (7-13 %), nausea and vomiting (6-11 %), and abdominal pain (6 %) (11). Other possible gastrointestinal manifestations of the disease in children are liver dysfunction or abnormal liver biochemical tests and ileitis (11).

These broad gastrointestinal manifestations may be caused by the direct invasion of SARS-CoV-2 into the intestine and liver cells that express ACE2 (7). Live viruses and viral RNA have been recovered from stool specimens in children, with longer RNA shedding than in respiratory samples. This demonstrates the presence of SARS-CoV-2 in the gastrointestinal tract and raises the possibility of fecal-oral transmission (12). However, liver disease may also be caused by the inflammatory response to the infection or multiple organ dysfunction in severe cases.

SEVERE DISEASE IN CHILDREN

Although most children have asymptomatic or mild illness, 10 % of those infected may develop serious or even critical illness leading to death (10). It is suggested that children with underlying conditions are at greater risk for more severe disease; however, these clinical observations are based on limited data and have insufficient evidence to support them (13). Some comorbidities suggested as risk factors for increased disease severity in children are chronic lung disease, severe immunocompromised status, cardiovascular disease, and obesity (13). Nevertheless, in children receiving immunosuppressive or immunomodulatory medication for cancer, renal disease, or inflammatory bowel disease, the proportion of patients with severe COVID-19 was low (14), probably due to modulation of the inflammatory response to the virus.

More recently, a multisystem inflammatory syndrome in children (MIS-C), as defined by the Centers for Disease Control and Prevention, has been reported as an uncommon but serious condition temporally associated with SARS-CoV-2 infection. MIS-C mainly occurs in older children and adolescents who have no apparent previous comorbidities (15-17). This syndrome is probably triggered by SARS-CoV-2, as some children have tested positive for viral infection by polymerase chain reaction (PCR) or serology (16,17). The high rate of IgG identification suggests a postviral or delayed immunological response to the virus (15-18). Children with this syndrome have elevated levels of the following inflammatory markers: C-reactive protein, procalcitonin, D-dimer, fibrinogen, ferritin, and interleukin 6. The levels of these inflammatory markers are presumed to correlate with the severity of disease (15,17). Clinically, patients may present manifestations resembling those of Kawasaki's disease: persistent fever, skin rash, bilateral conjunctival injection, oral mucosal changes, cervical lymphadenopathy, and peripheral extremity changes (15,17). However, gastrointestinal symptoms (abdominal pain, vomiting and diarrhea) are more common and are reported in 53-100 % of cases (15,17). Gastrointestinal manifestations precede the other symptoms, and respiratory symptoms may not be present (19,20). This reinforces the previous observation that GI symptoms are more common in patients with severe COVID-19 (21). Multiorgan damage, as seen in patients with MIS-C, includes myocarditis or myocardial injury, acute kidney injury, and shock (15-17,19,20). SARS-CoV-2 may directly cause these lesions, as these organs also express ACE2. However, organ dysfunction is seen after acute infection; therefore, the hyperinflammatory response and OS may be the leading causes of organ damage (22).

Table I summarizes the different characteristics associated with MIS-C in the reported cases (15-20,23-27). Notably, in a cohort of eight patients with MIS-C from London, 80 % of the patients were over the 75th percentile in terms of weight, suggesting that overweight and obesity are comorbidities associated with the syndrome (18). In 21 patients from France, 5 (24 %) met these criteria (17). Moreover, in another publication, 44 children with MIS-C were on average above the 75th percentile, and 39 % were above the 85th percentile (23). This suggests that overweight and obesity may be related to the severity of COVID-19 in children, as is seen in adults (28). Therefore, we reviewed the possible mechanisms underlying the development of severe COVID-19 in children, including MIS-C, and the role of nutrition.

INFLAMMATORY RESPONSE IN CHILDREN WITH SEVERE COVID-19 AND OBESITY OR UNDERNUTRITION

Obesity is defined as an abnormal or excessive fat accumulation that presents a risk to health (29). Studies indicate that children with obesity are at greater risk of developing severe COVID-19 (23), and the inflammation associated with obesity could be one of the factors that may worsen the symptoms of COVID-19 in children, as seen in adults. The expansion of adipose tissue occurs via hyperplasia, which is defined as an increase in the number of adipocytes, or hypertrophy, which is an increase in the size of adipocytes. The latter is related to hypoxia, fibrosis, and inflammation. Adipose tissue releases free fatty acids that activate Toll-like receptor 4 (TLR4) in macrophages, increasing the inflammatory response. Additionally, in obesity, polarization to M1 macrophages occurs in adipose tissue, and these macrophages release inflammatory molecules such as interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-α) and monocyte chemoattractant protein 1 (MCP1) (30). Therefore, obesity is considered a chronic low-grade inflammatory state, and this basal inflammation could lead to an exacerbated response to the virus and the development of severe COVID-19.

There is limited evidence about the levels of ACE2 in obese individuals. Studies in mice have shown that obesity increases the amount of ACE2 in lung epithelial cells (31), as well as ACE2 activity and protein levels in the adipose tissue (32). Interestingly, less information is available for humans. One study showed a tendency towards increased protein expression of ACE2 in the visceral adipose tissue of obese and malnourished humans; the same tendency was observed for other members of the RAS, such as angiotensinogen, ACE, and AT1 receptor (33). On the other hand, it is worthwhile to mention the opposite pole of obesity, when there is an energy deficit intake, such as an undernutrition status. In this condition, inflammation could worsen the symptoms of COVID-19 since protein-energy malnutrition has been strongly associated with inflammation. Additionally, the visceral adipose tissue of malnourished patients had elevated inflammatory markers such as IL-6 and TNF-α, similar to an obese condition (33). Nonetheless, more studies are needed to establish whether obesity or an undernutrition state may affect the amount of ACE2 in humans, and whether modulation of ACE2 and inflammation by nutrients could serve as a very attractive approach to the prevention of severe COVID-19.

ENDOTHELIAL DAMAGE IN CHILDREN WITH SEVERE COVID-19

Chronic cardiovascular diseases are related to the development of severe COVID-19, and a higher risk of thrombosis has also been described (34); therefore, endothelial cells have gained attention as a target to prevent complications of COVID-19.

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Table I. Characteristics associated in children with the multisystem inflammatory syndrome temporarily associated with SARS-CoV-2

	No. (%)										
	Whittaker et al. (15)	**Miller et al. (23)**	**Belhadjer et al. (16)**	**Toubiana et al. (17)**	**Grimaud et al. (19)**	**Cheung et al. (24)**	**Verdoni et al. (25)**	**Riphagen et al. (18)**	**Chiotos et al. (26)**	**Licciardi et al. (20)**	**Jones et al. (27)**
Country	England	USA	France and Switzerland	France	France	USA	Italia	England	USA	Italy	USA
Sample size	58	44	35	21	20	17	10	8	6	2	1
Median age (range), yrs	9 (3 mo-7 yrs)	7.3 (7 mo-20 yrs)	10 (2-16)	7.9 (3.7-16.6)	10 (2.9-15)	8 (1.8-16)	7.2 (2.9-16)	8 (4-14)	7.5 (5-14)	9.5 (7-12)	6 mo
Male	25 (43)	20 (45)	18 (51)	9 (43)	10 (50)	8 (47)	7 (70)	5 (63)	1 (17)	2 (100)	1 (100)
History of COVID-19 contact	NR	NR	13 (37) [g]	10 (48) [g]	NR	11 (65)	5 (50)	4 (50)	NR	NR	0
Comorbidities[a]	7 (12)	NR	4 (11)	0	0	3 (18)	1 (10)	2 (25)	0	1 (50)	0
Asthma	3 (5)		3 (8.5)			3 (18)	0	0		0	
BMI > 85th centile or overweight	NR	16 (36)	6 (17)	5 (24) [h]	NR	NR	NR	5 (63)	2 (33)	NR	NR
Kawasaki-like symptoms											
Fever	58 (100)	44 (100)	35 (100)	21 (100)	20 (100)	17 (100)	10 (100)	8 (100)	7 (100)	2 (100)	1 (100)
Rash or skin changes	30 (52)	31 (70)	20 (57)	16 (76)	10 (50)	12 (71)	8 (80)	4 (50)	2 (33)	2 (100)	1 (100)
Conjunctival injection	26 (45)	23 (52)	31 (89)	17 (81)	6 (30)	11 (65)	8 (80)	5 (63)	2 (33)	2 (100)	1 (100)
Lips or oral mucosal changes	17 (29)	23 (52)	19 (54)	16 (76)	5 (25)	9 (53)	6 (60)	NR	3 (50)	2 (100)	1 (100)
Cervical lymphadenopathy	9 (16)	NR	21 (60)	12 (57)	2 (10)	6 (35)	1 (10)	NR	0	NR	0
Peripheral extremity changes	9 (16)	NR	NR	10 (48)	NR	NR	5 (50)	NR	2 (33)	2 (100)	1 (100)
Respiratory symptoms[b]	12 (21)	NR	12 (34)	9 (43)	0	7 (41)	NR	NR	4 (67)	0	1 (100)
Gastrointestinal symptoms[c]		37 (84)	29 (83)	21 (100)	20 (100)	15 (88)	6 (60)	7 (88)	6 (100)	2 (100)	0
Abdominal pain	31 (53)	33 (75)			20 (100)		NR	6 (75)	5 (83)	2 (100)	
Diarrhea	30 (52)	18 (41)			NR		6 (60)	7 (88)	4 (67)	2 (100)	
Vomiting	26 (45)	25 (57)			20 (100)		NR	4 (50)	5 (83)	2 (100)	
Neurological symptoms[d]	15 (26)	13 (29)	11 (31)	6 (29)	NR	8 (47)	4 (40)	2 (25)	3 (50)	0	0
Myocarditis or myocardial injury[e]	29 (50)	22 (50)	35 (100)	16 (76)	20 (100)	11 (65)	5 (50)	7 (88)	4 (67)	2 (100)	0
Vasoactive or inotropic support	27 (47)	22 (50)	28 (80)	15 (71)	19 (95)	10	2 (20)	8 (100)	5 (83)	1 (50)	0
Coronary aneurysm (z-score ≥ 2.5)	7 (12)	NR	0	0	0	1	2 (20)	1 (12)	1 (17)	0	0
Invasive mechanical ventilation[f]	25 (43)	1 (2)	22 (62)	11 (52)	8 (40)	0	0	5 (63)	3 (50)	0	0
Acute kidney injury	13 (22)	7 (16)	NR	11 (52)	14 (70)	NR	NR	1 (12)	4 (67)	NR	0
Death	1 (2)	0	0	0	0	0	0	1 (12)	0	0	0
Positive microbiologic testing											
SARS-CoV-2 respiratory PCR	15 (26)	15 (34)	12 (34)	8 (38)	10 (50)	8	2 (20)	2	3 (50)	0	1 (100)
SARS-CoV-2 serology	40 (69)	31 (70)	30 (86)	19 (90)	15 (75)	9	8 (80)	NR	5 (83)	2 (100)	NR
Other viruses	2 (3.4)	0	NR	1 (5)	NR	3	0	1 (12)	NR	NR	0

SARS-CoV-2: severe acute respiratory syndrome by coronavirus 2; COVID-19: coronavirus disease 2019; No (%): number of patients displaying clinical features (percentage); mo: months; yrs: years; BMI: body mass index; PCR: polymerase chain reaction; NR: not reported; USA: United States of America. [a]Comorbidities not including overweight or obesity. [b]Respiratory symptoms: cough, coryza or dyspnea. [c]Gastrointestinal symptoms: abdominal pain, diarrhea or vomiting. [d]Neurological symptoms: headache, vision changes, meningeal irritation, cranial nerve palsy, confusion or altered mental status. [e]Myocardial injury: diminished ventricular function on echocardiogram or biochemical evidence of myocardial dysfunction. [f]Invasive mechanical ventilation for cardiovascular compromise or respiratory support. [g]History of COVID-19 contact or contact with a family member displaying viral-like symptoms. [h]BMI > 75th centile.

The available information shows that SARS-CoV-2 can infect human blood vessels *in vitro* (35). Since ACE2 is expressed in the endothelial cells that line the blood vessels in multiple organs, SARS-CoV-2 has the capacity to enter those blood vessels and activate an inflammatory response. Recently, an article suggested that SARS-CoV-2 facilitates the development of endotheliitis in several organs in adults. Histological analysis showed the recruitment of inflammatory cells, which can lead to endothelial dysfunction and apoptosis. This could in part explain the impaired microcirculatory function and ischemia found in COVID-19 patients. If we consider that patients with cardiovascular diseases are prone to endothelial dysfunction (36), it is understandable that SARS-CoV-2 infection worsens the inflammatory condition and contributes to the poor prognosis. It is still unknown why children with chronic ailments such as chronic pulmonary disease and obesity are prone to developing MIS-C (37), but a hypothesis is that the presence of a local RAS in endothelial cells and vascular smooth muscle cells (VSMCs) means that ACE2 is embedded in those cell membranes; hence, if SARS-CoV-2 is able to enter and replicate in those endothelial cells, it is plausible that when the virus leaves those cells, it will be able to infect the neighboring cells, the VSMCs. This could increase local inflammation and worsen vasculitis (Fig. 1).

OXIDATIVE STRESS IN CHILDREN WITH SEVERE COVID-19

OS is defined as an imbalance between ROS and antioxidants, leading to cell damage (38). This imbalance is related to the development of complications generated by obesity, inflammation, and the immune response. In addition, some viral infections are also known to contribute to increased OS, and have been associated with impaired immune responses (22). All of these factors are known to play major roles in the severity of COVID-19. OS increases the pathological inflammatory response, which is crucial for viral replication and the subsequent development of the disease associated with the virus. The association of severe cases of COVID-19 in children with an elevated BMI may be directly related to a predisposition to OS generation (39). In fact, there are associations between OS, inflammation, and the pathogenesis of SARS-CoV infection (22).

MIS-C, which is temporarily associated with SARS-CoV-2 infection, is similar to Kawasaki's disease, which is characterized by systemic vasculitis caused by inflammation of the blood vessels and subsequent damage to the coronary arteries (40). During the inflammatory process, cells release a number of ROS at the site of inflammation, leading to an exacerbation of OS (41). In addition, ROS can initiate an intracellular signaling cascade that increases the expression of pro-inflammatory genes through the activation of transcription nuclear factor B (NF-kB), resulting in an exacerbated inflammatory response of the host by inducing the expression of genes such as TNF-α and IL-6, and upregulating inflammatory molecules such as vascular cell adhesion molecule 1 (VCAM-1), intercellular adhesion molecule 1 (ICAM-1), and other genes that are overexpressed in SARS-CoV-2-infected patients (10).

These excessive ROS levels not only generate OS but also promote the generation of oxidative damage through the oxidation of various biomolecules such as lipids, proteins, and DNA. Oxidative

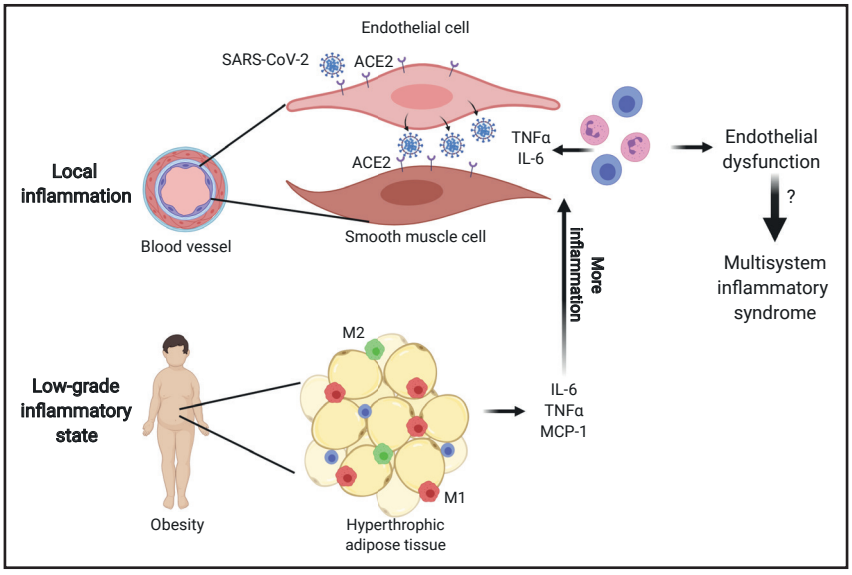

Figure 1.

Hypothesis on the pathogenesis of endothelial damage and vasculitis during obesity and SARS-CoV-2 infection. Blood vessels are constituted by an internal layer known as endothelium, and their neighboring cells are vascular smooth muscle cells (VSMC); both express a local RAS including ACE2. SARS-CoV-2 could infect endothelial cells, multiplicate, and infect smooth muscle cells, generating inflammation. A pre-existent condition such as obesity with hypertrophic adipose tissue, which releases inflammatory molecules, could worsen the local inflammatory response leading to the vasculitis that is present in the multisystem inflammatory syndrome of children. M1: macrophages M1; M2: macrophages M2; IL-6: interleukin 6; TNF-α: tumor necrosis factor alpha; MCP-1: monocyte chemoattractant protein 1.

damage to proteins and lipids causes alterations and dysfunction in cell signaling; several morphological and functional modifications are promoted by ROS, such as the oxidation of thiols and the downregulation of glycoproteins involved in processes such as cell adhesion, angiogenesis, inflammation, and apoptosis (42). During the infection process, the production of ROS is exacerbated because the activation of the immune system also involves the activity of pro-oxidant hemoproteins such as NADPH oxidase and myeloperoxidase. These enzymes are capable of participating in oxidative reactions leading to the formation of the oxidized protein 3-NitroTyr, which is associated with acute and chronic vascular and pulmonary diseases (43). In addition, excessively high ROS levels promote the oxidation of low-density lipoproteins, which in turn promotes a pro-inflammatory environment, inhibits endothelial nitric oxide synthase, promotes the retention of macrophages in the arterial wall, stimulates the proliferation of vascular smooth muscle cells, and disrupts endothelial function (44). This is very important because these alterations likely play important roles in disturbances in the redox homeostasis of red blood cells, resulting in anemia and the formation of blood clots, which may be associated with the inflammation of blood vessels seen in children with SARS-CoV-2 infection (20). Oxidative damage is increased in obese children due to reductions in the activity of enzymes in the endogenous antioxidant system, and in the levels of endogenous antioxidants such as glutathione (45). Thus, these data suggest that in children, chronic inflammation and OS are essential factors in the development of complications in the setting of SARS-CoV-2 infection. Therefore, regulation of the intake of macronutrients or micronutrients, including bioactive compounds with antioxidant or anti-inflammatory properties, could be used as a strategy to reduce the consequences of the severe inflammatory syndrome present in children during the late phase of SARS-CoV-2 infection.

IMPACT OF NUTRITION WITH REGARD TO REDUCING INFLAMMATION, OS, AND/OR ENDOTHELIAL DAMAGE

Can food and the bioactive compounds therein have an impact on reducing inflammation, OS, and/or the immune response? There is evidence to suggest that isolated nutrients, diet in general, and bioactive compounds could play important roles in the prevention of the inflammatory cascade due to their anti-inflammatory and antioxidant activities (46,47). Although there are conflicting data, the available evidence indicates that supplementation with multiple micronutrients that have immune support functions can modulate immune activity and reduce the risk of infection. The micronutrients and bioactive compounds with the strongest evidence suggesting their role in immune support, anti-inflammatory effects, and a reduction of ROS are vitamins C and D, zinc, and polyphenols. However, it is important to mention that it is necessary to satisfy the complex needs of the patient, including the synergy between macronutrients and micronutrients. Below, we focus on these bioactive nutrients/compounds with specific reference to the evidence regarding the factors underlying respiratory disease.

VITAMIN D

Evidence in children regarding vitamin D supplementation indicates that it reduces the incidence of influenza infection and other acute respiratory infections. This can be attributed to the fact that calcitriol (the active form of vitamin D) stimulates the expression of some antimicrobial peptides in epithelial cells, such as those that line the respiratory tract, protecting the lungs from infection (48). There is also evidence related to signals modulating the inflammatory response by modulating the activity of NF-kB through the upregulation of the NF-B inhibitor protein (IB); in this way, the production of molecules that amplify the inflammatory response, such as IL-6, IL-1, and TNF-α, is inhibited, influencing the production of enzymes such as iNOS, COX-2, and PLA2, that determine the production of free ROS resulting in tissue damage (49).

One of the comorbidities suggested as a risk factor for increased severity of disease in children with chronic lung disease is obesity. Moreover, there is an association between obesity and vitamin D deficiency, and it has been proposed that fat-soluble hormones, including vitamin D, are sequestered in adipose tissue. This results in decreased bioavailability (50) and insufficient serum concentrations of vitamin D, which could compromise the regulation of pathways that promote the innate immune response while suppressing the adaptive immune response (51).

VITAMIN C

Vitamin C is involved in the function of the epithelial barrier, which protects against pathogens, and the cellular functions of the innate and adaptive immune systems; in addition, it protects against OS (52). In particular, it has been documented that vitamin C may protect against lung infections due to its immunomodulatory function and activation of inflammatory mediators. In addition, during infection, vitamin C levels may be depleted, suggesting that vitamin C supplementation could attenuate infections (53).

A systematic review of randomized clinical trials that included studies with children aged 3 months to 18 years evaluated whether the administration of vitamin C had an impact on upper respiratory tract infections (URTIs), which are generally caused by a viral infection; they found that the duration of URTIs decreased by 1.6 days; however, there was no difference in the incidence of URTIs; no serious adverse events were reported (54).

POLYPHENOLS

Polyphenols are compounds that form one or more hydroxyl groups in one or more aromatic rings, and are found naturally in fruits, vegetables, grains, and roots. Polyphenols have antioxidant activity, which may depend on the structure of their functional groups; for example, the number of hydroxyl groups strongly influences various mechanisms of antioxidant activity, such as radical scavenging and the capacity to chelate metal ions. This antioxidant activity is related to the ability of polyphenols to eliminate a wide range of ROS.

Curcumin is a bioactive polyphenol found in the spice turmeric, and it has been documented that it has various biological functions, such as antioxidative and anti-inflammatory activities, in different organs, including the adipose tissue. A recent study found that curcumin could bind the target SARS-CoV-2 receptors, ACE2, and could therefore compete with the virus; this activity could be used to prevent infection (55). Curcumin has also been reported to inhibit influenza virus infection by activating the nuclear antioxidant erythroid factor 2-related factor 2 (Nrf2) pathway, and inhibiting virus-induced inflammatory pathways (56).

This bioactive compound has been evaluated in children and adolescents (7-18 years) with persistent asthma in a randomized clinical trial. In the trial, powdered *Curcuma longa* root (30 mg/kg/day) was administered for 6 months, and they observed that after 3 and 6 months of supplementation, children had less frequent nighttime awakenings, less frequent use of short-acting beta-adrenergic agonists (SA β AA), and better disease control. These results were due to anti-inflammatory and antioxidant effects, which alleviated bronchial hyperreactivity (57).

The synergy of the administration of these micronutrients could produce a better response in a patient; in fact, it is reported that a combination of three bioactive compounds, namely vitamin C, curcumin, and glycyrrhizic acid, showed a promising control over the production of interferons and regulated the inflammatory response, suggesting that these interventions may be useful for regulating the immune response to SARS-CoV-2 infection (58).

ZINC

Zinc is an essential trace element that plays an important role in the immune function, and the deficiency of this trace element has been associated with increased susceptibility to infectious diseases, specifically viral diseases. It has been observed that in pediatric patients with pneumonia on admission, zinc concentrations are below normal levels. Zinc depletion may be caused by the consumption of zinc by peripheral blood mononuclear cells during the inflammatory response (59). Zinc sulfate supplementation has been evaluated in children < 5 years old (10 mg for children younger than 1 year, 20 mg for children older than 1 year) with pneumonia, and improvements were observed in respiratory rate, oxygen saturation level, and disease duration; in addition, increases were observed in the concentrations of IFNγ and IL-2, resulting in an improvement of clinical symptoms mediated by the cellular immune response (60) (Fig. 2).

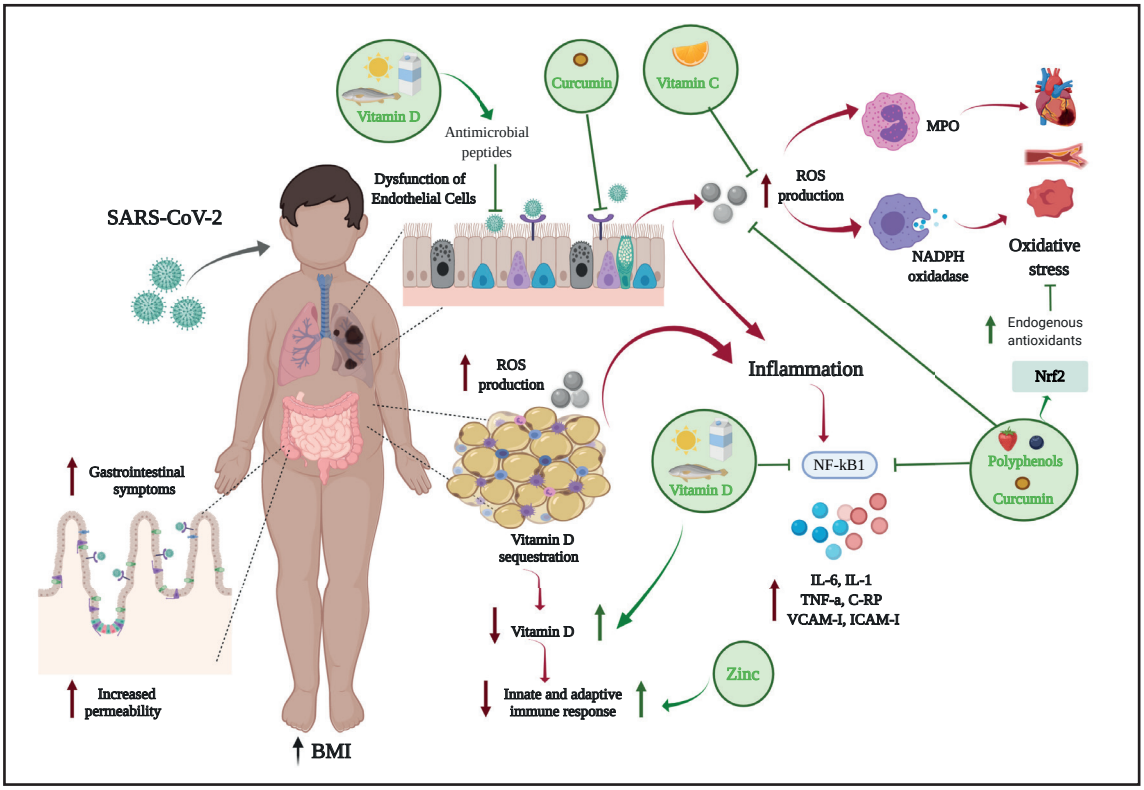

Figure 2.

Hypothesis of a possible interaction between the inflammatory process and oxidative stress in the complications caused by COVID-19 in children with obesity, and the impact of nutrition to reduce their response. ROS: reactive oxygen species; NF-KB: nuclear factor kappa B; IL-6: interleukin 6; IL-1: interleukin 1; TNF-α: tumor necrosis factor alpha; C-RP: C-reactive protein; VCAM-I: vascular cell adhesion molecule 1; ICAM-I: intercellular adhesion molecule 1; MPO: myeloperoxidase; NADPH oxidase: nicotinamide adenine dinucleotide phosphate oxidase; Nrf2: nuclear factor erythroid 2-related factor 2.

CONCLUSION

The pathophysiology of SARS-CoV-2 infection is characterized by aggressive inflammatory responses that are strongly implicated in the damage observed in the airways and organs; therefore, the severity of the disease in children is caused not only by the viral infection itself but also by the host immune response. Given this premise, it is reasonable to consider endothelial dysfunction, mediated by OS and inflammation, as a therapeutic target in COVID-19 patients. Therefore, it is important to discuss the role of nutrition as an adjunct therapeutic measure to decrease the inflammation and OS generated during infection. Additionally, another important factor affecting the severity of COVID-19 is the degree to which the patient is immunocompromised. In terms of nutrition, there is substantial controversy over whether specific nutrients could have an impact on 'improving' the immune system.

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Revisión

Efecto de las técnicas y estrategias de modificación de la velocidad al comer sobre la ingesta de alimentos o energía: revisión sistemática y metaanálisis

Effect of eating speed modification techniques and strategies on food or energy intake: a systematic review and meta-analysis

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Resumen

La evidencia científica indica que comer de modo lento reduce la ingesta de alimentos y de energía. Sin embargo, son pocas las investigaciones que han estudiado el efecto de las técnicas y estrategias que modifican la velocidad al comer sobre la ingesta. El objetivo de este estudio es analizar la relación entre estas técnicas y la ingesta de alimentos y/o energía. Para ello se realizó una revisión sistemática de 15 estudios de seres humanos y un metaanálisis de 7 estudios con 11 manipulaciones experimentales y 1 observacional. Se incluyeron únicamente los resultados de dos condiciones, "lenta" *vs.* "rápida", de la velocidad al comer y la ingesta. La estimación del efecto se expresó en OR con un IC del 95 % bajo el modelo de efectos aleatorios, y se evaluó la heterogeneidad con I^2. También se evaluó el sesgo de publicación con un gráfico de embudo y la prueba de la regresión lineal de Egger. Los resultados indican que comer de modo lento es un factor de protección (OR = 0,73) frente a la ingesta excesiva. Además, comer bocados pequeños con una cuchara chica (OR = 0,315), servir los guisados en platos separados (OR = 0,860 y OR = 0,831), usar un tenedor con retroalimentación vibrotáctil (OR = 0,847) y comer alimentos de textura dura (OR = 0,891) son las técnicas y estrategias que modifican la velocidad al comer y disminuyen la ingesta de alimentos o energía. El presente estudio confirma la premisa de que el comer de modo lento podrá reducir la ingesta excesiva de alimentos y de energía.

Palabras clave:

Técnicas y estrategias. Velocidad al comer. Ingesta de alimentos. Ingesta de energía. Modificación de la conducta.

Abstract

Scientific evidence indicates that eating slowly reduces food and energy intake. However, few investigations have studied the effect of techniques and strategies that modify eating speed on intake. The objective of this study is to analyze the relationship between these techniques and food and/or energy intake. Therefore, a systematic review of 15 human studies and a meta-analysis of 7 studies with 11 experimental and 1 observational manipulations were carried out. Only the results of two conditions were included, "slow" vs. "fast" of eating speed and ingestion. The estimation of the effect was expressed in OR with a 95 % CI under a random effects model, and heterogeneity was assessed with I^2. Publication bias was also assessed with a funnel plot and Egger's linear regression test. The results indicate that eating slowly is a protective factor (OR = 0.73) from excessive intake. Additionally, eating small bites with a small spoon (OR = 0.315), serving food preparations on separate plates (OR = 0.860 and OR = 0.831), using a vibrotactile feedback fork (OR = 0.847), and eating hard-textured foods (OR = 0.831) are the techniques and strategies that modify eating speed and decrease food or energy intake. The present study confirms the premise that eating slowly can reduce excessive food and energy intake.

Keywords:

Techniques and strategies. Eating speed. Food intake. Energy intake. Changing eating behavior.

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INTRODUCCIÓN

El fenómeno de la velocidad al comer ha sido de gran interés en los últimos años debido a que la evidencia procedente de estudios observacionales, revisiones sistemáticas y metaanálisis ha demostrado que el comer de modo rápido se asocia a la presencia de sobrepeso y obesidad (1-4). Además, se ha planteado que la velocidad al comer es el vínculo mediador entre el índice de masa corporal (IMC) y la ingesta de energía durante un episodio alimentario (5). No obstante, desde antes del siglo XX se argumentaba que el comer de modo rápido estimula una mayor ingesta de energía que, a su vez, promueve la ganancia de peso corporal y lleva al sobrepeso o la obesidad (6-10).

Aunado a lo anterior, se ha correlacionado la masa libre de grasa y la tasa metabólica basal con la velocidad al comer, sugiriéndose que las tasas de consumo alimentario (velocidad al comer) más rápidas promueven una mayor ingesta de energía como respuesta conductual adaptativa a los mayores requerimientos energéticos (11). También se ha señalado que el comer rápidamente tiene una base genética que aumenta el riesgo de factores conductuales para el aumento de peso, y este es un rasgo caracterizado como hereditario que se mantiene estable en el tiempo (12). Por otro lado, se ha observado que, cuando un individuo come rápidamente en una ocasión, es posible predecir que también comerá de modo rápido y con una ingesta elevada en comidas posteriores, independientemente de las diferencias de composición corporal (13).

Pero, independientemente de los aspectos genéticos y biológicos, la velocidad al comer se puede modificar por elementos del medio ambiente. Por ejemplo, se ha manipulado por el tipo de cubierto empleado (14), la forma de servir la comida (15), el tamaño de la porción (16), las propiedades nutricionales (16,17), las instrucciones verbales o computarizadas (18-20), la retroalimentación vibrotáctil de los cubiertos (21) y la textura de los alimentos (16,18,22-24).

Esto ha dado lugar a intervenciones clínicas y recomendaciones de salud pública para disminuir la velocidad al comer (25). Por ejemplo, en 2009, "The Obesity Society" recomendó a las personas con obesidad que disminuyeran la velocidad al comer como medio para controlar la ingesta de energía (26). Sin embargo, el análisis de las revisiones sistemáticas sobre los métodos elegidos para manipular la velocidad al comer es limitado, dado que dichas revisiones lo han planteado como un objetivo secundario de sus reportes (27). Por tanto, aunque la evidencia científica indica que la velocidad al comer afecta a la ingesta de energía y, por consiguiente, en la práctica clínica se recomienda disminuir la velocidad al comer para reducir la ingesta de energía, aún no se ha realizado un análisis detallado del efecto de los métodos que modifican la velocidad al comer sobre la ingesta. La realización de este análisis proporcionaría a los profesionales de la nutrición un sustento científico para la selección e implementación de técnicas y estrategias que modifiquen la velocidad al comer de los pacientes que necesiten reducir su ingesta de alimentos y energía. Por tal motivo, el objetivo principal de la presente publicación es analizar el efecto de los métodos que modifican la velocidad al comer sobre la ingesta de alimentos y de energía, mientras que el objetivo secundario es evaluar si hay evidencia científica que sustente la premisa de que comer de modo lento es un factor de protección frente a la ingesta de alimentos y de energía.

MÉTODOS

CRITERIOS DE INCLUSIÓN

Participantes

Se incluyeron estudios experimentales y observacionales con participantes de cualquier sexo, edad, composición corporal, actividad física y país. Se excluyeron los estudios que seleccionaron participantes con trastornos alimentarios clínicamente definidos.

Tipo de estudios

Se seleccionaron aquellos estudios experimentales en los que se manipuló la velocidad al comer por medio del alimento o el ambiente alimentario, y se observó su efecto sobre la ingesta de alimentos o de energía. Adicionalmente, se incluyeron estudios observacionales en los que se hubiera categorizado la velocidad al comer.

Comparación de grupos y medida de resultados

Los estudios observacionales o experimentales elegibles para el metaanálisis fueron los que habían incluido resultados de dos condiciones determinantes de la velocidad al comer (lenta frente a rápida) y su efecto sobre la ingesta de alimentos o de energía. En cambio, para la revisión sistemática se analizaron los resultados de todos los estudios que habían evaluado el efecto de la velocidad al comer sobre la ingesta de alimentos o de energía, independientemente de la categorización utilizada para el metaanálisis.

Diseño del estudio

Se eligieron estudios con diseños experimentales u observacionales aleatorios y no aleatorios, tanto de comparación entre grupos como de comparaciones intrasujetos o de medidas repetidas. En los estudios de medidas repetidas se realizó la comparación de los efectos de las condiciones (lenta *vs*. rápida) sobre cada participante: es decir, el sujeto participó en las dos condiciones. Por su parte, la comparación entre dos grupos independientes implica que un grupo comió conforme a la condición "lenta" y el otro según la condición "rápida".

Estrategia de búsqueda

Se realizó una búsqueda estratégica de publicaciones científicas en las bases de datos de PubMed (https://www.ncbi.nlm.nih.gov/pubmed/), BASE (https://www.base-search.net) y ScienceDirect (https://www.sciencedirect.com) durante los meses de julio, agosto y septiembre de 2019. La búsqueda incluyó una combinación de las palabras clave que hacen referencia a la velocidad al comer, "eating rate", "eating speed", "quick eating", "fast eating" y/o "rapid eating" en combinación con los términos de ingesta alimentaria o energética, "food intake" y/o "energy intake. El proceso de búsqueda se guío por los Ítems de referencia para publicar revisiones sistemáticas y metaanálisis, la declaración PRISMA (28).

SELECCIÓN DE ESTUDIOS Y EXTRACCIÓN DE DATOS

Dos autores (SPRE y HF) realizaron de forma independiente la búsqueda de la literatura y la extracción de datos utilizando un enfoque estandarizado. No se presentaron desacuerdos respecto a la elegibilidad o calidad de ningún estudio.

Clasificación de estudios

Se clasificaron como estudios de tipo 1 los observacionales o experimentales sin datos de la condición "rápida" *vs.* "lenta", y como estudios de tipo 2 los correspondientes del metaanálisis.

Datos registrados

Se registró el tamaño de la muestra de los participantes, la edad, el IMC y las características de la población, como la nacionalidad. Además, se especificó el método de manipulación de la velocidad al comer y los métodos de observación y registro de la ingesta de alimentos o de energía junto con los resultados de la velocidad al comer (g/min o kcal/min) y la ingesta de alimentos (g) o de energía (kcal).

Información adicional

El metaanálisis se realizó con la extracción de los datos de los resultados de las condiciones "lenta" *vs.* "rápida" de la velocidad al comer y la ingesta de alimentos o de energía.

ANÁLISIS ESTADÍSTICOS

Se utilizó el software STATA, versión 14.1 (Stata Corp, College Station, Texas, EUA), para administrar y analizar los datos. Se clasificaron la velocidad al comer y la ingesta de alimentos o de energía en dos condiciones: "lenta" *vs.* "rápida". La estimación del tamaño del efecto de la velocidad al comer sobre el riesgo de una mayor ingesta de alimentos o de energía se expresó como razón de momios (OR) con intervalos de confianza (IC) del 95 %. Se generó bajo el modelo de efectos aleatorios dado que se registró la ingesta de alimentos o de energía en diferentes medidas de valores numéricos (gramos, kcal, g/min, kcal/min). El índice de inconsistencia (I^2) se utilizó para evaluar la heterogeneidad entre los estudios, y su valor representa el porcentaje de diversidad observado entre los estudios que es consecuencia de la heterogeneidad además del azar. La heterogeneidad se consideró significativa si el I^2 era mayor del 50 %; un valor superior al 50 % significa un mayor grado de heterogeneidad. Finalmente, se realizó un gráfico de embudo o *funnel plot* y se calculó la prueba de Egger para evaluar el posible sesgo de publicación (29).

RESULTADOS

SELECCIÓN DE PUBLICACIONES CIENTÍFICAS

En la figura 1 se muestra el diagrama de flujo que detalla el proceso de selección de publicaciones para la revisión sistemática y el metaanálisis. La búsqueda estratégica encontró 553 publi-

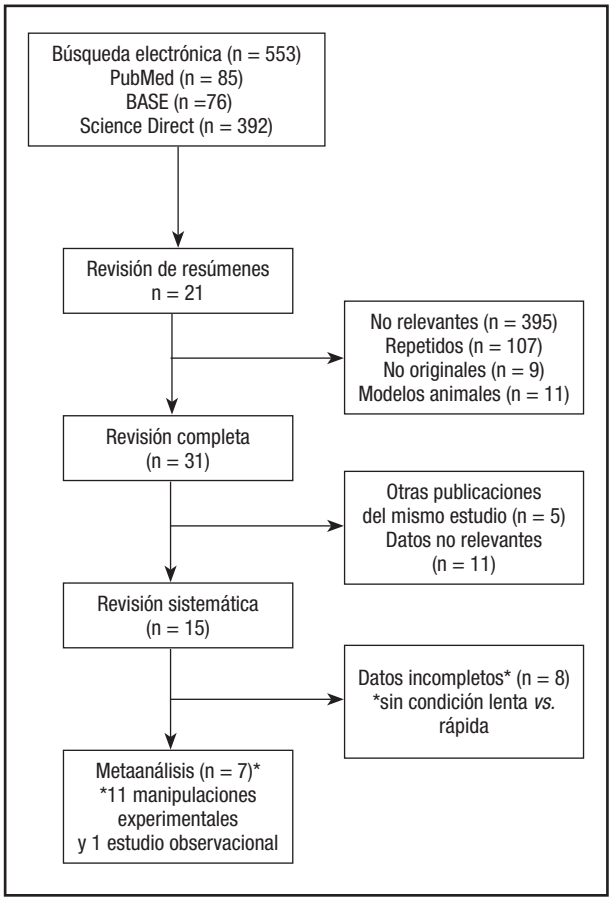


Figura 1.
Diagrama de flujo de la búsqueda y selección de publicaciones.

caciones, 85 en PubMed, 76 en BASE y 392 en ScienceDirect. Se realizó una revisión de los resúmenes, descartándose 395 no relevantes, 107 repetidos, 9 no originales y 11 de modelos animales. Posteriormente se efectuó una revisión completa de las 32 publicaciones restantes, excluyéndose 5 publicaciones del mismo estudio y 11 por datos no relevantes. Finalmente fueron 15 las publicaciones seleccionadas para la revisión sistemática del efecto de la velocidad al comer sobre la ingesta de alimentos y energía (2,3,5,14-24,30). Para el metaanálisis se eliminaron 8 publicaciones por datos incompletos para poder categorizar la velocidad al comer y la ingesta en dos condiciones (lenta *vs.* rápida). En consecuencia, el metaanálisis estuvo compuesto por 7 publicaciones en las que se habían realizado un total de 11 manipulaciones de la velocidad al comer y 1 estudio observacional (5,14,15,21,22,24,30).

CARACTERÍSTICAS DE LAS PUBLICACIONES INCLUIDAS

En la tabla I y la tabla II se muestra la información detallada de las 15 publicaciones elegidas para la revisión sistemática, que está constituida por los siguientes elementos: a) número de sujetos en general y por sexos; b) edad; c) IMC; d) características de la población, como la nacionalidad; e) tipo de manipulación experimental de la velocidad al comer; f) métodos de observación y registro de la ingesta de alimentos o de energía; y g) resultados del efecto sobre la ingesta de alimentos y energía.

Se registraron en total 13 estudios que habían medido la velocidad al comer de modo directo (5,14-24,30) y 2 que lo habían hecho por medio de cuestionarios autoadministrados (2,3). En 12 estudios se manipuló la velocidad al comer (14-24,30) por medio de: el tipo de cubierto (14), el tamaño del cubierto (30), la forma de servir la comida (15), el tamaño de la porción (16), las propiedades nutricionales de la comida (14,16,17,23), la textura de los alimentos (16,18,22-24), instrucciones verbales o computarizadas (19,20), y retroalimentación vibrotáctil del cubierto (21). En cuanto a las características de los participantes, 6 estudios estuvieron conformados únicamente por sujetos con normopeso (2,17,18,22-24), 2 por mujeres (15,30) y 1 por niños (5).

Las publicaciones se clasificaron en tipo 1 y tipo 2; las de tipo 1 estuvieron conformadas por estudios observacionales o experimentales sin datos de la condición "rápida" *vs.* "lenta (Tabla I) y las de tipo 2 correspondieron a las incluidas en el metaanálisis (Tabla II).

PUBLICACIONES DE TIPO 1: SIN DATOS DE LA CONDICIÓN "RÁPIDA" *VS.* "LENTA"

De las 15 publicaciones seleccionadas para la revisión sistemática (Tabla I y Tabla II), 8 presentaban datos incompletos sobre las condiciones "rápida" y "lenta" de la velocidad al comer y la ingesta de alimentos o energía (Tabla I). En 6 de ellas se había manipulado experimentalmente la velocidad al comer (16-20,23) y 2 eran sobre estudios observacionales (2,3). La edad de los participantes oscilaba entre los 18 y los 69 años; respecto al IMC, 7 estudios se habían realizado en sujetos con un IMC > 18,5 kg/m^2 (2,3,17-20,23), y, de estos, 2 se habían efectuado únicamente en sujetos con sobrepeso u obesidad (3,19) y 3 en sujetos con normopeso (2,17,18,23). En 1 publicación se incluían sujetos con un IMC categorizado como "delgadez" (16). Respecto a las características de la población, 5 se habían realizado en países asiáticos (2,3,16,18,23).

Análisis de subgrupos: métodos para manipular la velocidad al comer

En 6 publicaciones clasificadas como de tipo 1 se manipuló experimentalmente la velocidad al comer (16-20,23), por métodos de modificación de atributos de la textura de la comida (16,18,23) como la dureza (18) y la viscosidad, así como la densidad energética, el tamaño de la porción (16) e indicaciones verbales (19,20). Los resultados de estos estudios mostraron que disminuye la velocidad al comer y la ingesta cuando la textura de los alimentos o comidas es más dura (18), viscosa (16), masticable, resistente y menos elástica (23), y cuando el tamaño de la porción es más grande (16). Finalmente, el masticar más veces la comida disminuye la velocidad al comer (20) y, a su vez, el comer lentamente reduce la ingesta de alimentos y energía (19).

Análisis de subgrupo: estudios observacionales

De las 8 publicaciones sin datos de la condición rápida *vs.* lenta (tipo 1), en 2 estudios no se realizó ninguna manipulación experimental: es decir, se trata de estudios observacionales. En ellos se midió la velocidad al comer por medio de un cuestionario breve de historia dietética autoadministrado, denominado BDHQ (*brief self-administered diet history questionnaire*), y se categorizó como: 1) muy lenta, 2) lenta o relativamente lenta, 3) mediana, 4) rápida o relativamente rápida y 5) muy rápida. Los autores de estos estudios concluyeron que las personas que comen más rápido presentan una mayor ingesta de energía (2,3). Además, se observó una diferencia significativa según el sexo, demostrándose que los hombres comen más rápido que las mujeres (2).

PUBLICACIONES DE TIPO 2: METAANÁLISIS

Fueron 7 publicaciones con datos completos de condición "rápida" *vs.* "lenta" de la velocidad al comer y la ingesta de alimentos o energía las que se incluyeron en la revisión sistemática (Tabla II) y el metaanálisis (Figs. 2 y 3). En ellas se habían documentado 11 manipulaciones experimentales de la velocidad al comer (14,15,21,22,24,30) y 1 estudio era observacional (5).

[Nutr Hosp 2021;38(3):631-644]

Tabla I. Publicaciones tipo 1: sin datos de condición "rápida" *vs.* "lenta"

Autores	Sujetos (n) H/M	Edad (años)	IMC (kg/m²)	Características de la población	Tipo de manipulación experimental de la velocidad al comer	Métodos de observación y registro	Efecto sobre la ingesta de alimentos o energía
Bolhuis y cols., 2014 (18)	n = 50 11/39	20-29	21 ± 2	Población con nacionalidad china	Textura de comida: suave *vs.* dura pan blanco *vs.* pan artesanal (hamburguesas) verduras cocidas *vs.* crudas (ensalada de arroz)	Comida: *ad libitum,* servida en porciones de 4 hamburguesas y 600 g de ensalada de arroz (suave *vs.* dura) Cena: ad libitum, fideos con pollo y verduras Tiempo: almuerzo y cena (mismo día) Videograbación + microanálisis de la conducta por dos observadores	Se consumió en menor cantidad (16 %) el almuerzo de textura dura ($p < 0,001$), con una reducción de la ingesta energética de un 13 % ($p < 0,001$) y de la tasa de alimentación en un 32 % ($p < 0,001$). Se consumió más agua ($p = 0,09$) La reducción del consumo de energía en el almuerzo no se compensó en la cena ($p = 0,16$)
Maruyama y cols., 2008 (3)	n = 3287 1122/ 2165	30-69	> 25	Población japonesa que acude a revisión médica	Sin manipulación experimental	Velocidad al comer auto-reportada y categorizada como "muy lenta", "lenta", "mediana", "rápida" y "muy rápida" Ingesta energética medida por cuestionario dietético validado auto-administrado (BDHQ)	Las personas que comieron más rápidamente presentaron una mayor ingesta energética ($p < 0,05$)
Martin y cols., 2007 (19)	n = 48 22/26	18-64	25-34	Sin datos	Aplicación computarizada que indica cuándo comer cada pieza (sonido) 1) línea basal: velocidad al comer del participante 2) reducir al 50 % (condición lenta) 3) combinado (línea base y 50 % más lento)	Comida: *ad libitum,* servida en porciones de 1000 g de palomitas de pollo en bocados estándar de 8 g (2,32 kcal/g) Tiempo: hora del almuerzo (ayuno de 12 h) Monitores universales de alimentación (Universal Eating Monitor-UEM) registraron la ingesta de comida y la velocidad al comer	El comer lentamente (reducción 50 %) disminuyó la ingesta de alimentos (< 50 %), $F(1,45) = 6,00$, $p < 0,05$, y de modo combinado $F(1,45) = 4,92$, $p < 0,05$ El tamaño del efecto fue mediano en los hombres y pequeño en las mujeres
McCrickerd, Lim, Leong, Chia y Forde, 2017 (16)	n = 61 31/30 n = 53 53/0 Dos estudios	21-48 21-42	16-29 16-29	Población de Singapur	Textura: diluido *vs.* espeso Densidad energética: alta *vs.* baja Tamaño de la porción: regular *vs.* grande	Comidas *ad libitum,* servidas en diferentes porciones Estudio 1: porciones de 1000 g de gachas de arroz diluidas vs. espesas en combinación con una baja (0,57 kcal/g) y alta (1,01 kcal/g) densidad energética Estudio 2: gachas de arroz diluidas vs. espesas en combinación con porciones de tamaño regular (700 g) *vs.* grande (1050 g) Tiempo: desayuno de 20 min (ayuno desde las 23:00 h del día anterior) Videograbación con cámaras web y ELAN	Las gachas espesas y masticables se comieron más lentamente ($p < 0,001$), en menor cantidad ($p < 0,001$) y con una menor ingesta energética ($p = 0,001$) que las líquidas Se consumieron más gachas al servirse en porciones grandes ($p < 0,001$)

(Continúa en página siguiente)

Tabla I (Cont.). Publicaciones tipo 1: sin datos de condición "rápida" *vs.* "lenta"

Autores	Sujetos (n) H/M	Edad (años)	IMC (kg/m²)	Características de la población	Tipo de manipulación experimental de la velocidad al comer	Métodos de observación y registro	Efecto sobre la ingesta de alimentos o energía
Otsuka y cols., 2006 (2)	n = 4742 3737/ 1005	35-69	media H: 23,3 M: 21,8	Funcionarios públicos de Japón	Sin manipulación experimental	Velocidad al comer auto-reportada y categorizada como "muy lenta", "relativamente lenta", "mediana", "relativamente rápida", "rápida" Ingesta energética medida por cuestionario dietético validado auto-administrado (BDHQ)	El incremento en la velocidad al comer promovió una mayor ingesta energética en los hombres ($p < 0,001$) Los hombres comieron más rápido que las mujeres ($p = 0,001$)
Viskaal-van Dongen, Kok y de Graaf, 2011 (17)	n = 37 13/24	18-35	18,5-25	Población de Países Bajos	Comidas con diferentes características nutricionales	Comida: 45 muestras diferentes (50 g c/u) Tiempo: almuerzo (ayuno desde el desayuno) Tiempo de ingestión medido por cronómetro en una computadora	Asociación positiva de la velocidad al comer (g/min) con la ingesta de comida (g), $\beta = 0,55$, $p < 0,01$ y $R^2 = 0,37$, y la ingesta energética (log kJ) $\beta = 0,001$, $p < 0,01$ Los carbohidratos ($b = -0,012$), las proteínas ($b = -0,021$) y el contenido de fibra ($b = -0,087$) se asociaron inversamente con la velocidad al comer, mientras que la grasa no.
Wee, Goh Stieger y Forde, 2018 (23)	n = 27 10/17	21-45	20-25	Estudiantes universitarios de Singapur y voluntarios del Centro de Investigación Nestlé en Suiza	Comidas con diferentes texturas y características nutricionales	Comida: 59 muestras diferentes (50 g c/u) Tiempo: almuerzo (sin restricciones de ayuno y desayuno habitual en casa) Videograbación + software (The observer XT y ELAN)	La velocidad al comer disminuyó con las comidas que son menos elásticas ($p \leq 0,01$), masticables ($p \leq 0,05$) y resistentes ($p \leq 0,01$) La velocidad al comer aumentó con las comidas de texturas adhesivas ($p \leq 0,05$)
Zhu y Hollis, 2014 (20)	n = 47 24/23	18-45	> 18,5	Estudiantes universitarios estadounidenses	Indicación verbal del número de masticaciones por rollo (investigador) Número de masticaciones: 1) línea base (100 %) 2) 150 % de la línea base 3) 200 % de la línea base	Comida: *ad libitum,* rollos de pizza servidos en porciones de 85 g (6 rollos, 200 kcal) Tiempo: almuerzo (desayuno habitual en casa) Observación directa del número de masticaciones (movimiento mandíbula) y conteo de los participantes + duración del tiempo con cronómetro	La velocidad al comer disminuyó cuando se mastico más veces, en las sesiones del 150 % y el 200 % ($p < 0,001$)

N: tamaño de la muestra; H: hombres; M: mujeres; IMC: índice de masa corporal; kg: kilogramos; m: metros.

Tabla II. Publicaciones tipo 2: metaanálisis

Autores	Sujetos (n) H/M	Edad (años)	IMC (kg/m²)	Características de la población	Tipo de manipulación experimental de la velocidad al comer (condición rápida *vs.* lenta)	Métodos de observación y registro	Efecto sobre la ingesta de alimentos o energía y resultados de la condición rápida *vs.* lenta
Andrade, Kresge, Teixeira, Baptista y Melanson, 2012 (30)	n = 30 0/30	18-45	19-30	Mujeres universitarias estadounidenses	Ingesta de agua: controlada (300 ml con la comida) Cuchara grande + instrucción de comer rápido (sin pausas) *vs.* cuchara pequeña + indicación de comer lento (pequeños bocados, cuchara en la mesa entre bocados y de 20 a 30 masticaciones)	Velocidad al comer: auto-reportada como "lenta", "mediana" o "rápida" + registro en laboratorio en g/min y kcal/min Comida: 600 g de pasta (870 kcal) y 300 ml de agua Tiempo: almuerzo (ayuno de 4 h y desayuno estandarizado en casa) Hora de inicio y terminación de comida. Pesaje de comida restante	Mayor velocidad al comer y duración de la comida (min) en condición rápida *vs.* lenta ($p < 0,05$). **Condición rápida *vs.* lenta:** VC: 94 ± 5,6 *vs.* 29 ± 1,9 kcal/min IA: 488,2 ± 17,9 *vs.* 478,6 ± 22,5 g IE: 707,9 ± 26 *vs.* 694 ± 32,6 kcal
Bolhuis y Keast, 2016 (14)	n = 48 16/32	18-54	17,8-34,4	Estudiantes universitarios de Australia	Utensilios: cuchara *vs.* tenedor Contenido de sal y grasa: bajo *vs.* alto	Comida: *ad libitum,* pasta de macarrones + cuchara o tenedor (elección libre) Time: almuerzo (ayuno de 3 h y desayuno estandarizado en laboratorio) Pesaje de comida (antes y después) + cronómetro.	La velocidad al comer se correlacionó positivamente con la ingesta de comida (g) para el tenedor ($r = 0,45$, $p < 0,001$) y la cuchara ($r = 0,47$, $p < 0,001$) Comieron más cantidad los participantes que usaron la cuchara ($p = 0,09$) El contenido de sal y grasa no tuvo efecto sobre la ingesta (g) y la velocidad al comer. Pero la grasa sí tuvo efecto sobre la ingesta energética ($p < 0,001$) **Condición rápida *vs.* lenta: (cuchara *vs.* tenedor)** VC: 367 ± 13 *vs.* 332 ± 16 g/min IA: 62 ± 2,1 *vs.* 53 ± 2,8 g
Fogel y cols., 2017 (5)	n = 386 202/184	4.5 ± 2	Puntaje Z Normopeso ≤ 1,96 Sobrepeso/ obesidad > 1,96	Niños de Singapur de la cohorte GUSTO	Sin manipulación (observacional) Lenta *vs.* rápida	Comida: *ad libitum* buffet de 9 comidas y 3 bebidas comerciales Tiempo: almuerzo durante 20 min (ayuno de 3 h y desayuno habitual en casa) Videograbación y codificación del comportamiento del procesamiento oral con el software ELAN	Los niños que comieron más rápido consumieron más alimentos ($t \geq 1,8$, $p < 0,006$) y energía ($r = 0,61$, $p < 0,001$) **Condición rápida *vs.* lenta:** VC: 9,33 ± 2,44 *vs.* 4,43 ± 1,43 g/min IE: 306,76 ± 9,9 *vs.* 175,31 ± 6,09 kcal

(Continúa en página siguiente)

Tabla II (Cont.). Publicaciones tipo 2: metaanálisis

Autores	Sujetos (n) H/M	Edad (años)	IMC (kg/m²)	Características de la población	Tipo de manipulación experimental de la velocidad al comer (condición rápida *vs.* lenta)	Métodos de observación y registro	Efecto sobre la ingesta de alimentos o energía y resultados de la condición rápida *vs.* lenta
Hermans y cols., 2017 (21)	n = 114 44/70 Grupos: 60 *vs.* 58	18-80	18-35	63 % de estudiantes universitarios y 37 % del personal de la universidad y otras empresas de Países Bajos	Retroalimentación vibrotáctil* *vs.* sin retroalimentación *tenedor con suave vibración y luz roja cuando se come rápido	Comida: *ad libitum*, 800 g de pasta boloñesa (1616 kcal) o vegetariana (2216 kcal) Tiempo: almuerzo (ayuno de 3 h) Velocidad al comer auto-reportada y categorizada en una escala de 5 puntos, de 1 ("muy lenta") a 5 ("muy rápida") La velocidad al comer (número de bocados por minuto) y la duración de la comida fue registrada por el tenedor vibrotáctil. La ingesta (g) se midió con báscula (antes y después)	Los participantes con retroalimentación vibrotáctil consumieron menos bocados por minuto (velocidad al comer), p = 0,011. Sin embargo, estas diferencias no se reflejaron en la ingesta de alimentos (p = 0,797) Los participantes con retroalimentación vibrotáctil tardaron más tiempo comiendo (p = 0,16) **Condición rápida *vs.* lenta:** VC: 5,28 ± 1,49 *vs.* 4,55 ± 1,40 bocados/min IA: 428,21 ± 141,38 *vs.* 435,77 ± 156,84 g
Mosca y cols., 2019 (22)	n = 104 28/76	18-45	18,5-25	Nacionalidad holandesa de ascendencia europea, nacidos en Países Bajos	Textura (viscosidad) baja *vs.* alta Tamaño de las partículas: pequeño *vs.* grande	Comida: *Ad libitum*, servida en porciones de 1 kg de yogur (850 g de yogur y 150 g de granola) isocalórico con viscosidad baja o alta (1,57 x hasta 1.81 x) y con 15 % de granola en tamaño pequeño o grande (6 mm *vs.* 12 mm), 1149 kcal Tiempo: desayuno (ayuno desde las 22 h del día anterior) Videograbación con cámara web + el software "The Observer XT"	La velocidad al comer se correlacionó con la ingesta de alimentos (r = 0,62; p < 0,0001). Una disminución de la viscosidad y el tamaño de las partículas aumenta el número y la tasa de cucharadas (p < 0,0001) **Condición rápida *vs.* lenta:** **Textura (viscosidad baja *vs.* alta)** VC: 63 ± 1 *vs.* 62 ± 1 g/min IA: 349 ± 11 *vs.* 345 ± 10 g **Tamaño de las partículas (pequeño *vs.* grande)** VC: 60 ± 1 *vs.* 65 ± 1 g/min IA: 339 ± 10 *vs.* 356 ± 11 g

(Continúa en página siguiente)

Tabla II (Cont.). Publicaciones tipo 2: metaanálisis

Autores	Sujetos (n) H/M	Edad (años)	IMC (kg/m²)	Características de la población	Tipo de manipulación experimental de la velocidad al comer (condición rápida *vs.* lenta)	Métodos de observación y registro	Efecto sobre la ingesta de alimentos o energía y resultados de la condición rápida *vs.* lenta
Suh y Jung, 2016 (15)	n = 29 0/29	20-30	18-30	Mujeres coreanas	Forma de servir la comida: Separada *vs.* mezclada (varios platos *vs.* 1 plato)	Comida: arroz blanco y guarniciones (500 g) Tiempo: almuerzo (sin restricción de alimentos entre comidas y desayuno habitual)	Los sujetos comieron más rápido la comida en forma mezclada que en forma separada ($p < 0,05$). Más ingesta de comida en un solo plato que en varios platos ($p < 0,05$). **Condición rápida *vs.* lenta:** VC: 22,4 *vs.* 16,2 g/min IA: 285 *vs.* 244 g IE: 575 *vs.* 492 kcal
Zijlstra, Mars, Stafleu y de Graaf, 2010 (24)	n = 106 45/61	18-50	18,5-25	Población de Países Bajos	2 versiones de cada alimento (textura): blanda *vs.* dura	Comida*: Ad libitum,* carne (dura), sustituto de carne (suave), dulces duros y dulces suaves o blandos (similar contenido de calorías, densidad energética y macronutrientes) Tiempo: cena Ingesta: pesaje de comida (antes y después) Velocidad al comer: cantidad de comida fija (6 piezas de carne, 6 piezas de sustituto de carne y 4 dulces) y reloj digital	Se correlacionó la velocidad al comer con la ingesta de comida ($r = 54$, $p < 0,0001$) Los participantes comieron más cantidad de alimentos blandos que duros ($X^2 < 07,25$, $p < 0,01$) Se comió más lentamente la carne dura que la suave $F(1, 98) = 21,4$, $p < 0,0001$ **Condición rápida *vs.* lenta: (suave *vs.* dura)** **Carne** VC: 25 ± 13 *vs.* 21 ± 10 g/min IA: 157 ± 125 *vs.* 148 ± 121 g **Carne vegetariana** VC: 19 ± 16 *vs.* 19 ± 9 g/min IA: 171 ± 111 *vs.* 160 ± 109 g **Dulces** VC: 8 ± 4 vs. 8 ± 4 g/min IA: 143 ± 90 *vs.* 138 ± 83 g

N: tamaño de la muestra; H: hombres; M: mujeres; IMC: índice de masa corporal; kg: kilogramos; m: metros; VC: velocidad al comer; IA: ingesta de alimentos; IE: ingesta de energía; g: gramos; kcal: kilocalorías; g/min: gramos por minuto; kcal/min: kilocalorías por minuto; bocados/min: bocados por minuto; media ± desviación estándar.

En cuanto al sexo, 2 estudios se realizaron exclusivamente con mujeres (15,30); respecto a la edad, 1 estudio se había llevado a cabo en niños de 2,5 a 6,5 años (5) y 6 en adultos de 18 a 80 años (14,15,21,22,24,30). Referente al IMC, 2 publicaciones se referían únicamente a sujetos con normopeso (22,24), 2 a sujetos con IMC de normopeso, sobrepeso u obesidad (5,30), y 3 a sujetos con delgadez, normopeso, sobrepeso y obesidad (14,15,21). En relación con las características de la población, 1 estudio se había realizado en estadounidenses (30), 1 en australianos (14), 2 en asiáticos (5,15) y 3 en la población de los Países Bajos (21,22,24).

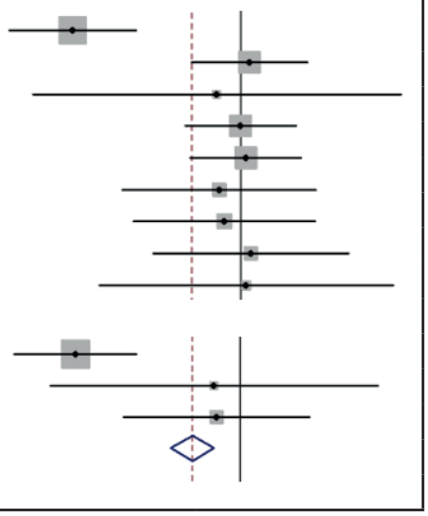
Análisis de subgrupos: métodos para manipular la velocidad al comer

En las publicaciones de tipo 2 se realizaron 11 manipulaciones experimentales de la velocidad al comer, las cuales se especifican a continuación: a) cuchara grande frente a cuchara chica; b) cuchara frente a tenedor (30); c) tenedor con retroalimentación vibrotáctil cuando se come rápido frente a sin retroalimentación vibrotáctil (21); d) viscosidad baja frente a alta; e) tamaño de la partícula pequeño frente a grande (22); f) comida en un solo plato frente a varios platos de estilo asiático (15); g) comidas con textura suave frente a dura (carne, carne vegetariana, dulces) (24). Si bien, los resultados de estos manuscritos mostraban una mayor ingesta de alimentos o energía en la condición rápida, el metaanálisis realizado en el presente estudio (Fig. 2) muestra que las técnicas y estrategias de modificación de la velocidad al comer que disminuyen eficazmente (OR < 1) la ingesta de alimentos o energía son: a) comer pequeños bocados con una cuchara chica, realizando entre 20 a 30 masticaciones por bocado y dejando la cuchara en la mesa entre bocados (30); b) servir los guisados en platos separados o al estilo asiático (15); c) usar un tenedor que emita una suave vibración y encienda una luz roja cuando el sujeto come de modo rápido (21); y d) comer alimentos con textura dura (24).

Análisis de subgrupos: estudios observacionales

De las 7 publicaciones que cumplían los criterios de inclusión para el metaanálisis (Figs. 1 y 2), 1 estudio era observacional, es decir, no se realizó en él ninguna manipulación experimental. En él se registró la velocidad al comer por medio de la videograbación de una sesión de comida *ad libitum* y se procesó con el software ELAN. Los autores concluyeron que los niños que habían comido más rápidamente habían tenido una mayor ingesta de energía (5). Además, el análisis realizado en el presente manuscrito (Fig. 2) con los resultados de este estudio observacional confirma que una velocidad lenta al comer reduce la ingesta de energía (OR = 0,831; IC 95 %: 0,264-2,613).

	OR	IC (95 %)		% peso
Ingesta de alimentos				
Andrade y cols. (30)	0,315	0,204	0,486	19,81
Bolhius y Keast (14)	1,058	0,713	1,572	11,47
Hermans y cols. (21)	0,847	0,240	2,988	1,26
Mosca y cols. (22)	0,996	0,680	1,457	12,73
Mosca y cols. (22)	1,032	0,705	1,510	12,50
Suh y Jung (15)	0,860	0,443	1,671	4,54
Zijlastra y cols. (24)	0,891	0,478	1,660	5,06
Zijlastra y cols. (24)	1,069	0,546	2,092	3,95
Zijlastra y cols. (24)	1,036	0,378	2,838	1,78
Ingesta de energía				
Andrade y cols. (30)	0,315	0,205	0,483	20,53
Fogel y cols. (5)	0,831	0,264	2,613	1,58
Suh y Jung (15)	0,845	0,441	1,620	4,78
M-H RM agrupado	0,713	0,615	0,827	100



Heterogeneidad chi-cuadrada = 41,04 (d.f. = 11) p = 0,000
I^2 (variación en OR atribuible a heterogeneidad) = 73,2 %
Test de OR = 1: z = 4,46 p = 0,000

Figura 2.

Diagrama de bosque del efecto de la velocidad al comer sobre la ingesta de alimentos y de energía. Metaanálisis por OR con IC del 95 % y modelo de efectos aleatorios (M-H: Mantel-Haenszel; OR: *odds ratio;* IC: intervalo de confianza).

EFECTO DE LA VELOCIDAD AL COMER SOBRE LA INGESTA DE ALIMENTOS O ENERGÍA

En la figura 2 se observa el análisis de 7 publicaciones en relación con dos condiciones —"rápida" *vs.* "lenta"— de la velocidad al comer y la ingesta de alimentos o energía (5,14,15,21,22,24,30); en ellas se realizaron 11 manipulaciones experimentales diferentes (14,15,21,22,24,30) y 1 estudio fue observacional (5). Los estudios con una OR < 1 fueron 5 (5,15,21,22,24,30) y esto significa que sus técnicas y estrategias para modificar la velocidad al comer se consideraron como "factores de protección frente a la ingesta excesiva (riesgo menor)", es decir, como eficaces para disminuir la ingesta de alimentos o energía. Estos fueron: comer con una cuchara chica en lugar de grande (OR = 0,315) (30); servir los guisados en platos separados en lugar de en el mismo plato (OR = 0,860 y OR = 0,831) (15); usar un tenedor con retroalimentación vibrotáctil en lugar de uno sin retroalimentación vibrotáctil (OR = 0,847) (21), y comer alimentos de textura dura en lugar de suave (carne) (OR = 0,891) (24).

Por otro lado, las manipulaciones experimentales de la velocidad al comer que mostraron un efecto indiferente sobre la ingesta de alimentos (OR = 1) fueron el utilizar una cuchara en lugar de un tenedor (OR = 1,058) (14), el comer alimentos (granola) de partículas pequeñas en lugar de partículas grandes (OR = 1,032) (22), la textura de los alimentos suave en lugar de dura (carne vegetariana, OR = 1,069; dulces, OR = 1,036) (24) y la viscosidad alta en lugar de baja (OR = 0,996) (22).

Finalmente, el OR agrupado fue de 0,713 (IC 95 %, 0,615-0,827), lo que indicó la presencia de asociación al factor de protección con un I^2 del 73,2 % (p = 0,000), que exhibe heterogeneidad entre los estudios, demostrando que el comer de modo "lento" es un factor de protección frente a la ingesta excesiva de alimentos y de energía.

SESGO DE PUBLICACIÓN

Se evaluó el sesgo de publicación por medio de un gráfico de embudo o *funnel plot* (Fig. 3), que produjo una representación gráfica asimétrica sugestiva de sesgo según el tamaño del efecto. Este resultado se puede deber a la limitada publicación de manuscritos sobre el tema de la velocidad al comer y de la ingesta, a que se publiquen únicamente artículos con resultados positivos o a que haya defectos en la calidad de dichos artículos. Sin embargo, los gráficos de embudo son una técnica visual subjetiva, por lo cual se complementaron con la prueba de la regresión lineal de Egger, que indicó la ausencia de sesgo de publicación (p = 0,728, IC = 95 %).

DISCUSIÓN

El principal hallazgo de la presente revisión sistemática y metaanálisis fue la identificación de las técnicas y estrategias de modificación de la velocidad al comer que tienen un efecto sobre la ingesta de alimentos o de energía. Estas fueron el tamaño del cubierto, el número de platos en los que se sirve la comida, la dureza de los alimentos y el uso de cubiertos con retroalimentación vibrotáctil. Además, se proporcionó evidencia científica que sustenta la premisa de que el comer de modo lento es un factor

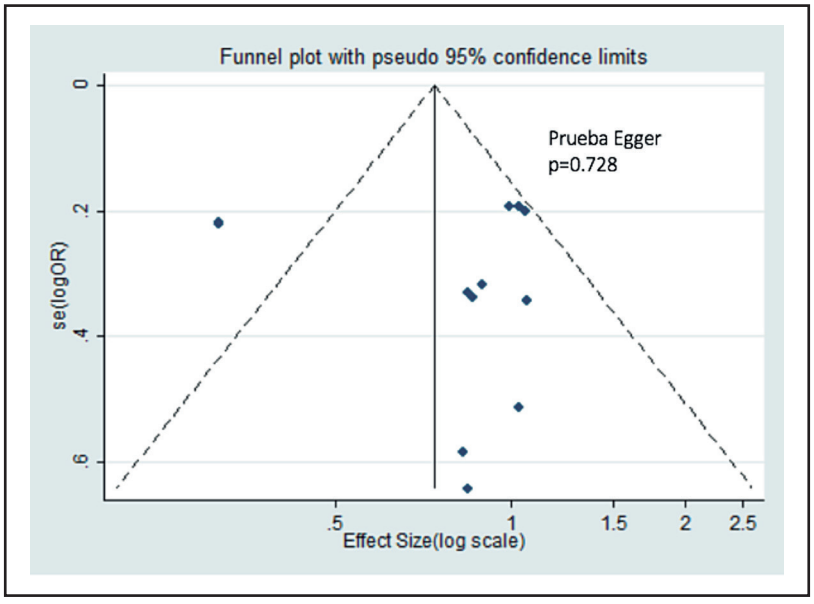


Figura 3.

Gráfica de embudo del sesgo de publicación. Nota: en el eje de las abscisas se observa la medida del efecto y en el eje de las ordenadas, la medida de la precisión.

de protección frente a la ingesta excesiva, planteándose que, cuando los individuos comen de modo lento, ingieren menos comida y energía. Ahora bien, se encontró heterogeneidad entre los estudios analizados debido a que midieron la ingesta y la velocidad al comer con diferentes unidades de medida, tales como gramos, kilocalorías, cucharadas, gramos por minuto, kilocalorías por minuto, cucharas por minuto, etc. No obstante, independientemente de la heterogeneidad de los estudios incluidos en este metaanálisis, la evaluación del sesgo de publicación realizada indicó ausencia del mismo.

Los resultados mencionados anteriormente concuerdan con los del metaanálisis realizado por Ronbinson y cols. en el año 2014, en el que sus autores concluyeron que la velocidad al comer afecta a la ingesta de energía y sugirieron la necesidad de identificar las técnicas y estrategias de modificación de la velocidad al comer que pudieran utilizarse en la vida cotidiana para limitar la ingesta excesiva de energía. Aunque en su revisión sistemática se muestran los resultados de los métodos de manipulación de la velocidad al comer sobre la ingesta energética, y su metaanálisis señala el efecto de los estudios incluidos, los autores no discutieron este aspecto detalladamente, dado que no era el objetivo principal de su estudio. También es relevante mencionar que hubo heterogeneidad entre los estudios que analizaron, por lo que realizaron un análisis de subgrupos que demostró un efecto consistente de la velocidad al comer sobre la ingesta de energía, independientemente del tipo de manipulación experimental realizada (27). Por su parte, Ohkuma y cols. (2015) asociaron los resultados de su metaanálisis de la velocidad al comer con la obesidad y también sugirieron que se debían realizar investigaciones con el objetivo de determinar las técnicas y estrategias eficaces para disminuir la velocidad al comer (1), objetivo que se cumple con la presente investigación.

La presente revisión sistemática y metaanálisis incluye estudios que midieron tanto la velocidad al comer como la ingesta de alimentos o energía. Sin embargo, es importante mencionar que se han realizado diversas investigaciones en las cuales se ha medido únicamente la velocidad al comer o la ingesta, con lo cual se ha determinado que los factores principales que logran modificarlas son el volumen de la porción percibido o la expectativa de saciedad (8,31-34), el tamaño del bocado (14,30), la palatabilidad de la comida (8), las propiedades sensoriales y nutricionales de los alimentos (14,16-18,22-24,34) como el contenido de fibra (4,34), y la textura de estos (16,18,22-24,34); respecto a la textura, se han reportado atributos como la dureza y la viscosidad que ya se discutieron en el presente metaanálisis, pero también se ha señalado la complejidad textural como un factor que influye sobre la ingesta de alimentos (35,36).

Con respecto a los programas de intervención clínica, en el estudio de Torbahn y cols. (2017) se proporcionó tratamiento nutricional centrado en cambios de la conducta alimentaria y de la actividad física a pacientes pediátricos con obesidad. Se analizó la asociación de los cambios de la velocidad al comer con el tamaño de las porciones y los hábitos dietéticos con el IMC. Sus resultados mostraron que la disminución de la velocidad al comer y el tamaño de las porciones se asociaban con la reducción del IMC a los 2 años de la intervención, proponiendo los autores que los programas de educación nutricional debían centrarse en la reducción de la velocidad al comer y el tamaño de las porciones (37).

En cuanto a los posibles mecanismos de acción, los hallazgos del presente manuscrito y de las investigaciones previas señalan que una velocidad lenta al comer se caracteriza por bocados pequeños y un mayor tiempo de masticación, sugiriéndose que mejora la capacidad de saciarse gracias a un tiempo más largo de exposición orosensorial a los alimentos (38-41), pues los alimentos o calorías que se ingieren rápidamente no son percibidos por el sentido del gusto durante la fase cefálica de la digestión (41). Además, se ha asociado el comer rápidamente con un vaciamiento gástrico rápido y una respuesta disminuida de las hormonas gastrointestinales de la saciedad (42-46), junto con una disminución de la termogénesis posprandial y la acumulación de tejido adiposo blanco (47,48), mientras que en el caso contrario, cuando se come de modo lento, el sentido del gusto registra adecuadamente la cantidad de nutrientes y de energía, se promueve un vaciamiento gástrico lento con una respuesta pronunciada de hormonas gastrointestinales de efecto anorexigénico y se aumenta la termogénesis posprandial (33,38-48). Por otro lado, se ha propuesto que la velocidad al comer esta mediada por la retroalimentación visual y no es simplemente una respuesta refleja de la estimulación orosensorial, demostrándose que la velocidad al comer es un proceso que se corrige con cambios más rápidos o más lentos conforme al volumen remanente percibido en los cubiertos. Con lo cual, al parecer las personas también usan el sentido de la vista para contar el volumen o las calorías, produciéndose una expectativa de saciación (8,31-34).

Finalmente, en el presente metaanálisis no se identificó ninguna limitación importante dado que la mayoría de los estudios analizados fueron experimentales y los análisis fueron intrasujetos, aunque en algunos se manipuló la velocidad al comer por medio de modificaciones de las propiedades sensoriales de la comida, específicamente de los atributos de textura y dureza, viscosidad y tamaño de las partículas, lo que puede ocasionar cambios en la ingesta independientemente de la tasa de alimentación. Los resultados de los demás estudios mostraron una mayor ingesta de comida o energía en la condición "rápida" con respecto a la "lenta"; asimismo, el análisis grupal indicó que comer de modo "lento" es un factor de protección frente a la ingesta excesiva. Otra limitación es que todos los estudios experimentales midieron las variables durante una sesión de comida, por lo cual no se puede concluir que estás técnicas y estrategias de modificación de la velocidad al comer producen cambios constantes de la ingesta en otro ambiente diferente al laboratorio. Por tanto, es relevante mencionar que McCrickerd y Forde (2017) comprobaron la hipótesis referente a la constancia de la velocidad al comer en el tiempo, demostrando que el comer rápido es un factor consistente entre los individuos y que, cuando se registra que un individuo comió rápidamente en una ocasión, se puede predecir que también comerá de modo rápido y con una ingesta elevada en subsiguientes comidas. Sin embargo, en este estudio se utilizó el mismo platillo de comida en todas las medicio-

nes como control del experimento; por tanto, los resultados de este estudio predicen la velocidad al comer de un sujeto con un determinado platillo, y esta se podría modificar cuando el sujeto consume otra comida con diferentes propiedades sensoriales o por medio de manipulaciones en el medio ambiente alimentario (13). Ahora bien, aunque hay que tener cuidado al extrapolar los datos, los estudios incluidos en el presente metaanálisis revisaron muestras tanto de adultos jóvenes como de adultos mayores y niños. Asimismo, el rango de IMC fue amplio, desde el bajo peso al normopeso, el sobrepeso y la obesidad. Por último, la heterogeneidad presente entre los estudios sugiere que el efecto de la manipulación de la velocidad al comer sobre la ingesta de alimentos o energía depende de la técnica o estrategia utilizada, aunque es posible que la consistencia individual de la velocidad al comer de cada sujeto influya sobre esto. Por ello es pertinente realizar más investigaciones sobre el tema para determinar la causa de esta variabilidad.

CONCLUSIÓN

Los estudios publicados acerca de las técnicas y estrategias de modificación de la velocidad al comer y su efecto sobre la ingesta de alimentos o energía han sido variados con respecto a características de la población tales como el sexo, la edad y el país de origen, y también en lo referente al tamaño de la muestra y el IMC. Asimismo, se han utilizado diversos métodos para manipular la velocidad al comer, enfocándose estos principalmente en las propiedades sensoriales y nutricionales de los alimentos y el ambiente alimentario. Adicionalmente, los estudios observacionales han categorizado la velocidad al comer por medio de cuestionarios autoadministrados y se ha evaluado la ingesta con cuestionarios dietéticos, si bien la evidencia aún es limitada y es necesario realizar más investigaciones referentes a este tema con un mayor número de participantes y metodologías más homogéneas. La presente revisión sistemática y metaanálisis confirma la premisa de que comer de modo lento es un factor de protección frente a la ingesta excesiva de alimentos y de energía. Asimismo, cumplió su objetivo principal al proporcionar técnicas y estrategias de intervención nutricional-conductual, eficaces para disminuir la velocidad al comer y la ingesta de alimentos o energía, que pueden ser útiles en el tratamiento o la prevención de enfermedades como el sobrepeso o la obesidad.

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ARÁN

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Artículo Especial

Posicionamiento sobre la definición de azúcares añadidos y su declaración en el etiquetado de los productos alimenticios en España

Position statement on the definition of added sugars and their declaration on the labelling of foodstuffs in Spain

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Resumen

Introducción: actualmente existe una gran preocupación relacionada con el contenido de azúcares de los alimentos y bebidas ya que un consumo excesivo se asocia con una mayor prevalencia de enfermedades crónicas no transmisibles. Además, hay una gran confusión tanto en los datos científicos publicados como en las informaciones que aparecen en los medios de comunicación sobre diversos conceptos tales como azúcares libres, azúcares intrínsecos o endógenos y azúcares añadidos a los alimentos, así como sobre el tipo de monosacáridos y disacáridos que forman parte de ellos. El término azúcares libres se refiere a aspectos de salud pública mientras que el de azúcares añadidos se relaciona con la información nutricional incluida en el etiquetado regulado en el Reglamento 1169/2011, aplicable a la información alimentaria facilitada al consumidor.

Material y métodos: análisis de la legislación vigente en la Unión Europea y en España, así como en Estados Unidos y México, junto con los posicionamientos de la Organización Mundial de la Salud (OMS), la *European Food Safety Authority* (EFSA) y la Agencia Española de Seguridad Alimentaria y Nutrición (AESAN), así como de sus comités científicos sobre la definición y declaración de azúcares totales, azúcares libres y azúcares añadidos.

Resultados: los azúcares añadidos se declaran en el etiquetado en países como en Estados Unidos y México. En el caso de Estados Unidos hay una propuesta de modificación del porcentaje que deben contribuir a la dieta, pasando del 10 % al 6 %. En el caso de la Unión Europea solo está establecida la ingesta de referencia para los hidratos de carbono: 45-65 %, al igual que ya lo ha hecho el Comité Científico de la AESAN. Solo en el caso del estudio ANIBES hay un dato aproximado del consumo de azúcares añadidos para la población española: un 7,3 %.

Conclusiones: se deben establecer ingestas de referencia para los azúcares añadidos y hacer que se declaren en la información del etiquetado de los productos alimenticios, para poder trabajar con datos fidedignos en las tablas de composición de alimentos, conocer la ingesta real por parte de la población española, y así implementar medidas de salud pública que permitan reducir la ingesta de los mismos en todos los productos alimenticios que los contengan.

Palabras clave:

Azúcares. Azúcares libres. Azúcares añadidos. Etiquetado.

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**Ver Anexo I al final.*

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Abstract

Introduction: there is currently great concern about the sugar content of food and beverages as excessive consumption is associated with a higher prevalence of chronic non-communicable diseases. In addition, there is a great deal of confusion both in published scientific data and in media reports about various concepts such as free sugars, intrinsic or endogenous sugars, and sugars added to food, as well as the type of monosaccharides and disaccharides that are part of them. The term "free sugars" refers to public health aspects whereas the term "added sugars" relates to the nutritional information included in the labelling covered by Regulation 1169/2011 as applicable to food information provided to the consumer.

Material and methods: an analysis of the legislation in force in the European Union and Spain, as well as in the United States and Mexico, together with the position statements of the World Health Organization (WHO), the European Food Safety Authority (EFSA), and the Spanish Agency for Food Safety and Nutrition (AESAN), as well as their Scientific Committees on the definition and declaration of total sugars, free sugars, and added sugars.

Results: added sugars are declared on the label in countries such as the United States and Mexico. In the case of the United States, there is a proposal to modify the percentage they should contribute to the diet from 10 % to 6 %. In the case of the European Union, only the reference intake for carbohydrates is established: 45-65 %, as has already been done by the Scientific Committee of AESAN. Only in the case of the ANIBES study is there an approximate figure for the consumption of added sugars by the Spanish population: 7.3 %.

Conclusions: reference intakes for added sugars should be established and declared in the information provided on food product labels in order to work with reliable data in the food composition tables, and to assess their real intake by the Spanish population, and thus implement public health measures to reduce their intake in all food products containing them.

Keywords:

Sugars. Free sugars. Added sugars. Labelling.

INTRODUCCIÓN Y JUSTIFICACIÓN

El consumo excesivo de azúcares, tanto por la población infantil como por la adulta, se relaciona con una mayor prevalencia de algunas enfermedades crónicas no transmisibles (ECNT), especialmente el sobrepeso y la obesidad, el síndrome metabólico, la diabetes de tipo 2 y las enfermedades cardiovasculares (1). Esto ha motivado que numerosas agencias y autoridades de seguridad alimentaria y nutrición de todo el mundo establezcan recomendaciones para limitar su consumo (2-6). Existen un gran número de términos utilizados para describir los azúcares de los alimentos y sus componentes: azúcar o azúcares, azúcares totales, azúcares totales disponibles, azúcares libres, azúcares añadidos, azúcar(es) refinado(s), azúcares simples, azúcar discrecional, azúcares intrínsecos, azúcares extrínsecos y azúcares extrínsecos no lácteos (7).

La existencia de estos numerosos términos y su uso en diferentes países ha dado lugar a una amplia literatura sobre ingestas de azúcares que limita las comparaciones entre diferentes naciones y el análisis de las tendencias a lo largo del tiempo. Del mismo modo, las posibilidades de comparar las ingestas con las recomendaciones y de establecer vínculos entre la ingesta y los factores de riesgo de las ECNT son, en consecuencia, limitadas.

Las definiciones y recomendaciones en las guías alimentarias de los países desarrollados para los azúcares, y en particular para los azúcares libres y los azúcares añadidos de los alimentos, varían ostensiblemente. En cualquier caso, la variabilidad es mayor en la terminología que se refiere a las definiciones que la relacionada con las recomendaciones de ingesta. Por otro lado, sorprendentemente, son hasta el momento muy pocos los Estados que han regulado la obligatoriedad de declarar en el etiquetado los azúcares añadidos. Estados Unidos de América (2) y México (3) tienen definidos los azúcares añadidos y contemplan la obligatoriedad de incorporarlos en el etiquetado de los productos alimenticios en el apartado de hidratos de carbono, a continuación de los azúcares totales (2,3).

Con estos antecedentes, el objetivo del presente documento es establecer un posicionamiento actualizado sobre la definición de azúcares añadidos y establecer las bases para su declaración en el etiquetado de productos alimenticios aplicable al territorio español.

RECOMENDACIONES NACIONALES E INTERNACIONALES SOBRE LA INGESTA DE AZÚCARES

En general, todos los países, bien directamente a través de su legislación alimentaria, o bien a través de los alimentos y bebidas, recomiendan la reducción del consumo de azúcares, aunque solo algunos establecen cantidades o límites de cantidad en la ingesta diaria recomendada (4).

La Organización Mundial de la Salud (OMS) en el año 2003 estableció, dentro del Informe Técnico sobre Dieta, Nutrición y Enfermedades Crónicas, los objetivos de ingesta de nutrientes para la población en forma de porcentaje sobre la cantidad de energía total (6). En el caso de los azúcares, los fijó en función de la cantidad máxima diaria de "azúcares libres", definidos como "azúcares añadidos a alimentos y bebidas por el fabricante, el cocinero o el consumidor, más los azúcares naturalmente presentes en la miel, los jarabes (siropes) y los zumos de frutas", excluida la lactosa naturalmente presente en la leche y en los productos lácteos. Dicho objetivo establece un límite máximo del 10 % de la energía total proveniente del aporte diario de la dieta. Si se considerara una ingesta diaria de 2.000 kilocalorías, sería equivalente a 50 g de azúcares libres/persona/día (según la definición de la OMS) (6). Esta recomendación, determinada como "firme", fue ratificada por la propia OMS en el año 2015 con la misma denominación de "azúcares libres". En este caso, además, se incluye una "recomendación condicional", fijada en una cantidad inferior al 5 % de la energía proveniente de los azúcares libres, lo que supondría para una dieta de 2.000 kilocalorías unos 25 g/persona/día (8).

En el caso de los Estados Unidos de América, en las guías alimentarias de 2015-2020 propuestas por el *U.S. Department of Health and Human Services* y el *U.S. Department of Agriculture* (USDA), se incluyen diferentes limitaciones para conseguir un

patrón de alimentación saludable, siendo una de ellas la cantidad de azúcares añadidos. Estos componentes son de particular preocupación para la salud pública en este país y los límites especificados pueden ayudar a las personas a lograr patrones de alimentación saludable sin desviarse de los límites energéticos. En ese sentido, se recomienda consumir menos de un 10 % de calorías diarias provenientes de azúcares añadidos (2). Posteriormente, en el año 2018, la *Food and Drug Administration* (FDA) aprobó la incorporación obligatoria en el etiquetado de la declaración de los azúcares añadidos, como un apartado incluido en la información nutricional sobre la cantidad de hidratos de carbono, a continuación del punto de azúcares totales, como se puede comprobar comparando una etiqueta anterior con una posterior al año 2018 (9-12) (Fig. 1).

Al mismo tiempo, contempla la definición de azúcares añadidos: "incluyen azúcares que se agregan durante el procesamiento de los alimentos (como la sacarosa o la dextrosa), alimentos envasados como endulzantes (como el azúcar de mesa), azúcares de siropes y miel, y azúcares de zumos de concentrados de frutas o verduras" (9-12). Estos no incluyen los azúcares naturales que se encuentran en la leche, las frutas y las verduras. El valor máximo diario para los azúcares añadidos es de 50 gramos por día, basado en una dieta de 2.000 kilocalorías diarias.

En el mes de julio de 2020, el *U.S. Department of Health and Human Services* y el *U.S. Department of Agriculture* han aprobado un primer borrador de las guías alimentarias de 2020-2025 para la población estadounidense (13), y al igual que las vigentes para el periodo 2015-2020 (9), la importancia del tipo de azúcares

Figura 1.

Evolución de la etiqueta de productos alimenticios en Estados Unidos de América, incorporando los azúcares añadidos (2).

recae en los azúcares añadidos, pues son sobre los que se puede actuar para reducir claramente su ingesta.

Además, se incluye la definición y nueva recomendación de ingesta diaria de azúcares añadidos. Así, recoge que los "azúcares añadidos" son los azúcares que se añaden durante el procesado de productos alimenticios (tales como la sacarosa o dextrosa), azúcar envasado o de mesa (terrones o sobres de azúcar), azúcares de jarabes y miel y azúcares de zumos de concentrados de frutas o verduras (13). No incluyen los azúcares que están presentes de forma natural en leche y lácteos, frutas y verduras (13). La recomendación de la cantidad máxima de ingesta diaria en este primer borrador la USDA la rebajaba a un 6% de la ingesta total de energía, que para una dieta de 2.000 kilocalorías, serían 30 gramos de azúcares añadidos (13).

Las *Dietary Guidelines for Americans* las ha aprobado definitivamente la USDA en el mes de diciembre de 2020, manteniendo una recomendación de una ingesta de azúcares añadidos por debajo del 10 % de las kilocalorías, lo que implica que en el etiquetado para los productos alimenticos en USA se mantenga el 10 % como ingesta de referencia para los azúcares añadidos para una dieta de 2.000 kcal, lo que supone una cantidad de 50 g (14).

Otro ejemplo, relacionado con las definiciones de los azúcares, de reciente aprobación, publicación y entrada en vigor de la normativa que lo contempla, es el caso de México. Con fecha de 27 de marzo de 2020, la Secretaría de Economía, la Secretaría de Salud y la Comisión Federal para la protección de riesgos sanitarios, a través de la modificación de la Norma Oficial Mexicana NOM-051-SCI/SSA1-2010, sobre especificaciones generales de etiquetado para alimentos y bebidas no alcohólicas, preenvasados, información comercial y sanitaria, publicada el 5 de abril de 2010, han recogido en la modificación de la norma de etiquetado la definición de azúcares añadidos: "azúcares libres agregados a los alimentos y a las bebidas no alcohólicas durante la elaboración industrial".

Para el caso de los azúcares libres se propone: "monosacáridos y disacáridos disponibles añadidos a los alimentos y a las bebidas no alcohólicas por el fabricante, más los azúcares que están presentes naturalmente en miel, siropes y zumos de frutas u hortalizas" (3). En la misma norma recoge que en el etiquetado, en la información nutricional, se reflejará la cantidad de hidratos de carbono disponibles, indicando la cantidad correspondiente de azúcares totales y azúcares añadidos (3).

En el año 2009, a petición de la Comisión Europea, el panel de productos dietéticos, nutrición y alergias de la Autoridad Europea de Seguridad Alimentaria ("*European Food Safety Authority*", EFSA) publicó un dictamen científico sobre el límite de la ingesta de azúcares totales para aspectos relacionados con el etiquetado, y establece una ingesta de referencia diaria de 90 g de azúcares totales, referida a la información nutricional en el etiquetado de productos alimenticios, lo que correspondería a una cantidad del 18 % de las calorías proveniente de azúcares en una dieta de 8.400 kJ o 2.000 kcal/día. La propuesta se aprobó a partir de un valor medio dentro de un rango de ingesta de azúcares totales para los países de la Unión Europea, situado en el 17-26 % de la ingesta total energética (5). En este caso, la cantidad de azúcares totales incluye los denominados azúcares intrínsecos (naturalmente presentes en alimentos y bebidas tales como frutas, vegetales, cereales, leche y productos lácteos) y los azúcares añadidos. Según recoge el mismo dictamen científico publicado, el límite de la ingesta de azúcares añadidos, para diferentes autoridades a nivel mundial, es del 10 %, aunque hay otras que indican que la ingesta de azúcares añadidos o de ciertos alimentos con azúcares añadidos debe limitarse, si bien no establecen un límite máximo recomendado (5).

En el caso de la Unión Europea, en el año 2010 se establecen por primera vez, junto con otros nutrientes, las ingestas de referencia (porcentaje respecto a la energía total) de hidratos de carbono y fibra dietética: en el primer caso, un 45-60 %; sin embargo, por la alta frecuencia de la ingesta de azúcar contenida en alimentos y bebidas y su potencial de incrementar el riesgo de caries dental, se indica que habría que recomendar la reducción del consumo de azúcar, aunque en ese momento no había datos suficientes para establecer un límite máximo para la ingesta de azúcares, en concreto de los añadidos (15).

La EFSA, para los denominados azúcares libres, aprobó una declaración institucional, como base del protocolo para la elaboración de un dictamen científico, con el fin de establecer el nivel superior tolerable de la ingesta dietética de azúcares, incluyendo en la definición de azúcares libres la lactosa y la galactosa, además del resto de monosacáridos y disacáridos ya contemplados en otras definiciones de azúcares libres (16). Esta situación se daría en las leches, los productos lácteos y las leches fermentadas que contienen lactosa, y también en aquellas leches, productos lácteos y leches fermentadas en los que la lactosa, bien por acción de la lactasa o bien por acción de microorganismos, ha sido hidrolizada y que contienen tanto glucosa como galactosa. También hay que señalar que, en las mermeladas y confituras, el procesamiento de las frutas hace que se liberen los disacáridos y monosacáridos presentes en las mismas y que no estén unidos o presentes en estructuras celulares, por lo que la sacarosa, la glucosa y la fructosa se comportarían como azúcares libres.

Finalmente, para la EFSA, en el año 2010, en el dictamen científico sobre valores de ingesta dietética de referencia para hidratos de carbono y fibra alimentaria, se recoge que "azúcares añadidos" es el término que describe a "la sacarosa, la fructosa, la glucosa, los hidrolizados de almidón (sirope de glucosa, sirope alto en fructosa) y otros azúcares aislados usados en preparaciones o añadidos durante el procesado y la preparación de productos alimenticios" (15).

Recientemente, Amoutzopoulos y cols. (2020) han establecido que habría que fijar las definiciones de azúcares, azúcares añadidos y azúcares libres para su utilización en las guías dietéticas del Reino Unido, basándose en las definiciones establecidas por la EFSA, la OMS y el *Scientific Advisory Committee on Nutrition* (SCAN) del Reino Unido (17). Según sus resultados, concluyen que las diferencias entre las ingestas de azúcares añadidos y de azúcares libres son grandes, y que por este motivo, el uso de las definiciones de cada uno de los dos grupos necesita tenerse en consideración para poder monitorizar la ingesta de azúcar y su relación con la salud pública (17).

En el caso del Comité Científico de la Agencia Española de Seguridad Alimentaria y Nutrición (AESAN), en el año 2014, la

definición de azúcares libres contempla la establecida en el año 2003 por la OMS, incluida en el informe sobre objetivos y recomendaciones nutricionales y de actividad física frente a la obesidad en la estrategia NAOS del año 2014 (18). En el caso de los azúcares añadidos, el Comité Científico de la AESAN indica, en este mismo informe, que "tomados de forma separada o utilizados como ingredientes en los alimentos procesados o preparados (por ejemplo, azúcar blanco, azúcar moreno, azúcar no refinado, siropes de maíz, sirope de malta, sirope de arce, edulcorantes de fructosa, fructosa líquida, miel, melazas, dextrosa anhídrida y dextrosa cristalizada). Puede contender oligosacáridos" (18).

El Comité Científico de la AESAN, en su informe de muy reciente publicación sobre la revisión y actualización de las recomendaciones dietéticas para la población española, recoge información y datos sobre las guías alimentarias de los Estados Unidos de América, China, Finlandia, Noruega, Suecia, Reino Unido, Alemania, Países Bajos, Francia, Portugal y España, en las que la variabilidad de las definiciones y recomendaciones es patente para el azúcar, los azúcares totales, los azúcares añadidos y los azúcares libres (4). En este informe se ha incluido como recomendación un consumo de azúcar libre inferior al 10 % de la ingesta calórica total como objetivo para conseguir una dieta saludable. Para obtener mayores beneficios se recomienda reducir su consumo a menos del 5 % de la ingesta calórica total (4). Quizás en este caso sería conveniente unificar las recomendaciones para el consumidor, que deben realizarse a partir de mensajes simples y directos sobre la cantidad expresada en gramos, y para el profesional de la salud, donde las informaciones deben establecerse en los porcentajes del aporte sobre la dieta, partiendo del cálculo individualizado de las necesidades de cada persona.

El Comité Científico de la AESAN incluye en las conclusiones unas recomendaciones para la población española dentro de las cuales se indica, como una de ellas, que para los azúcares añadidos, como en el caso del azúcar, se establece una cantidad inferior a 30 g/día, evitando los alimentos con azúcar añadido. También menciona que, además del seguimiento de las recomendaciones dietéticas propuestas por dicho Comité Científico, se asumen en parte las recomendaciones de la OMS y se recomienda que el consumo de azúcares libres sea inferior al 10 % de la ingesta calórica total que forma parte de una dieta saludable. Para obtener mayores beneficios se recomienda reducir su consumo a menos del 5 % de la ingesta calórica total (4). La unificación de los mensajes puede suponer una acción positiva de salud pública, como ha ocurrido con la adopción de la declaración de la sal, en vez de sodio, a partir de la aprobación del Reglamento 1169/2011, ya que el dirigir un único contenido de mensaje al consumidor, ha dado lugar a la sensibilización sobre la sal, lo que ha conllevado una redución del consumo de sodio, cuya ingesta excesiva tiene probados efectos negativos sobre la salud (19).

De acuerdo con los resultados recopilados a partir de los escasos estudios disponibles y con metodología suficientemente válida para poder valorar cual sería la recomendación del rango de ingesta de azúcares añadidos más adecuada para la población española, este puede oscilar entre el 10 %, que hasta ahora es el valor más común usado en los países que han incorporado la recomendación de ingesta dietética, y el 7 %, que es el obtenido en el año 2017 en el estudio científico ANIBES, una encuesta dietética con representatividad de todo el territorio nacional y para la población de entre 9 y 75 años (20). Sin embargo, siempre que fuese posible, sería muy conveniente establecer recomendaciones de consumo máximo de acuerdo con los distintos grupos de edad y situaciones fisiológicas, ya que los efectos sobre la salud pueden diferir de forma muy marcada.

En cuanto a las ingestas de referencia para la población española referentes a hidratos de carbono, en el año 2019 el Comité Científico de la AESAN (21) adoptó las mismas que previamente había aprobado la EFSA para la población de la Unión Europea (15), siendo estas del 45-60 % de las calorías de la dieta total.

Por último, en el plan de mejora de la AESAN, la industria alimentaria consensuó y aprobó en el año 2017, bajo la estrategia NAOS, una acción coordinada para la reducción de azúcares, implementada sobre los azúcares añadidos. Por este motivo, y para planes futuros, sería imprescindible tener la información de los mismos en el etiquetado de los productos alimenticios, para que los cálculos sean lo más fidedignos posibles, tanto sobre la cantidad presente en los alimentos y bebidas, como sobre la reducción de los azúcares añadidos en los mismos (22).

CONCLUSIONES Y RECOMENDACIONES

- Para los azúcares totales, se propone que la definición debería establecerse como la suma de los azúcares naturalmente presentes más los azúcares añadidos en los alimentos y bebidas.
- En el caso de los azúcares naturalmente presentes, estos serían aquellos disacáridos y monosacáridos que forman parte intrínseca de los alimentos y bebidas.
- En relación con la definición de azúcares añadidos, se propone: todos los monosacáridos y disacáridos añadidos a los productos alimenticios en sus procesos de elaboración y preparación culinaria, que aparecen reflejados en el listado de ingredientes. Su cantidad total deberá estar indicada en la información nutricional, en el apartado de hidratos de carbono, a continuación del punto "de los cuales azúcares", quedando estructurada dicha información de la forma que se refleja en la tabla I.
- Resulta necesario y urgente poder unificar el criterio de la utilización como ingrediente e información nutricional de los azúcares añadidos.
- Se propone incluir la declaración de azúcares añadidos en la información nutricional del etiquetado de los productos alimenticios no solo para conocer su cantidad, sino como herramienta válida para los cálculos reales de ingesta en la población española.
- Se propone establecer recomendaciones de ingesta diaria máxima de azúcares añadidos en las guías alimentarias para la población española, así como fortalecer los programas de reformulación de los productos alimenticios para reducir el contenido de azúcares añadidos y ayudar a las

políticas y estrategias de reducción y prevención del sobrepeso y la obesidad.
- La declaración de los azúcares añadidos en la información nutricional del etiquetado de los productos alimenticios servirá al consumidor para conocer la cantidad presente en los alimentos y bebidas, y así poder tomar decisiones de compra adecuada y responsable, máxime en los grupos de riesgo y en las poblaciones en que se lleven a cabo actuaciones preventivas de control y reducción del peso.
- De acuerdo con la cantidad de azúcares añadidos presentes en alimentos y bebidas, se propone establecer iconos que realicen llamadas de atención, bajo criterios de límites adecuados, para conocer si un producto alimenticio tiene un contenido bajo, medio o alto de azúcares añadidos.

Tabla I. Información nutricional para los azúcares y azúcares añadidos por 100 g/100 ml

Hidratos de carbono	X (g)	Y %IR. IR= [225 g-300 g (45-60 %)]
de los cuales azúcares	X (g)	Y %IR. IR= [90 g (18 %)]
de los cuales azúcares añadidos	X (g)	Y %IR. IR= [35 g (7 %)]

IR: Ingesta de Referencia Diaria para un adulto medio (8.400 kJ/2.000 kcal).

ANEXO I.

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ARÁN

Nutrición Hospitalaria

Grupo de trabajo SENPE

Standards of the nutritional support process in Spain — Towards benchmarking

Estándares del proceso de soporte nutricional en España: hacia el "benchmarking"

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Abstract

Introduction: quality indicators have been proposed in Spain for assessing the various stages of clinical nutrition. However, reference standards for these indicators (feasible and relevant) based on daily practice of artificial nutrition are not available.

Goals: the goal of this study was to propose quality indicators standards for their routine application to artificial nutrition in clinical practice.

Material and methods: a multicenter, cross-sectional study—based on a survey applied to health professionals in the field of clinical nutrition—on the fulfilment of eight quality criteria was carried out during 2018 and 2019. The total number of processes and those that were correctly accomplished were assessed and compared with the corresponding proposed theoretical standard.

Results: fifteen centers were assessed. Of eight indicators assessed, five were within the theoretical standard (correct identification of parenteral nutrition bags, semi-upright position of patients on enteral nutrition, administration of micronutrients in ready-to-use parenteral nutrition bags, checking placement of feeding tubes, and days with glycemia below 60 mg/dL). Two indicators were very close to the theoretical standard. One indicator, hyperglycemia in patients with parenteral nutrition, was far removed from its theoretical standard (15.7 % vs. 5 %).

Conclusion: the administration of artificial nutrition in Spanish hospitals was performed with a high quality level. Therefore, standards based on daily clinical practice regarding artificial nutrition in Spain are proposed.

Keywords:

Quality indicators. Health care. Healthcare surveys. Nutrition therapy. Standards. Patient care team.

Resumen

Introducción: en España se han propuesto indicadores de calidad para evaluar las diversas etapas de la asistencia en nutrición clínica. Sin embargo, no se encuentran disponibles estándares de referencia de estos indicadores (factibles y relevantes) basados en la práctica diaria de la nutrición artificial.

Objetivos: ofrecer estándares de indicadores de calidad para su aplicación rutinaria en la práctica clínica de la nutrición artificial.

Material y métodos: estudio transversal multicéntrico, basado en una encuesta remitida a profesionales sanitarios del ámbito de la nutrición clínica, sobre el cumplimiento de 8 criterios de calidad durante el año 2018 y 2019. Se analizó el número total de procesos evaluados y los que se cumplieron correctamente, y se compararon con el estándar teórico propuesto.

Resultados: se estudiaron 15 centros. De los 8 indicadores estudiados, 5 estuvieron dentro del estándar teórico (identificación correcta de las bolsas de nutrición parenteral, posición semi-incorporada de los pacientes con nutrición enteral, administración de micronutrientes en las bolsas de nutrición parenteral "listas para su uso", comprobación de la colocación de las sondas, y días de glucemia por debajo de 60 mg/dl); dos indicadores estuvieron muy próximos al estándar teórico y, uno, la hiperglucemia en los pacientes con nutrición parenteral, lejos del estándar teórico (15,7 % *vs.* 5 %).

Conclusión: la aplicación de la nutrición artificial se realiza en los hospitales españoles con un elevado nivel de calidad. De esta manera, se ofrecen unos estándares basados en la práctica clínica diaria de la nutrición artificial en España.

Palabras clave:

Indicadores de calidad. Cuidados sanitarios. Encuestas de salud. Terapia nutricional. Estándares. Equipos de salud.

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INTRODUCTION

In recent years, the need to improve the quality and efficiency of health systems has led to a growing interest in the application of various tools for achieving a better management. Quality indicators that express the extent of achievement for key objectives in organizations stand out among these instruments. In general terms, these indicators focus on specific quality dimensions (accessibility, patient satisfaction, health outcomes, safety, etc.). They are intended to meet key requirements such as relevance, feasibility, and reliability, and meant to be based on evidence (1).

In order to achieve correct interpretations, the results of the indicators should be compared with reference standards that indicate the limit beyond which the levels of compliance can be considered adequate. This comparison allows determining corrective measures to improve outcomes in organizations. The standards are intended for use in practice. When they are defined, not only the level of compliance that is convenient from a theoretical point of view should be taken into account, but also the degree of real difficulty they pose. In this sense, there are many factors that can promote compliance with quality indicators. These factors may depend on: the organizations (management involvement, leadership style, institutional culture of quality improvement, and availability of resources); the professionals (awareness and recognition of recommendations in clinical guidelines, time restrictions, previous experiences); or the activity being monitored (coherence and strength of scientific evidence, associated technical complexity) (2).

In Spain, quality indicators have been proposed for assessing the various stages of clinical nutrition care (3,4). The reference standards for these indicators are mostly theoretical values obtained from arbitrary criteria or from research studies. Therefore, the goal of the present study was to obtain sufficient information to determine standards, based on daily practice, for relevant and feasible indicators in routine application.

MATERIALS AND METHODS

The present multicentre cross-sectional study was conducted between 2018 and 2019. First, a questionnaire was prepared and sent to the members of the Spanish Society of Clinical Nutrition and Metabolism (SENPE) by email. Subsequently, the responses included in the study were those sent by health professionals that belonged to SENPE and were performing their professional activity in the field of clinical nutrition, either in public or private hospitals nationwide.

The questionnaire included eight quality criteria (29 items in total) extracted from the document "Process of Clinical Nutrition. Self-assessment guide" prepared by the SENPE Management working group. It was based on the relevance and feasibility criteria for indicators used in nutrition units that were obtained in 2012 (5).

Table I shows the quality indicators included in the survey. The level of compliance with each indicator (process completed/process assessed x 100) was compared with the theoretical standard proposed by the existing literature (theoretical standard). Based on this result, but also taking into account the relevance of compliance with indicators and the difficulty they entail, standards were proposed for each indicator (proposed standard).

RESULTS

Responses were obtained from 15 health centers, of which: one had less than 200 beds (6.7 %); three had 201 to 500 beds (20.0 %); six had 501 to 1,000 beds (40.0 %); and five had more than 1,000 beds (33.3 %). Nutrition units or multidisciplinary nutritional support teams were responsible for nutritional support in 13 of the centers (86.7 %). In the other two centers nutritional support was in the hands of professionals not organized in a functional unit.

IDENTIFICATION OF PARENTERAL NUTRITION BAGS

Data were obtained from 12 centers. The assessment included 2,380 parenteral nutrition bags, which meant an average of 198.5 (330.5) bags per center assessed (minimum 4 bags/center, maximum 1,101 bags/center). Of these bags, 2,374 had an identifying label. This fact indicated a degree of compliance of 99.7 % (theoretical standard = 100 %).

SEMI-UPRIGHT POSITION OF PATIENTS WITH ENTERAL NUTRITION BY NASOGASTRIC TUBE

Data were obtained from 12 centers, with a total of 620 patients (mean, 57.7 [82.4] patients/center; minimum 6 patients/center, maximum 278 patients/center). The degree of compliance was 96.8 % (theoretical standard > 90 %).

CORRECT MONITORING OF NUTRITIONAL SUPPORT

This item was answered by 13 centers. A total of 1,050 visits to patients were analyzed, corresponding approximately to 80.7 (107.8) visits per center (minimum 9, maximum 400), of which 988 were considered correct according to the definition of the criterion. Compliance with the standard was 94.1 % (theoretical standard = 100 %).

MEETING THE CALORIC GOAL WITH ENTERAL NUTRITION

Data from seven centers were analyzed, with a total of 429 days of enteral nutrition (61.3 [54.4] days/center; minimum 15 days/center, maximum 137 days/center).

Table I. Data and quality indicators included in the survey

Organizational criteria	
– Affiliation data – Center size – Organizational structure: • Nutrition unit nutritional support team • Group of professionals belonging to one or more services (without nutrition units) • Other professionals	
Quality criteria	
Criterion 1:	Patient identification in parenteral nutrition bags. *Method:* visual confirmation of correct labeling in patients with parenteral nutrition on the day of referral. *Instruction:* correct identification must include the following items: hospitalization unit; room and bed; composition; date of preparation
Criterion 2:	Semi-upright position in patients with enteral nutrition via a nasogastric tube. *Method:* visual verification of the correct position of patients with enteral nutrition on the day of referral. *Instruction:* semi-upright position: patient with the torso at > 30 ° with respect to the horizontal plane during the administration of enteral nutrition and one hour afterwards
Criterion 3:	Correct monitoring of patients receiving artificial nutrition (enteral or parenteral). *Method:* checking by reviewing the patient's medical records for evidence on the correct monitoring of patients with artificial nutrition. *Instruction:* each visit counts independently, so more than one event (monitoring visit) can be performed per patient. Visits for intercurrent events, e.g., due to loss of enteral access, do not count. Correct monitoring should include assessment of tolerance and compliance with nutritional requirements, as well as periodic laboratory determinations. Assessment of tolerance involves a systematic screening of the most frequent complications caused by enteral nutrition (gastrointestinal problems, etc.) and parenteral nutrition (fluid status, hyperglycemia, etc.)
Criterion 4:	Meeting caloric goals in patients with artificial nutrition (enteral or parenteral). *Method:* checking by reviewing the patient's medical records regarding the administration of an artificial nutrition formula in sufficient amount to meet nutritional requirements. *Instruction:* all treatment days are taken into account, so more than one event per patient can be considered. Interruptions justified by the protocol or periods of artificial nutrition do not count. Compliance implies a systematic calculation of caloric requirements. The goal is considered reached when the necessary calories were administered (± 10 %)
Criterion 5:	Checking the placement of enteral feeding tubes before start of enteral nutrition. *Method:* checking out in medical records the corresponding radiological technique before start of enteral nutrition. *Instruction:* the reference technique to ascertain an enteral tube's correct position is radiography. Valid only for nasogastric and nasoenteral tubes. Tubes placed under radiological or endoscopic control are not included in the calculation
Criterion 6:	Checking the administered 'ready-to-use' parenteral nutrition bags do provide micronutrients. *Method:* visually checking the records related to micronutrient contents in the 'ready-to-use' parenteral nutrition bags administered on the day of referral. *Instruction:* micronutrients should include: electrolytes, vitamins, and trace elements
Criterion 7:	Glycemic control in patients with parenteral nutrition. *Method:* checking by reviewing medical records for maintenance of adequate glycemic levels in patients with parenteral nutrition, on the day of referral. *Instruction:* each day with parenteral nutrition counts as an isolated event (regardless of the number of glycemic determinations performed)
Criterion 8:	Control of venous access-related infections for parenteral nutrition. *Method:* assessment by reviewing medical records and the microbiological results of catheter removals due to suspected infection and its possible confirmation. *Instruction:* each day of parenteral nutrition counts in isolation. The confirmation of catheter-related infection is given by the existence of a positive culture of its tip or by bacteremia. Different types of catheters (jugular, subclavian, PICC) are assessed independently

Caloric requirements were met in 369 days, which represented a standard of 86.0 % (theoretical standard > 90 %).

MEETING THE CALORIC GOAL WITH PARENTERAL NUTRITION

Six centers submitted data for this criterion, including 380 days of parenteral nutrition (63.3 [50.8] days/center; minimum 12 days/center, maximum 148 days/center). Caloric requirements were met by administering parenteral nutrition for 335 days (88.2 %) (theoretical standard > 90 %).

CHECKING THE PLACEMENT OF ENTERAL FEEDING TUBES

Eleven centers answered this item, with a total of 218 patients and a mean of 19.8 (18.2) patients per center (minimum 5 patients/center, maximum 61 patients/center). Correct probe checking had been performed in 188 patients, which represented a standard of 86.2 % (theoretical standard = 100 %).

MICRONUTRIENT SUPPLY IN 'READY-TO-USE' PARENTERAL NUTRITION BAGS

These data were only obtained from four hospitals, and a total of 160 bags of parenteral nutrition were assessed (40.0 [72.0] bags/center; minimum 2 bags/center, maximum 148 bags/center). Micronutrients had been added to 158 bags (98.8 %) (theoretical standard = 100 %).

GLYCEMIC CONTROL IN PATIENTS WITH PARENTERAL NUTRITION

Twelve centers sent data related to glycemic control. A total of 3,782 days with parenteral nutrition could be assessed, with 315.2 (424.2) days/center (minimum 5 days/center, maximum 1,226 days/center). Hyperglycemia (> 180 mg/dL) was observed during 595 days (15.7 %), and hypoglycemia (< 60 mg/dL) during 18 days of follow-up (0.5 %) (theoretical standard = 5 % in both cases).

INFECTION OF PARENTERAL NUTRITION CATHETERS

Data from six hospitals were analyzed. The results are shown in table II. Table III shows the theoretical and proposed standards for the most relevant indicators of a hospital's artificial nutritional support process.

DISCUSSION

In the last decade, quality management has been progressively established in health systems. This fact promoted important changes in their organization. These changes have directly affected clinicians, whose objectives have gone from providing healthcare based on the best available scientific evidence to also incorporating the satisfaction of different stakeholders (patients, relatives, managers, providers, healthcare teams, and society). This way, in recent years, both scientific societies and health agencies have created indicators for controlling healthcare quality.

In conjunction with the Spanish Society of Hospital Pharmacy (SEFH), the Spanish Society of Clinical Nutrition and Metabolism (SENPE) has developed the "Guidelines for the assessment of the clinical nutrition process", which discusses the sub-processes involved in nutritional support for hospitalized patients (3). Each sub-process is accompanied by one or more quality criteria, with their definition, indicators, and theoretical standards.

The goal of the present study was to propose standards based on clinical practice, applying those quality indicators considered most relevant and feasible (5). Responses were obtained from 15 centers distributed throughout the different Spanish auton-

Table II. Parenteral nutrition catheter-related infection

Indicator	No.	No. of days with PN	Recorded incidence	Theoretical standard
Total catheters removed due to suspected infection	20	2852	0.7/100 days	-
Confirmed infections*	24	2852	0.8/100 days	5/100 days
Jugular catheters removed due to suspected infection (jugular)	1	105	0.9/100 days	-
Confirmed infection caused by jugular catheters	0	105	0/100 days	5/100 days
Subclavian catheters removed due to suspected infection	2	158	1.3/100 days	-
Confirmed infection caused by subclavian catheters*	3	158	1.9/100 days	5/100 days
PICC removals due to suspected infection	0	31	0/100 days	-
Confirmed infections caused by PICC	0	31	0/100 days	5/100 days

**Confirmed infections outnumber catheters removed due to suspected infection as a result of culturing the tip of catheters removed for other reasons. The frequency of infection is expressed per 100 days of use; PICC: peripherally inserted central catheter; PN: parenteral nutrition.*

Table III. Theoretical and proposed standards for the most relevant indicators of a hospital's nutritional support process

Indicator	Theoretical standard	Proposed standard
PN bags correctly identified	100 %	100 %
Patients with EN in semi-upright position	> 90 %	> 90 %
Days of correct PN/EN monitoring	100 %	> 90 %
Days of compliance with caloric goals (EN)	> 90 %	> 85 %
Days of compliance with caloric goals (PN)	> 90 %	> 85 %
Nasogastric tubes checked by radiologic imaging before initiating EN	100 %	> 90 %
Ready-to-use PN bags with micronutrients	100 %	100 %
Days with glycaemia > 180 mg/dL in patients with PN	< 5 %	< 10 %
Days with glycemia < 60 mg/dL in patients with PN	< 5 %	< 1 %
Catheter removal due to suspected infection after 100 days of use		< 2
Confirmed infection caused by catheters per 100 days of use	< 5	< 2

PN: parenteral nutrition; EN: enteral nutrition.

omous communities, 11 of which had more than 500 beds and a nutrition unit. This fact indicates that the data presented can be considered representative of the nutritional care provided by medium/large centers with structured and recognized units for nutritional support (2).

Among the results obtained, the high degree of compliance with some of the indicators stood out, namely: correct identification of parenteral nutrition bags; semi-upright position of patients with enteral nutrition; administration of micronutrients in ready-to-use parenteral nutrition bags; and days of glycemia below 60 mg/dL. Use of protocols and systematization of activities, mainly in hospital pharmacies, may have contributed to these results.

On the other hand, compliance with other indicators was slightly lower. Examples are: correct monitoring of artificial nutrition; radiographic assessment of the correct position of feeding tubes; and compliance with caloric goals in parenteral and enteral nutrition. Therefore, it is considered advisable to propose a lowering of the standard because, possibly, the underlying difficulties were fundamentally due to the workloads for the case of monitoring. The interruption of support may have occurred due to various complications and diagnostic or therapeutic procedures in the case of compliance with caloric goals. Radiographic probe testing should be performed due to frequent pull-outs that can make further compliance difficult in some cases.

Regarding the control of hyperglycemia, the proposed standard was raised to 10 % of days instead of the 5 % theoretically proposed. During the administration of parenteral nutrition, 50 % of patients exhibited some elevated glycemia values, especially those with previous diabetes, greater intravenous blood glucose supply, hyperglycemic drugs, or infectious complications (6). Hyperglycemia during parenteral nutrition is an independent factor for in-hospital mortality, hence the relevance of its control (7). The control of hyperglycemia is counterbalanced by the risk of developing hypoglycemia. The latter has been addressed by studies in up to 7 % of patients with parenteral nutrition, and is also a risk factor for mortality in hospitalized patients (8,9). The lower degree of hyperglycemia control with respect to hypoglycemia may have resulted from a conservative use of hypoglycemic treatment, in addition to the difficulty in controlling it due to clinical factors and hyperglycemic drugs.

Regarding the infection rate of the central venous catheters used for administering parenteral nutrition, multiple data are available on the rate of complications of these catheters in home parenteral nutrition. In Spain, the most frequent complication in patients with home parenteral nutrition has been infection, with a rate of 0.64 infections per 1,000 days of central venous catheter use (10). In hospitalized patients, the reported infection rate has been highly variable, between 0 and 4.9 infections per 1,000 days (11-13). Variability may depend on factors such as the type of central venous catheter, local catheter management protocols, underlying diseases, or the definition of infection associated with the catheter used. According to the data found in the present study, infection rates have been lower than reported in other studies, which could be due to the lower number of hospitals that provided data for this indicator, their having implemented infection control programs, or a different recording method. Even so, the standard has been significantly lowered in the present proposal.

The strengths of the present study include the number of centers that answered the survey and, above all, the number of patients included. Among its limitations, the fact stands out that responses were mainly obtained from larger hospitals that had nutrition units among their healthcare services. However, the study did not provide enough data about nutritional support in smaller hospitals without a defined structure for the provision of nutritional support, nor were data recorded for all the indicators analyzed in all hospitals.

In conclusion, the data obtained in the present study suggest that nutrition units in Spain perform their activity with a high quality degree. In addition, this work promotes the creation of initiatives to assess the quality of nutritional support in Spain, providing quality standards based on actual data. An immediate objective for the future should be obtaining information from the maximum number of centers possible, determining which are the best ones, learning from them, and ultimately benchmarking.

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ARÁN

Nutrición Hospitalaria

Nota Clínica

Pelagra: una enfermedad antigua en un mundo moderno

Pellagra: an ancient disease in a modern world

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Resumen

Introducción: la pelagra es una enfermedad sistémica secundaria a la deficiencia de vitamina B3 o de su precursor, el triptófano. La vitamina B3 es necesaria para varios procesos metabólicos, de señalización celular y reparación del ADN. Se caracteriza por la tétrada clásica de dermatitis, diarrea, demencia y muerte. La misma es considerada una enfermedad rara hoy en día; sin embargo, con el auge de las dietas restrictivas sin la adecuada suplementación, como es el caso del veganismo, se ha visto un aumento de los casos en los últimos años.

Caso clínico: exponemos el caso de una paciente adulta joven, vegana estricta, a la cual se le realizó el diagnóstico de pelagra y se le instauró un tratamiento de forma precoz, con una excelente evolución.

Discusión: el interés del caso radica en la importancia de la sospecha clínica y la anamnesis dirigida a factores sociales y nutricionales, adaptados a la época actual, para poder hacer el diagnóstico de una enfermedad rara e infradiagnosticada que es potencialmente mortal de retrasarse el inicio del tratamiento.

Palabras clave:

Pelagra.
Dieta vegana.
Fotodermatosis.
Niacina.

Abstract

Background: pellagra is a systemic disease due to deficiency of vitamin B3 or tryptophan, its precursor. Vitamin B3 is needed for several metabolic processes, cell signaling, and DNA repair. It is characterized by a classic tetrad of dermatitis, diarrhea, dementia, and death. Pellagra is considered rare nowadays; however, due to the popularity of restrictive diets without necessary supplementation such us veganism, there has been an increase in cases in recent years.

Case report: we report the case of a young strict vegan female patient in which a pellagra diagnosis was made, and early treatment was administered with an excellent outcome.

Discussion: the interest of this case lies in the importance of clinical suspicion and directed history taking focused on social and nutritional factors, as adapted for the current times, in order to make the diagnosis of a rare, subdiagnosed disease that is life-threatening if treatment is delayed.

Keywords:

Pellagra. Vegan diet.
Photodermatosis.
Niacin.

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INTRODUCCIÓN

La pelagra, también conocida como la enfermedad de las cuatro D (dermatosis, diarrea, demencia y defunción) fue descrita por primera vez en 1735 por el médico español Gaspar Casal. Está causada por el déficit de vitamina B3, también denominada ácido nicotínico y niacina, o de su precursor, el triptófano (1-3).

Esta vitamina se encuentra ampliamente en los alimentos, sobre todo en los de origen animal. Fuentes ricas en ella son las carnes, el pescado, los lácteos, los huevos, las semillas de gramíneas y los vegetales verdes (2,4).

La pelagra, a nivel mundial, tiene una prevalencia cada vez menor, estando casi erradicada en los países desarrollados gracias al enriquecimiento de los alimentos con niacina.

Se ve sobre todo en ancianos, alcohólicos y pacientes de estrato socioeconómico muy bajo. Sin embargo, los nuevos hábitos alimenticios y las dietas de moda han hecho resurgir esta entidad (2,5).

CASO CLÍNICO

Presentamos el caso de una paciente de 31 años, vegana no suplementada, que se presentó con una dermatosis bilateral y simétrica de los miembros a nivel distal, caracterizada por máculo-placas eritemato-violáceas, bien definidas, de bordes irregulares, con descamación amarronada en collarete y con clara distribución en las zonas expuestas a la luz solar (Fig. 1). La mucosa oral se observó hipocoloreda, con borde lingual depapilado, queilitis y glositis. Este cuadro tenía 6 meses evolución y se asociaba a ardor y prurito. En lo sistémico, la paciente refería astenia, adinamia, anorexia, náuseas, vómitos y dolor abdominal; el cuadro se acompañó además de síntomas depresivos y ansiosos. En función de la dermatosis descrita y de los síntomas gastrointestinales y neurológicos, se hizo un diagnóstico de pelagra en una paciente vegana. Se solicitó paraclínica (análisis clínicos) en búsqueda de déficits nutricionales, mostrando los resultados anemia ferropénica y déficit de B12 y vitamina D, lo que respaldó el diagnóstico (Tabla I).

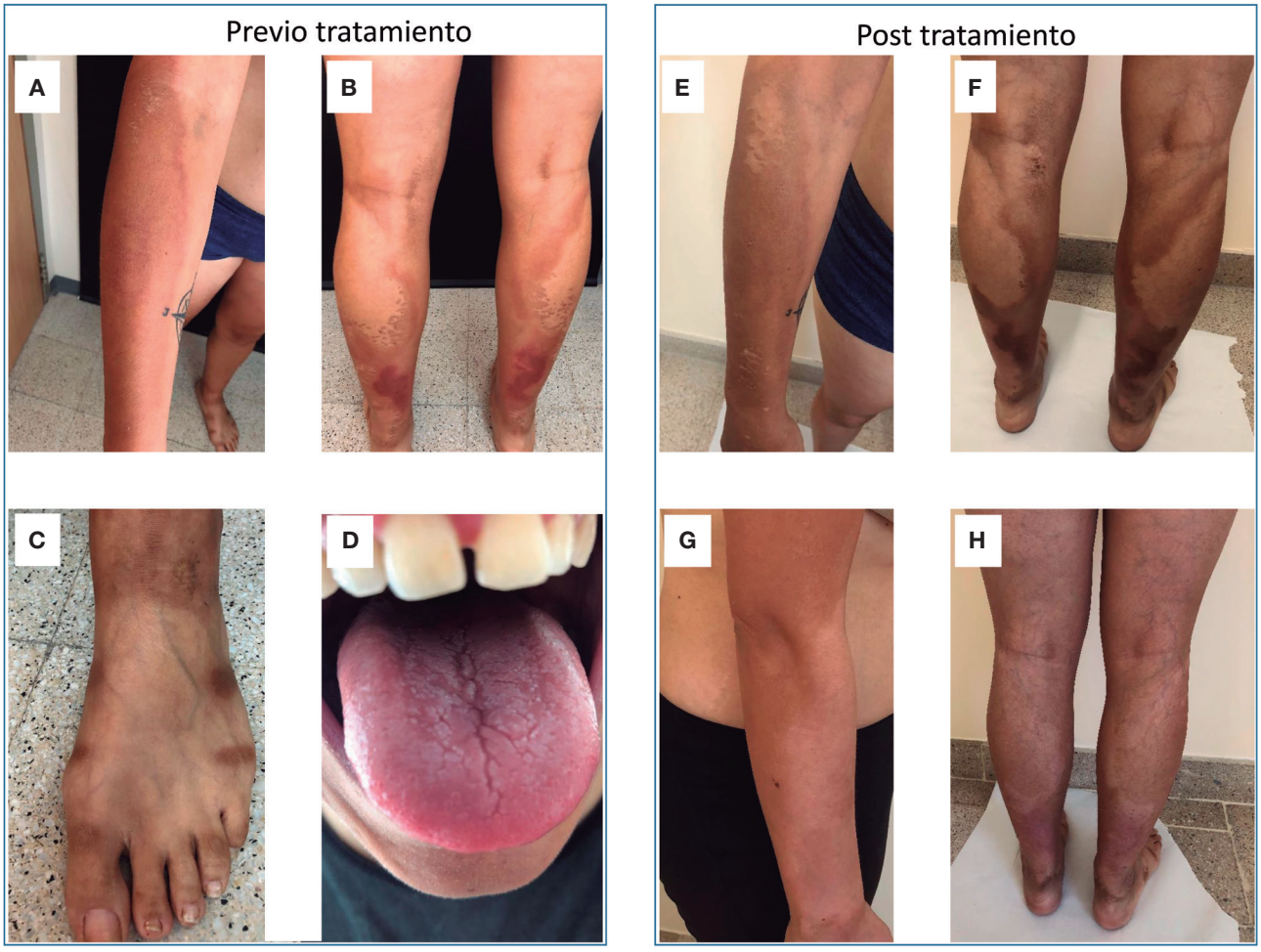

Figura 1.

Comparación entre antes y después del tratamiento.

Tabla I. Análisis clínicos

Paraclínica	Resultado	Valor de referencia	Paraclínica	Resultado	Valor de referencia
Hemoglobina	7,6 g/dl	12,0-16,0	Sideremia	21 µg/dl	33-193
Hematocrito	27,8 %	36,0-46,0	Ferritina	2 ng/ml	15-150
VCM	68,9 fL	80,0-100,0	Transferrina	378 mg/dl	200-360
HCM	18,9 pg	26,0-34,0	IST	4 %	20-55
TSH	> 100 Ul/ml	0,27-4,20	Vitamina D	16 ng/ml	> 29
T4 libre	0,15 ng/dl	0,93-1,70	Vitamina B12	116,6 ng/ml	197-771

Se realizó tratamiento con ácido nicotínico en dosis de 500 mg/día, complejo B, vitamina D, hierro y fotoprotección, obteniéndose una rápida y excelente evolución, lo que certificó nuestro diagnóstico. Al mes de tratamiento se encontraba asintomática, sin elementos de actividad, observándose únicamente hipopigmentación postinflamatoria (Fig. 1).

DISCUSIÓN

La pelagra es una enfermedad causada por el déficit de vitamina B3 o de su precursor, el triptófano, que puede producirse por una dieta deficiente o por trastornos metabólicos o malabsortivos.

El compromiso cutáneo suele ser el inicial y el que domina el cuadro, y se manifiesta como una dermatosis fotodistribuida que se caracteriza por presentar piel eritematosa, áreas hiperpigmentadas y placas queratósicas y/o costrosas, a veces fisuradas, como fue el caso de nuestra paciente. También pueden observarse vesículas y/o ampollas (2-6).

La afectación de las manos es la más frecuente (77-97 %), configurando los llamados "guantes de Casal", mientras que el compromiso de los pies se denomina "botas de Casal", ambos signos presentes en nuestro caso clinico (1,5-7). La afectación de la zona del escote es lo más característico de la pelagra, configurando el "collar de Casal"; puede extenderse al esternón, denominándose "corbata de Casal". Estos elementos habitualmente no están presentes en las pelagras secundarias a dietas restrictivas, como en el caso de nuestra paciente, en donde los signos son menos típicos y floridos (1,4).

En un tercio de los pacientes existe afectación de la cavidad oral. Puede haber compromiso de la mucosa anal y vaginal, y en ocasiones de las faneras. Nuestra paciente solo presentaba compromiso oral (1,5-8)**.**

Los síntomas neurológicos se observan en el 50 % de los casos, aproximadamente. Son bastante inespecíficos, como los presentados por nuestra paciente. Es importante su pesquisa ya que pueden evolucionar hacia trastornos neuropsiquiátricos severos y pueden ser irreversibles, llevando incluso a la muerte (1,4,6,9,10).

La afectación gastrointestinal es frecuente y se manifiesta inicialmente como anorexia (clásico de la enfermedad), pudiendo además asociarse a otros síntomas digestivos como en nuestro caso. En ocasiones pueden evolucionar a diarrea severa (1,6,9).

El diagnóstico de pelagra es clínico y se realiza por la clínica y la rápida respuesta al tratamiento. La concentración plasmática de niacina y las concentraciones urinarias de sus metabolitos apoyarían el diagnóstico; sin embargo, no contamos en el país con dichos estudios (1,4,5).

El diagnóstico en este caso se realizó precozmente, lo cual difiere de lo descrito en la literatura, y con ello se evitó la aparición de manifestaciones sistémicas graves (2,4).

Existen varios esquemas de tratamiento con niacina (1,3-5,7,10). Además, se recomienda administrar preparaciones con complejos de vitamina B por la asociación con el déficit de otras vitaminas (3,10).

Nuestra paciente presentó la respuesta clásica al tratamiento que aparece reportada en la literatura, observándose la resolución de las manifestaciones gastrointestinales y neurológicas en las primeras 48 horas, y la de las cutáneas en la primera semana (1,4,6,10).

CONCLUSIÓN

La pelagra es una enfermedad poco frecuente que generalmente no se encuentra entre nuestros diagnósticos diferenciales.

Comunicamos este caso con la finalidad de recordar que, a pesar de ser una enfermedad rara, aún existe y que el diagnóstico y el tratamiento de forma precoz es fundamental por su potencial mortalidad. Las causas de pelagra se han modificado y se está viendo un nuevo perfil de presentación asociado al consumo de dietas restrictivas, por lo que se trata de una enfermedad reemergente en la actualidad.

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Carta al Director

LAS REDES DE RELACIÓN ESTADÍSTICA EN LA INVESTIGACIÓN DE NUTRICIÓN

Sr. Editor:

En el volumen 37 de la presente revista se presentaron dos estudios que evaluaban los modelos de medición de instrumentos clínicos nutricionales (1,2). Estas investigaciones reportaron, mediante el análisis factorial exploratorio (AFE), la cantidad de factores extraídos para examinar la estructura del test, los cuales están conformados por variables asociadas con el mismo factor, cuyo rasgo subyacente común permite la correlación entre tales variables. La metodología del AFE está vinculada al área de la psicometría que ha impulsado la evaluación de los modelos de variables latentes (no medibles directamente) y esto ha generado el desarrollo de nuevos modelos estadísticos más robustos, como el análisis de ecuaciones estructurales. Este método se basa en análisis de rutas y la regresión múltiple, que refiere la inclusión de relaciones y efectos entre una serie de variables para evaluar múltiples hipótesis clínicas más allá del análisis factorial (3,4).

Los análisis de variables latentes presentan similitud estadística con los modelos de red de correlaciones (5). Este modelo de red no solo incorpora relaciones de orden cero sino también asociaciones parciales causales (6,7) entre un conjunto de variables de diferentes medidas clínicas interconectadas (antropométricas, nutricionales, test, entre otros) (6,7), cuya representación gráfica facilita la interpretación de manera sencilla: mientras más gruesa sea la conexión entre los nodos (variables), mayor será la relación estadística (6,7).

El modelo de red es un análisis multivariante compuesto por múltiples relaciones no lineales regularizadas (eliminación de relaciones más espurias mediante el estimador LASSO) después del control multivariado de los elementos de la red (6,7). Esto favorece la inclusión de variables de diversa naturaleza que evalúen múltiples aspectos relacionados con la salud nutricional (por ejemplo, los trastornos de la conducta alimentaria) (8) y la interacción entre sus múltiples factores etiológicos y moduladores (6-8). Asimismo, es posible estimar los elementos "puente" (altos índices de centralidad) que refieren una mayor implicancia clínica de interés. Aquellos elementos afectan a las interacciones de los demás componentes; es decir, una mayor medida de este elemento "puente" aumenta la probabilidad de fortalecer las demás relaciones y viceversa: su disminución o una menor medida es posible que reduzcan las demás conexiones e incluso que generen un colapso en toda la estructura de la red (6-8).

El análisis de red ha dado origen al modelo gráfico exploratorio (MGE). Este método es alternativo al AFE y ambos permiten extraer una estructura de un conjunto de variables según un marco teórico previo, (9) lo que permite estimar un determinado número de dimensiones cuyos elementos —los de cada dimensión— presentan un color específico (9).

Se utilizaron los datos de una investigación en curso que incluye una medida de síntomas de riesgo de la conducta alimentaria en adultos peruanos durante la cuarentena de la COVID-19 (10) con la finalidad de representar un ejemplo de MGE, el cual identifica tres factores (Fig. 1).

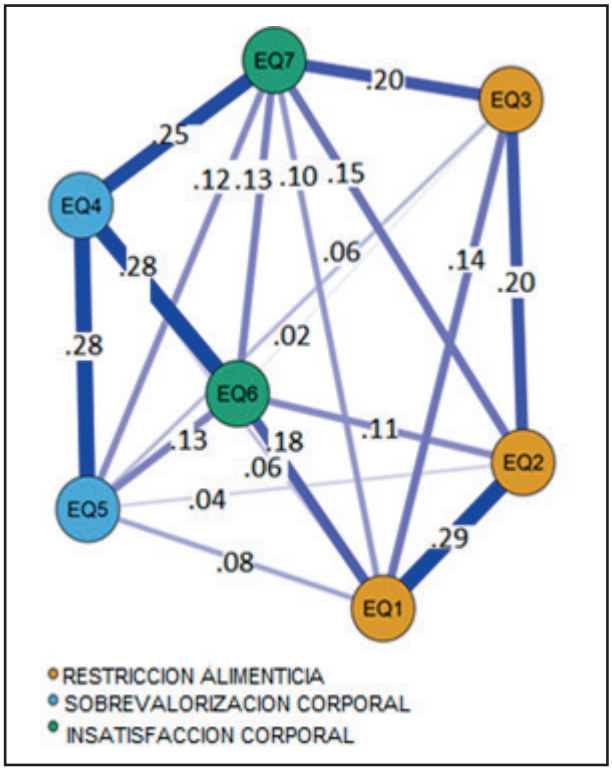

Figura 1.

MGE del "Eating Disorder Examination Questionnaire" (EDE-Q7) en adultos peruanos durante la cuarentena.

El autor refiere no tener ningún conflicto de intereses.

En conclusión, el análisis de red supone una valiosa contribución metodológica y práctica para la investigación en el campo de la nutrición, cuyo uso inclusivo brindará una mayor explicación dinámica de las condiciones clínicas y del impacto psicológico en el ámbito de la salud nutricional.

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Carta al Director

BARRERAS PARA LA MEDICIÓN DE LA FUERZA DE PRENSIÓN EN LA POBLACIÓN MEXICANA

Sr. Editor:

Existe un creciente interés en el estudio de la sarcopenia entre los profesionales de la salud. Sin embargo, a pesar de los avances que representa la publicación de *Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People Sarcopenia* (EWGSOP) y *Sarcopenia: Revised european consensus on definition and diagnosis* (EWGSOP2), siguen existiendo barreras para su implementación en el contexto mexicano (1,2). Un paso fundamental para el diagnóstico de la sarcopenia es la evaluación de la fuerza. La medición de la fuerza de prensión es una de las herramientas más accesibles en la práctica clínica. Sin embargo, la falta de consenso en torno a la técnica de medición de la fuerza de prensión ha limitado el desarrollo de valores de referencia. Se ha reportado que la variación en el procedimiento de medición puede asociarse a diferencias significativas en los resultados obtenidos por lo que, al utilizar una determinada técnica, deberían utilizarse también valores de referencia desarrollados con base en una población local específica para la misma. Se realizó una revisión de la literatura y se pudieron identificar dos técnicas con mayor difusión: la propuesta por Roberts y cols. y la de la American Society of Hand Therapists (ASHT) (3,4). Ambas son muy parecidas. Sin embargo, en la propuesta por Roberts y cols. es necesaria una silla con descansabrazos (3). Este requerimiento es una limitante para su implementación y, debido a la gran variedad de diseños de sillas, puede actuar como un factor de error y disminución de la precisión de las mediciones. En muchos centros del primer nivel de atención no se cuenta con sillas con descansabrazos, y variables como la altura del descansabrazos pueden impactar en la capacidad para ejercer fuerza. Tras discutir esta disyuntiva con el Grupo de Estudio de Sarcopenia en Población Mexicana, se decidió elegir el uso de la técnica sugerida por la American Society of Hand Therapists (ASHT) por ser la más adecuada para el contexto mexicano.

Por todo lo expuesto anteriormente, es prioritario homogenizar la técnica de medición de la fuerza de prensión mediante el uso de la técnica de la ASTH y desarrollar valores de referencia basados en la población local. A continuación se describe dicha técnica.

TÉCNICA DE EVALUACIÓN DE LA FUERZA DE PRENSIÓN DE LA ASHT

El sujeto deberá estar sentado con los hombros aducidos y rotados neutralmente, el codo flexionado en 90 °, el antebrazo en posición neutral y la muñeca entre 0 y 30 ° de dorsiflexión (4) (Fig. 1). Se tomarán 3 mediciones en ambos brazos con un minuto de intervalo entre cada medición. Antes de empezar, el examinador le mostrará al paciente cómo se realiza la prueba y le indicará verbalmente: "Sostén el mango y presiona tan fuerte como puedas". Posteriormente le dará el dinamómetro al sujeto y, después de que el sujeto esté debidamente posicionado, el examinador

Figura 1.
Técnica de evaluación de la fuerza de prensión de la ASHT.

Conflicto de intereses: los autores declaran no tener conflictos de interés.

le indicará verbalmente: "¿Estás listo? Presiona tan fuerte como puedas". Cuando el sujeto comience a presionar, el examinador lo animará verbalmente diciéndole: "¡Presiona fuerte!… ¡Fuerte!… Relajado". Al finalizar cada medición, el examinador le solicitará el dinamómetro para tomar y registrar la lectura de la fuerza de prensión. Para la clasificación de los sujetos se reportará el valor máximo de medición, ya que hay menor probabilidad de que el valor máximo se vea afectado por el número de mediciones en comparación con el valor promedio (5).

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Carta al Director

AKKERMANSIA MUCINIPHILA, UNA VENTANA DE INVESTIGACIÓN PARA LA REGULACIÓN DEL METABOLISMO Y ENFERMEDADES RELACIONADAS

Sr. Editor:

Desde hace más de una década, *Akkermansia muciniphila* se ha identificado como una bacteria que coloniza la microbiota intestinal. Esto es importante debido a que conforma del 1-4 % de la microbiota intestinal y tiene actividades relacionadas con el metabolismo (1).

A. muciniphila es una bacteria gramnegativa perteneciente al filo *Verrucomicrobia*, cuya fuente de energía es la mucina del epitelio intestinal: la degrada para nutrirse y libera en el ambiente monosacáridos, aminoácidos y ácidos grasos de cadena corta (AGCC). Estos nutrientes liberados son usados por otras bacterias de la microbiota, estimulando sus funciones metabólicas (1).

Ahora bien, se han realizado intervenciones nutricionales buscando aumentar la concentración de *A. muciniphila* para ver sus efectos sobre el metabolismo. Se ha demostrado que el incremento de esta bacteria en el organismo ayuda a disminuir el nivel de triglicéridos en sangre (2). También se ha comprobado su papel en la regulación de la homeostasis del metabolismo de la glucosa y del tejido adiposo (3,4). Se encontró que la presencia de *A. muciniphila* está inversamente relacionada con la obesidad, la diabetes mellitus de tipo 2, las enfermedades hepáticas, los procesos inflamatorios y la arteriosclerosis (1). En una intervención nutricional realizada en México en pacientes diabéticos de tipo 2 se incrementó la presencia de *A. muciniphila* en la microbiota fecal en un 125 % y la intervención se relacionó con reducciones de las AUC de glucosa, triglicéridos, colesterol total y c-LDL; con aumentos de la actividad antioxidante plasmática, y con disminución de las concentraciones de LPS, pudiendo ayudar a reducir la endotoxemia metabólica (5).

Incluso para la obesidad, ya se ha demostrado que la administración oral de *A. muciniphila* como probiótico es factible y segura, demostrando efectos benéficos en pacientes obesos tales como una mejoría de la sensibilidad a la insulina, niveles bajos de colesterol plasmático, reducción de los marcadores de disfunción hepática y una ligera disminución de la circunferencia de la cadera, de la masa y del peso corporal (6).

Con todo esto nos percatamos que la bacteria representa un papel benéfico en el estado nutricio, por lo que la pregunta que surge es: ¿Cómo podemos aumentar la concentración de *A. muciniphila* en la microbiota intestinal? Se ha demostrado que la dieta restrictiva en calorías; la suplementación con extracto de granada, resveratrol, polidextrosa, EpiCor o butirato de sodio, y la dieta alta en FODMAP (oligo, di, monosacáridos y polioles fermentables) aumentan la concentración de *A. muciniphila* (7). De igual manera, la ingesta de alimentos como el nopal, la semillas de chía y la proteína de soya han demostrado su capacidad de modificar la composición de la microbiota intestinal, aumentando el porcentaje de esta bacteria (8).

Concluimos que una intervención alimentaria dirigida a aumentar esta bacteria puede ser clave en la mejora de los parámetros cardiometabólicos de los pacientes con obesidad y/o diabetes (6).

Por todo ello, se busca hacer énfasis en la importancia de investigar más a fondo los efectos de esta bacteria, ya que tal vez pueda ser la piedra angular perdida en el tratamiento de estas enfermedades.

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Carta al Director

A PROPÓSITO DE LAS REVISIONES SISTEMÁTICAS, LOS METAANÁLISIS Y LOS RESÚMENES DE REVISIONES SISTEMÁTICAS

Sr. Editor:

Tiempo atrás se publicó en su prestigiosa revista el siguiente artículo: "¿Revisión sistemática, metaanálisis o resumen de revisiones sistemáticas?" (1). El manuscrito citado previamente plasma la importancia que presenta la investigación secundaria, considerando que esta pueda resumir toda la evidencia existente sobre un área específica del conocimiento. También nos encontramos con que divide y explica las diferencias existentes entre una revisión narrativa, una revisión sistemática con metaanálisis y una revisión sistemática sin metaanálisis, y finaliza describiendo los resúmenes de las revisiones sistemáticas u "Overview".

En relación con esto, el Manual Cochrane de revisiones sistemáticas de intervenciones, en su capítulo 22 (2), define lo siguiente: "Los resúmenes de las revisiones Cochrane tienen como objetivo principal resumir múltiples revisiones Cochrane de intervenciones y abordar el efecto de dos o más posibles intervenciones sobre un problema de salud" (en caso de no existir revisiones sistemáticas Cochrane, se pueden incluir revisiones sistemáticas publicadas en otros recursos). Por tanto, ¿cuáles son las diferencias metodológicas entre una revisión sistemática y un resumen de revisiones sistemáticas ("Overview")?

Para dar respuesta a la pregunta planteada anteriormente, nos basaremos en los siguientes aspectos metodológicos: a) objetivos; b) criterios de selección; c) búsqueda; d) obtención de los datos; e) evaluación de las limitaciones; e) calidad de la evidencia y f) análisis (Tabla I).

A modo de conclusión, debemos recordar que una revisión sistemática no es lo mismo que un resumen de revisiones. Ambos

Tabla I. Comparación de los métodos de las revisiones sistemáticas de intervenciones y los resúmenes de revisiones ("Overview")

Aspectos metodológicos	Revisiones sistemáticas	Resúmenes de revisiones sistemáticas
Objetivos	Resume la evidencia procedente de estudios sobre los efectos de las intervenciones	Resume la evidencia procedente de revisiones sistemáticas sobre los efectos de las intervenciones
Criterios de selección	Describe los criterios de elegibilidad de los estudios	Describe los criterios de elegibilidad de las revisiones sistemáticas
Búsqueda	Búsqueda exhaustiva de los estudios que son relevantes	Búsqueda solo de revisiones sistemáticas de intervenciones que sean relevantes
Obtención de los datos	Los obtiene a partir de los estudios incluidos	Los obtiene a partir de las revisiones sistemáticas incluidas
Evaluación de las limitaciones	Evaluación del riesgo de sesgo en los estudios incluidos	Evaluación en las revisiones sistemáticas incluidas
Calidad de la evidencia	La evaluación es entre los estudios para cada resultado de interés	Las evaluaciones presentadas en las revisiones sistemáticas incluidas
Análisis	Se realiza una síntesis de los resultados incluidos para cada resultado de interés importante	Se resumen los resultados de las revisiones. También se pueden realizar análisis adicionales para las comparaciones entre las revisiones, generalmente comparaciones indirectas de múltiples intervenciones

Tabla adaptada de: "Comparación de los métodos de las revisiones Cochrane de intervenciones y los resúmenes de revisiones Cochrane" (2).

Conflicto de intereses: los autores declaran no tener conflicto de intereses.

diseños de investigación secundaria presentan diferencias metodológicas en su elaboración. Por un lado, las revisiones sistemáticas resumen la evidencia procedente de estudios primarios sobre los efectos de las intervenciones, mientras que los resúmenes de revisiones tienen como propósito resumir la evidencia procedente de revisiones sistemáticas de los efectos de las intervenciones y abordar el efecto de dos o más intervenciones sobre determinado problema de salud. Por tanto, ambos diseños no se deben confundir.

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Carta al Director

BODY MASS INDEX AND BODY FAT PERCENTAGE OF POLICE FORCE IN MONTENEGRO IN DIFFERENT AGE GROUPS

Dear Editor-in-Chief,

The prevalence of obesity is increasing among the global population, regardless of their living in developed or underdeveloped countries, or rural or urban areas. In the USA, for example, from 1999-2000 through 2017-2018, the prevalence of obesity increased from 30.5 % to 42.4 %, and the prevalence of severe obesity increased from 4.7 % to 9.2 % (1). Montenegro is no exception, so it is reasonable to expect that this problem will not bypass Montenegrin police officers as well. The lifestyle of people of all ages and all professions has changed in general. People are much less physically active on a daily basis, while media consumption and eating fast food are increasing (2). Police officers also face different tasks today than they used to in the past, due to the increasing rate of cybercrime relative to street crime. Therefore, the activity of a police officer at work is far less today than it was before, and now a police officer is more active off duty than at work (3). However, the seriousness of certain tasks that a member of the police forces must be ready to carry out at crucial moments points to the fact that occurrence of obesity is absolutely undesirable. Therefore, preventive action has to be undertaken continuously for ensuring significant improvements in the efficiency of police officers when it comes to performing professional tasks.

As body mass index (BMI) and body fat percentage (FAT%) represent significant indicators, used for the assessment of nutritional status among members of the police, the main goal of this study was to apply these indicators, for the first time, to perform a comprehensive analysis of the nutritional status of police officers relative to their age, primarily because this global problem is likely to vary with age. The sample of 115 members of the police forces of Montenegro included in the analysis was divided into seven age groups: I (aged to 24 yrs.), II (25-29 yrs.), III (30-34 yrs.), IV (35-39 yrs.), V (40-44 yrs.), VI (45-49 yrs.), and VII (50 yrs. or older). Body mass index and body fat percentage were calculated according to the standard formula (4). Descriptive statistics were used to calculate the socio-demographic and body composition characteristics, while the ANOVA and *post hoc* test were applied to determine differences between age groups. The significance level was set at $p < 0.05$. Mean age, BMI, and FAT% of the subjects (in total) were: 31.54 years, 27.57 kg/m^2, and 16.81 %. Amongst 115 tested subjects (based on the BMI classification of WHO), not one was underweight (< 18.50 kg/m^2), while 16 subjects (13.91 %) were normal weight (18.50-24.99 kg/m^2), 80 subjects (69.57 %) were overweight (25.00-29.99 kg/m^2), and 19 subjects (16.52 %) were obese (≥ 30.00 kg/m^2). On the other hand, age groups had specific mean BMI and FAT% values: I: 26.17 kg/m^2 and 13.03 %; II: 28.01 kg/m^2 and 15.9 %; III: 28.28 kg/m^2 and 18.08 %; IV: 29.15 kg/m^2 and 22.14 %; V: 28 kg/m^2 and 17.99 %; VI: 28.6 kg/m^2 and 21.16 %; and VII: 29.19 kg/m^2 and 23.92 %). Judging from the age perspective, no group exhibited values in the normal range. All age groups were approaching 25.0 (over-weight or pre-obese) and over, but never beyond 30.0 (obese) on average. Furthermore, groups I and V were described as "very good" (based on the normative FAT% of ACSM), while all others were described as "good", which was a surprise since at least two age groups were expected to be described as "excellent", especially because of doubts about the adequacy of applying WHO normative values to the Western Balkan's population, which has a specific body composition (5). An ANOVA was performed, which showed significant differences in both tested variables, while the *Post Hoc* test showed no significant differences in all age groups, except for BMI between the first group (aged to 24 yrs.) and all other groups except the fifth group (aged 40-44 yrs.), and for FAT% between the first group (aged to 24 yrs.) and all other groups except the second group (aged 25-30 yrs.).

In conclusion, this study indicates that the situation with regard to overweight (69.57 %) and obesity (16.52 %) among the police forces is alarming, and may lead to a decrease in their physical fitness and effectiveness when on duty. It should be noted that, together with shift work, poor sleep, and exposure to a range of

Conflicts of interest: the authors declare no conflicts of interest.

Author contributions: Veselin Veljovic designed and led the study, performed statistical analyses, and wrote the manuscript. Zeljko Spalevic reviewed previous studies, wrote the manuscript, and discussed the results. Marija Bubanja reviewed previous studies and discussed the results. Bojan Masanovic collected the data, did the presentation of the results, discussed the results, and revised the manuscript.

stressors, this could indeed have an impact on their health in the future. Finally, it should definitely be noted that this study is limited due to the fact that measurements were taken during the ongoing COVID-19 pandemic, so it is likely that, under regular circumstances, police officers would be more active and their body composition might be different.

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In Memoriam

Prof. Manuel Serrano Ríos (1935-2021)

El profesor Manuel Serrano Ríos nacido en Málaga en 1935 y fallecido en Madrid en 2021, fue uno de los más destacados y brillantes referentes españoles en diabetes y obesidad. Hijo de maestros, de padre cordobés y madre granadina, él se describía humorísticamente como un "andaluz heterocigoto de alelos granadino y cordobés". Desde muy pequeño cultivó una intensa afición por la lectura y el estudio, claramente reflejada en la brillante carrera de Medicina que cursó en la Universidad Complutense de Madrid, donde obtuvo la calificación de Sobresaliente y Premio Extraordinario en el año 1959. Fue admitido a continuación en el internado en Medicina Interna de la Fundación Jiménez Díaz (FJD) hasta el año 1964, permaneciendo en esa misma institución en los años sucesivos como médico adjunto, junto al maestro Carlos Jiménez Díaz. De su paso por el New York Medical College (1965-1966) en EE. UU., con una beca en Endocrinología concedida por la Fundación Lilly Internacional, nos queda su trabajo sobre el "Radioinmunoanálisis de la insulina y su aplicación a la investigación diabetológica".

Como especialista en Medicina Interna y Endocrinología accede a la plaza de Jefe Asociado de Medicina Interna de la FJD (1968). Dos años después es nombrado Profesor Adjunto de Patología y Clínica Médicas de esa misma institución, cargo en el que permanece hasta el año 1975, cuando obtiene el grado de Profesor Adjunto Numerario por concurso-oposición del Cuerpo Nacional de Profesores Adjuntos de Patología y Clínica Médicas de la Facultad de Medicina de la Universidad Autónoma de Madrid. Pocos años antes, en 1971, había optado al grado de Doctor por la Universidad Complutense con su tesis que fue calificada como Sobresaliente "Cum Laude".

Tras cesar como profesor de la Universidad Autónoma ocupa en los años sucesivos las plazas de profesor agregado numerario por concurso-oposición de Patología y Clínica Médicas en la Universidad Autónoma de Barcelona (1976-1978), Profesor Agregado Numerario de Patología General y Propedéutica Clínica, por concurso de traslado en la Universidad Complutense de Madrid (1978-1979), Profesor Agregado Numerario encargado de Cátedra de Patología General y Propedéutica Clínica -2.ª Cátedra- (1979-1981) y Catedrático de Patología General y Propedéutica Clínica en la Facultad de Medicina de la Universidad de Oviedo hasta 1987. Durante estos años también fue jefe en los servicios de Medicina Interna de la FJD (1976-1977) y por concurso oposición del Hospital Universitario Ramón y Cajal, donde permanece desde 1977 a 1987, año en el que obtiene la Cátedra y Jefatura de Medicina Interna en el Hospital Clínico San Carlos de la Universidad Complutense, plazas que ocupa hasta su jubilación en el año 2005. Nombrado entonces Profesor Catedrático Emérito de Medicina (2005-2008) y posteriormente Académico de Número de la Real Academia Nacional de Medicina (2009) donde ocupa el sillón número 6 de Endocrinología, Metabolismo y Nutrición, Académico Honorario Extranjero de la Real Academia Nacional de Medicina de Argentina (2010) y Académico de Honor de la Real Academia Medicina de Andalucía Oriental (2016).

Entre las distinciones recibidas destacan los Doctorados *Honoris Causa* por las Universidades de Granada (España), Cayetano Heredia de Lima (Perú) y Cluj-Napoca (Rumanía), así como las Medallas de Oro de la Mediterranean Group Study of Diabetes (MGSD) y de la Sociedad Española de Nutrición Básica y Aplicada (SENBA), y las Lecturas Conmemorativas de la Fundación Jiménez Díaz y Magistral Dr. Laguna de la Universidad de Alcalá de Henares.

Miembro de multitud de sociedades nacionales e internacionales en Diabetes, Endocrinología, Aterosclerosis y Medina Interna, fue presidente de las Sociedades Española de Diabetes y de Nutrición Básica y Aplicada. Así mismo, vicepresidente en la Federación Internacional de Diabetes y otros numerosos cargos en diversos organismos nacionales e internacionales entre los que podemos destacar la Presidencia del Instituto Danone Internacional.

También fue miembro del Consejo Científico de la Fundación Lilly y de diversos comités editoriales de numerosas revistas científicas, entre las que cabe destacar *Diabetes Research and Clinical Practice, Diabetes, Diabetologia, Nutrition and Metabolism, Revista Clínica Española,* etc. Así mismo fue revisor en estas mismas

revistas y otras del máximo nivel científico, como Diabetes y Diabetes Care, entre otras.

Manuel Serrano Ríos lideró como investigador principal el grupo de CIBERDEM (Red Nacional de Diabetes) del Hospital Clínico San Carlos de Madrid, puesto que ocupó por su brillante y destacada trayectoria científica en las áreas de fisiopatología de la secreción de insulina, genética de la diabetes *mellitus* y obesidad, así como epidemiología de estas enfermedades y el síndrome metabólico. Sin lugar a dudas fue un referente nacional e internacional en estos campos, participando también en el estudio de la resistencia a la insulina en lipodistrofia en pacientes VIH. Sirvan como notables ejemplos de su actividad científica, la descripción por primera vez, de la disminución de la secreción de insulina como el marcador más temprano de prediabetes genética, y del síndrome genético Mendenhall con resistencia extrema a la insulina, como consecuencia de un fallo en la unión de la insulina a receptores específicos en varios sistemas celulares. Posteriormente demostró que el defecto se debía a una mutación puntual (sin sentido) en la subunidad beta del receptor de insulina. Este hallazgo fue uno de los primeros defectos moleculares descubiertos en la resistencia a la insulina determinada genéticamente. Asimismo, y de gran relevancia fue, la primera descripción de genes de susceptibilidad asociados a HLA de diabetes mellitus tipo 1 en población española. Impulsor del estudio di@bet.es, uno de los mas importantes realizados en España sobre epidemiología.

En 1978 promovió la creación de la Federación Española de Educadores en Diabetes en aquella reunión inolvidable para muchos en Segovia. En 2002 como vicepresidente de la IDF promocionó un acercamiento con los países más necesitados en una primera reunión en Cuba, donde trabajó como un verdadero "residente de batalla".

Quedarán para siempre en nuestra memoria la claridad, rigor y entusiasmo que transmitía en sus presentaciones en congresos y reuniones científicas, así como su capacidad de síntesis, notables aptitudes que siempre nos impresionaron. De la etapa en el Hospital Clínico San Carlos llegó a afirmar que "fue la más equilibrada, productiva y gratificante para mi vida personal, académica e investigadora". En esta etapa, estableció fructíferos programas de cooperación internacional con grupos de EE. UU., Europa y Australia.

Maestro de innumerables médicos e investigadores, también fraternales amigos, que hoy ocupan destacados lugares en la asistencia y la investigación, y contribuyen con su labor a mejorar la atención a las personas con "diabesidad" y/o síndrome metabólico, supo transmitir, con frecuente y cálida simpatía, su pasión por el estudio y la investigación de estas enfermedades pandémicas. Sin olvidar que ante todo fue médico, profesión que desarrolló desde una perspectiva humanista, porque parafraseando al célebre Platón, amando el arte de la Medicina, amó también la humanidad.

Maestro, descanse en paz.

María Teresa Martínez Larrad, Arturo Corbatón Anchuelo,
Alfonso L. Calle Pascual; entre otros tus discípulos
del CIBERDEM

Hospital Clínico San Carlos. Madrid