Nutrición Hospitalaria

Original/*Valoración nutricional*

Body fat and its relationship with clustering of cardiovascular risk factors

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Abstract

Background: Body mass index (BMI) and waist circumference (WC) are the most commonly measured anthropometric parameters given their association with cardiovascular risk factors (RFs). The relationship between percentage body fat (%BF) and cardiovascular risk has not been extensively studied.

Aims: This study evaluated %BF and its relationship with cardiometabolic RFs in healthy subjects and compared these findings with the relationship between BMI/WC and cardiovascular RFs.

Methods: This was a cross-sectional study of 99 males and 83 females (mean age 38 ±10 years) evaluated in a preventive cardiology program. All subjects completed a survey about RFs and lifestyle habits. Anthropometric parameters, systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting lipid profile, and blood glucose were collected. Body fat was determined using four skinfold measurements. Fat mass index (FMI) was also calculated.

Results: Percentage body fat was significantly and directly associated with total cholesterol (R^2=0.11), triglycerides (R^2=0.14), low-density lipoprotein cholesterol (R^2=0.16), non-high-density lipoprotein cholesterol (R^2=0.24), fasting blood glucose (R^2=0.16), SBP (R^2=0.22), and DBP (R^2=0.13) ($p<0.001$ for all) and inversely related to high-density lipoprotein cholesterol (R^2= 0.32; $p<0.001$). When the models of %BF, FMI, WC, and BMI were compared, all of them were significantly related to the same cardiometabolic RFs and the clustering of them.

Conclusion: Percentage body fat and FMI were significantly associated with biochemical variables and to the clustering of RFs. However, these associations were similar but not better than WC and BMI.

(*Nutr Hosp.* 2015;31:2253-2260)

DOI:10.3305/nh.2015.31.5.8625

Key words: *Body fat. Lipid profile. Cardiovascular risk factors. Metabolic syndrome.*

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GRASA CORPORAL Y SU RELACIÓN CON LA AGREGACIÓN DE FACTORES DE RIESGO CARDIOVASCULAR

Resumen

Introducción: El índice de masa corporal (IMC) y la circunferencia de cintura (CC) son los parámetros antropométricos que se miden con mayor frecuencia dada su asociación con los factores de riesgo cardiovascular (RC). La relación entre el porcentaje de grasa corporal (%GC) y el riesgo cardiovascular no se ha estudiado ampliamente.

Objetivo: Evaluar el %GC y su relación con los FR cardiometabólico en sujetos sanos y comparar estos resultados con la relación IMC/CC y FR cardiovascular

Métodos: Se realizó un estudio transversal en 99 hombres y 83 mujeres participantes asistentes a un programa de cardiología preventiva (edad 38 ± 10 años). Todos los sujetos completaron una encuesta sobre los FR y hábitos de estilos de vida. Se evaluaron antropométricamente, se les tomo presión arterial sistólica (PAS) y diastólica (PAD), perfil lipídico y glicemia en ayunas. La grasa corporal se determinó a través de cuatro mediciones de pliegues cutáneos. También se calculó el índice de masa grasa (IMG).

Resultados: El porcentaje de grasa corporal se asoció significativamente y directamente con el colesterol total (R^2=0,11), triglicéridos (R^2=0,14), colesterol LDL (R^2=0,16), colesterol VLDL (R^2=0,24), glicemia (R^2=0,16), PAS (R^2=0,22) y PAD (R^2=0,13) ($p<0,001$ para todos) e inversamente relacionada con HDL (R^2=0,32; $p<0,001$). Cuando se compararon los modelos de %GC, IMG, CC e IMC, todos ellos se asociaron en forma significativa a los mismos FR cardiometabólico y a la agregación de los mismos.

Conclusión: El %GC e IMG se asociaron en forma significativa con las variables bioquímicas y la agregación de FR. Sin embargo, estas asociaciones eran similares pero no mejor que la CC y el IMC.

(*Nutr Hosp.* 2015;31:2253-2260)

DOI:10.3305/nh.2015.31.5.8625

Palabras claves: *Grasa corporal. Perfil lipídico. Factores de riesgo cardiovascular. Síndrome metabólico.*

Introduction

From decades, the main risk factors (RFs) associated with cardiovascular disease are well known and include: smoking, overweight/obesity, diabetes, dyslipidemia, and hypertension (1-8). The majority of these RFs are preventable and modifiable by lifestyle changes. Evidence has shown that both overweight and physical activity affect most cardiometabolic variables associated with cardiovascular RFs, such as serum lipids, blood pressure (BP), and insulin resistance (3, 9, 10). Frequently, overweight is diagnosed using body mass index (BMI), which is the relationship between the weight and height of a subject; however, this parameter has been criticized due to its low specificity regarding body composition. For example, studies have shown that, although some ethnic groups have a lower BMI compared with Caucasians, they have a higher body fat percentage (11-13).

Visceral fat has been identified as a key factor in cardiovascular risk due to its higher lipid turnover which alters serum lipids (14-16). Waist circumference (WC) has a strong correlation with visceral fat in both men and women (17); thus, it has often been used with BMI to determine cardiovascular risk and metabolic syndrome. However, similar to BMI, WC does not represent total body fat. The relationship between total body fat—or, percentage body fat (%BF)—and cardiovascular risk has not been extensively studied. Two studies determined the association among %BF, cardiovascular RFs, and RF clustering and suggested that the association is direct and stronger than that seen with body weight or BMI (18, 19). However, these studies were limited to male subjects, and the methodology used was hydrostatic weight and/or seven skinfolds thicknesses measurement, approaches that are not generally applicable in ambulatory practice. Other studies have determined %BF using dual X-ray absorptiometry (DXA) and compared it with BMI and WC as predictors of CV risk factors reporting different results (20-22). Although DXA is the most reliable method for measuring %BF, it is both expensive and not readily applicable in the ambulatory setting. The estimation of %BF with the measurement of 4 skinfold thicknesses (tricipital, bicipital, subscapular, and suprailiac) is efficient and relatively low cost (23). Moreover, it is easily measured during the ambulatory nutritional assessment, requires little time to perform and has been previously validated (29). (Lean et al. 1996). When determining %BF, it is also possible to calculate fat mass index (FMI), a parameter that incorporates both %BF and BMI (24). Fat mass index calculates the total fat mass of a subject according to his or her height. To our knowledge there are scarce data in Latin American population evaluating the association of %BF with cardiometabolic RFs.

The present study was developed to complement the available data on %BF and its relationship to cardiovascular risk. The main objectives were to: 1) determine the association between %BF and cardiovascular risk parameters determined by biochemical variables and BP; 2) determine the relationship between %BF and FMI with cardiometabolic RF clustering; 3) compare the strength of the association of %BF and FMI with BMI and WC as predictors for the same cardiometabolic RFs in healthy young subjects.

Methods

This was a cross-sectional study of 182 adult subjects (99 male and 83 female) who were evaluated in a preventive cardiovascular health program in Santiago de Chile between April and August of 2013. Exclusion criteria were subjects with BMI >34.9 kg/m^2, history of bariatric surgery, and previous medical treatment for dyslipidemia, hypertension, diabetes, or other chronic diseases. Subjects provided written informed consent that data could be used anonymously for academic purposes. The original and follow-up research protocol was approved by the Pontificia Universidad Católica de Chile, Chile.

Data collection

Subjects, assisted by a trained program nurse, answered a survey about cardiovascular RF, medical history, and use of medication. Fasting blood samples were taken to determine lipid profiles and blood glucose. Systolic and diastolic blood pressure (SBP and DBP, respectively) were measured using a sphygmomanometer and following the protocol as described in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (25).

Blood samples were analyzed in the laboratory using the following methods:

Total cholesterol, high-density lipoprotein cholesterol (HDL-C), and triglycerides were determined using standard enzymatic methods with ad-hoc reactives (Hitachi analyzer).

Low-density lipoprotein cholesterol (LDL-C) was calculated using Friedwald's formula when triglycerides were <400 mg/dL.

Blood glucose was calculated using the glucose-oxidase method.

Nutritional and Physical Activity Assessments

All subjects were evaluated by the program dietitian who took anthropometric measurements and conducted a survey about dietary and physical activity habits. Physical activity level was calculated according to the guidelines of the American College of Sports Medicine and the American Heart Association where intensity of reported exercise is determined in meta-

bolic equivalents (METs) then multiplied by the total time performed during the week[26]. To determine the effect of exercise on %BF, subjects were divided by gender in: a) BMI tertiles (T1: 18 to 24 kg/m²; T2: 24 to 27 kg/m²; T3: 27 to 34 kg/m²) and b) physical activity level tertiles (inactive: <148 METs · minutes per week; moderate: 148-880 METs · minutes per week; vigorous: >880 METs · minutes per week).

Anthropometric Measurements

BMI and WC: weight and height were measured using a standard scale with a capacity of 160 kg (DETECTO 3P704, Webb city, Missouri, USA) and precision (0.1 kg and 0.1 cm, respectively). BMI was calculated using the following formula: BMI=Weight/(Height)². Waist circumference was evaluated in the mid-point between the last rib and the iliac crest with a precision of 0.1 cm.

Skinfold thicknesses measurement: tricipital, bicipital, subscapular, and suprailiac skinfolds were measured using a Harpenden caliper with a precision of 0.2 mm (John Bull British Indicators Ltd., St Albans, United Kingdom) in the right side of the body with the subject standing in a supine position (23). Two measurements were taken and the mean was calculated based on the criteria of the International Society for the Advancement of Kinanthropometry (27). To reduce errors of measurements, skinfold thicknesses were measured by the same dietitian, whose intra-observer error is 3.5 ± 1.1%.

Total body fat percentage and FMI: Body density (D_b) was calculated according to the age and gender of each subject, using the sum of the four skinfold thicknesses, as described by Durnin and Womersley in 1974 (23). Percentage body fat (%BF) was calculated applying the formula described by Siri in 1956 (28), and FMI was calculated using %BF and BMI.

%BF= [(4.95/D_b)-4.5] · 100
FMI (kg/m²)=(%BF · BMI)/100

An excel spreadsheet was developed with the described formulas to reduce the time of calculation. Subjects with BMI ≥ 34.9 were excluded from analysis as %BF estimation using skinfold thicknesses has shown to underestimate real body fat in extremely obese subjects (29).

Cardiovascular and metabolic syndrome risk factors

The following criteria were used to determine the number of cardiovascular RFs: dyslipidemia, any subject with LDL-C ≥130 mg/dL, HDL-C <40 in men or <50 mg/dL in women, or non-HDL-C ≥160 mg/dL; diabetic, any subject with fasting glucose ≥126 mg/dL; hypertensive, any subject with SBP ≥140 mm Hg or DBP ≥90 mm Hg on alternate days during the present evaluation; active smoker, those subjects smoking

daily during the last month; physical inactivity, those subjects with a frequency of physical activity <1 time per week.

The harmonized criteria put forth by the International Diabetes Federation Task Force on Epidemiology and Prevention, the National Heart, Lung, and Blood Institute, the American Heart Association, the World Heart Federation, the International Atherosclerosis Society, and the International Association for the Study of Obesity (30) were used to determine the number of metabolic syndrome RFs, excluding WC since it was an anthropometric variable being analyzed in this study: triglycerides ≥150 mg/dL, HDL-C <40 mg/dL in men and <50 mg/dL in women, fasting blood glucose ≥100 mg/dL, and SBP ≥130 mm Hg or DBP ≥85 mm Hg.

Statistical Analysis

Linear regression models (adjusted for gender, age, physical inactivity, and smoking) were developed to determine the relationship between each anthropometric parameter and cardiometabolic variables. In addition, the group was divided by gender in %BF tertiles to compare cardiometabolic variables using ANOVA test with a post-hoc test. A proportional odds cumulative logistic regression model (likelihood ratio $p<0.05$) for each predictor (%BF, FMI, WC, BMI), adjusted for age and gender, was applied to determine the probability of increasing the number of cardiovascular RFs by 0, 1 to 2, and 3+, and the probability of increasing the number of metabolic syndrome RFs by 0 to 1 and ≥2. The models for each anthropometric variable were compared. Statistical software R, version 3.0.1 (R Foundation for Statistical Computing, Vienna, Austria) was used for the statistical analysis.

Results

182 adult subjects (99 male and 83 female) were included in this analysis with a mean age of 38 ±10 years (range: 22 to 68 years old). Demographic, biochemical, and anthropometric characteristics of the group are described in table I. The prevalence of "newly diagnosed" RFs was: dyslipidemia 50%, hypertension 3%, diabetes 1%, overweight 59%, smoking 27%, and metabolic syndrome 12%. Overall, women had lower LDL-C ($p<0.01$), triglycerides ($p<0.01$), SBP ($p<0.0001$), and DBP ($p=0.02$) levels than men. In addition, HDL-C was higher in women than men ($p<0.0001$). Body mass index and WC were significantly lower in women compared with men ($p=0.01$ and $p<0.0001$, respectively). However, %BF was significantly higher in women compared with men: 35% versus 25%, respectively ($p<0.0001$).

Associations between %BF, FMI, WC, and BMI with the biochemical variables and BP, according to

Table I

Demographics and characteristics of a young adult population (n=182)

Demographical, biochemical and anthropometrical variables	Total (n=182)	Women (n=83)	Men (n=99)	p-value
Age, years	38 ± 10	37 ± 9	40 ± 10	0.03
Biochemical Variables				
Systolic blood pressure, mm Hg	133 ± 14	108 ± 13	117 ± 13	<0.001
Diastolic blood pressure, mm Hg	70 ± 8	69 ± 7	71 ± 9	0.023
Blood glucose, mg/dL	87 ± 10	86 ± 13	88 ± 7	0.072
Total-C, mg/dL	192 ± 34	188 ± 32	195 ± 36	0.182
Triglycerides, mg/dL	122 ± 73	104 ± 51	137 ± 85	0.001
HDL-C, mg/dL	55 ± 15	63 ± 14	48 ± 11	<0.001
LDL-C, mg/dL	113 ± 33	104 ± 29	119 ± 34	0.002
Non-HDL-C, mg/dL	138 ± 38	126 ± 31	137 ± 40	<0.001
Physical inactivity (<1 time/week), %	41%	46%	37%	0.184
Smokers, %	27%	31%	25%	0.387
Overweight and obesity, %	59%	50%	66%	0.025
Dyslipidemia, %	50%	44%	55%	0.156
Hypertension, %	3%	1%	4%	0.258
Diabetes, %	1%	1%	0%	0.266
Metabolic syndrome, %	12%	6%	17%	0.026
Physical activity (METs · min per week)	566 ± 643	412 ± 490	691 ± 723	0.002
Anthropometric variables				
BMI, kg/m^2	26 ± 3	25 ±4	26 ±3	0.011
Waist circumference, cm	86 ± 11	81 ± 11	91 ± 9	<0.001
Percentage body fat, %	30 ± 7	35 ± 5	25 ± 5	<0.001
Fat mass index, kg/m^2	8 ± 3	9 ± 2	7 ± 3	<0.001

Abbreviations: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MET, metabolic equivalent; SD, standard deviation; total-C, total cholesterol.
Data are mean ± SD, except where indicated. T-tests were used to determine differences between men and women.

linear regression models (adjusted for gender, age, physical inactivity, and smoking), are presented in table II. Overall, %BF was directly and significantly related to total cholesterol, triglycerides, LDL-C, non-HDL-C, fasting blood glucose, SBP, and DBP and was inversely related to HDL-C (Table II). Fat mass index, WC, and BMI were also significantly related to these variables.

When %BF tertiles were compared, subjects in the highest tertile (Tertile 3: %BF ≥27% and ≥37% for men and women, respectively) had significantly higher total cholesterol, triglycerides, LDL-C, non-HDL-C, fasting blood glucose, SBP, and DBP, and lower HDL-C (Table III). Moreover, a higher prevalence of dyslipidemia and metabolic syndrome was observed in this group.

BMI and physical activity were directly related to %BF in men such that when BMI increased, %BF

also increased (p<0.0001) and when physical activity increased, %BF decreased independently from BMI (p<0.0001). However, in women physical activity did not significantly affect %BF.

All of the anthropometric parameters studied (%BF, WC, BMI, and FMI) were significantly associated with the clustering of cardiovascular RFs (p<0.0001) (Figure 1). The odds ratio (OR) and 95% confidence intervals for each variable as a predictor of the number of RFs are: FMI (OR: 1.26; 1.06 to 1.50; p<0.01); %BF (OR: 1.11; 1.02 to 1.20; p=0.01); WC (OR: 1.06; 1.03 to 1.10; p<0.001); and BMI (OR: 1.16; 1.05 to 1.28; p<0.01). Figure 2 displays the cumulative logistic regression models (proportional odds) that compare the relationship of anthropometric variables with the number of metabolic syndrome RFs. Each chart shows the probability of increasing the number of components for the metabolic syndrome (to present 1 or more

components or 2 or more) according to each anthropometric predictor, adjusted for gender and age (mean age of 37 years for women and 40 years for men). Although changes in FMI showed the greater explanation for variability of number of metabolic syndrome components (OR: 1.48; 1.24 to 1.76), from a statistical point of view, all anthropometric parameters were equally significant predictors of metabolic syndrome components (p<0.0001).

Discussion

Our results show that all the studied anthropometric parameters are strongly and significantly associated with cardiometabolic risk factors. Moreover, we also demonstrated that %BF and FMI were significantly related to serum lipids, fasting blood glucose, and BP and to the clustering of cardiovascular and metabolic RFs. The same relationship was confirmed for BMI and WC. These results provide further evidence to confirm that excessive total body fat increases individual risk for cardiovascular disease and metabolic syndrome in a population of young subjects without a history of cardiovascular disease. However, we cannot negate that BMI and WC were as good predictors as %BF in determining RF load.

There is a substantial body of evidence demonstrating that increased BMI is not only associated with but is also a predictor of increased cardiovascular risk (1, 25, 27). In addition, increased BMI is a predictor of diabetes and increased cardiac mortality (1, 5, 6). Further, it is known that WC is a predictor of cardiovascular risk, with numerous studies demonstrating that WC is closely associated with visceral obesity and cardiovascular morbidity and mortality (14-16, 31). To date, there have been few investigations into the association between total adiposity (defined by FMI) or %BF and cardiovascular risk. This is important because some populations (eg, elderly patients) have a greater percentage of subjects with normal BMI but high %BF coupled with a high number of cardiovascular RFs. For these individuals, there is a risk that their BMI would not be calculated into their risk profile; however, they are known to be at higher risk because of their high %BF and increased prevalence of cardiometabolic RFs. It has been reported that these subjects may have a lower BMI due to sarcopenia, where muscle mass loss has been replaced by fat (32).This situation is often seen in patients with heart disease, sedentary
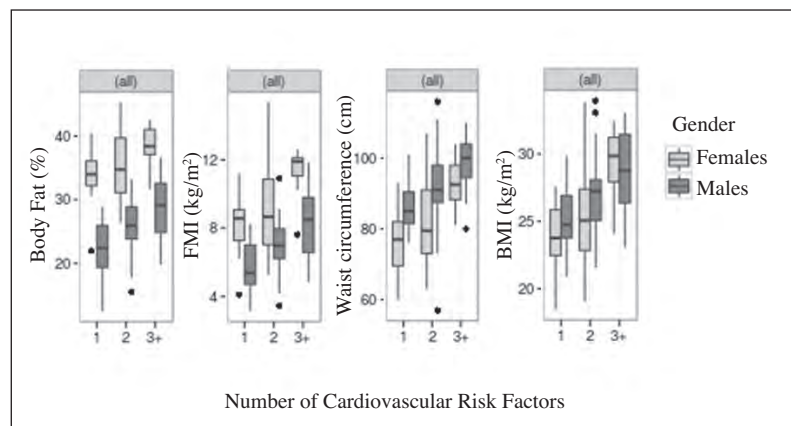

Fig. 1.—Association among anthropometric variables (body mass index, waist circumference, percentage body fat, and fat mass index) and the clustering of cardiovascular risk factors in a young adult population (n=l 82).

Biochemical variables and cardiovascular risk factors	% Body fat (Tertiles)			p-value
	Tertile 1 M:<23%W: <32%	Tertile 2 M:23%– <27% W: 32%–<37%	Tertile 3 M:≥27% W: ≥37%	
Total-C, mg/dL	183	192	199	0.030
Triglycerides, mg/dL	98	128	136	0.017
HDL-C, mg/dL	59	55	50	0.005
LDL-C, mg/dL	104	111	122	0.010
Non-HDL-C, mg/dL	124	137	149	0.001
Blood Glucose, mg/dL	84	87	90	0.024
SBP, mm Hg	108	111	119	<0.001
DBP, mm Hg	67	69	73	<0.001
Physical activity, METs · min per week	879	571	314	<0.001
Dyslipidemia, %	34%	46%	65%	0.003
Metabolic syndrome, %	2%	9%	23%	0.002
Glycemia ≥100 mg/dL %	0%	2%	12%	0.003

Abbreviations: DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M, men; MET, metabolic equivalent; SBP, systolic blood pressure; total-C, total cholesterol; W, women.
P-value indicates differences between tertile 1 and tertile 3. ANOVA was used to determine differences between percentage body fat tertiles.

elderly patients, and those with chronic obstructive pulmonary disease (32-34).

Segal et al. reported that male subjects who are overweight (diagnosed by BMI) with a high %BF had higher insulin resistance and serum lipids compared with those individuals with the same BMI but normal %BF. This study suggested that BMI could overestimate cardiovascular risk in men with normal %BF as they have higher BMI due to higher proportions of muscle mass rather than fat. This is a common phenotype in young men, particularly in those who perform moderate to intense physical activity. Discordance between

Odds ratios and 95% confidence intervals for each anthropometric parameter.
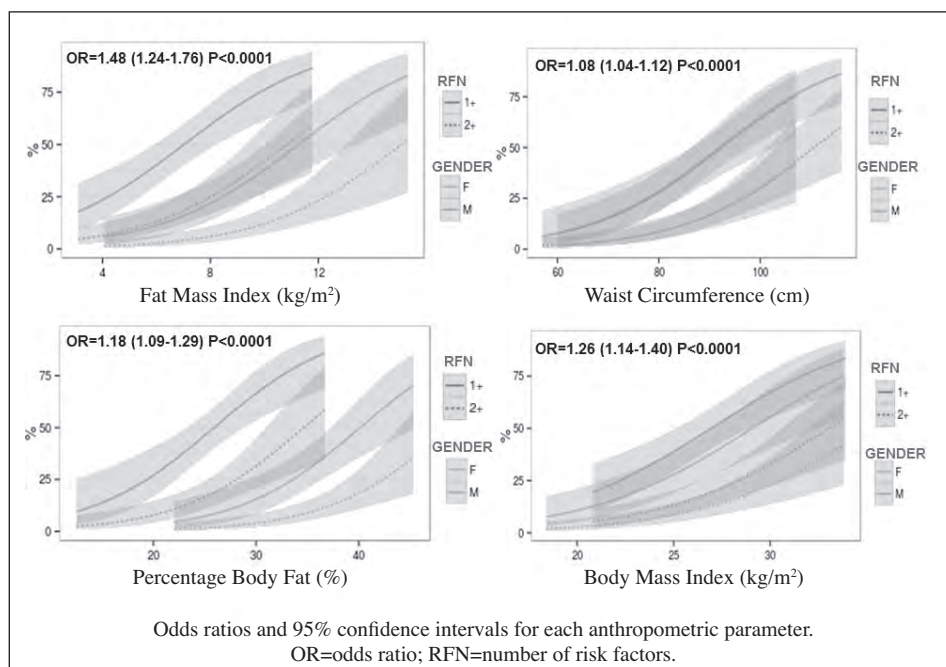OR=odds ratio; RFN=number of risk factors.

Fig. 2.—Cumulative logistic regression (proportional odds), adjusted for gender and age, for the probability of increasing the number of risk factors for metabolic syndrome according to each anthropometric parameter in a young adult population (n=l82).

BMI and %BF has also been described by Zeng et al (35), who demonstrated that %BF was a better predictor than BMI for determining CV risk in a Chinese population. Similarly to our results, Shea et al. recently reported in a Canadian population that normal-weight subjects in the two highest %BF tertiles had an increased risk of cardiometabolic disease. However, this last statement should be carefully considered because in obese patients, %BF was not as accurate in classifying risk as it was in normal weight subjects. This was the reason why we decided to exclude morbidly obese subjects from our study. Although, BMI should not be replaced as a predictor of CV risk in epidemiological studies (20, 36), our results underline the importance of having not only a normal BMI, but also the lowest possible %BF, especially in normal or near normal weight subjects. The mind-set that has currently predominated in preventive cardiovascular research and clinical practice is mainly focused on BMI and/or body weight. However, abdominal obesity, defined by WC and total adiposity (represented by FMI and/or %BF in our study), should be assigned greater importance , particularly in some populations with high prevalence of sedentary "normal-weight", who present with higher %BF or FMI, and thus, presumably with CV risk.

The importance of WC has been highlighted in the INTERHEART study which demonstrated that WC was an important attributable RF for myocardial infarction (15, 16). Waist circumference is a marker for intra-abdominal adiposity, which is closely associated with systemic inflammation, serum lipids, and insulin resistance. In our study, WC was significantly associated with cardiometabolic parameters. However, it was not a better predictor of cardiometabolic alterations than %BF, BMI, or FMI. We believe that %BF and FMI measurements could have benefits for further refining cardiometabolic risk profile in certain populations, such as those with normal BMI, normal WC, and high %BF. This phenotype could be attributed to physical inactivity and sarcopenia, which have been also associated with increased risk of insulin resistance (6, 32, 34). Lee and colleagues investigated WC and %BF and their relationship with cardiovascular mortality and found that both parameters were predictors of mortality (19). Of note, however, sedentary subjects with a normal or low WC had a much higher relative risk of cardiovascular events compared with physically active subjects with a high WC. In our study, 41% of the total population was categorized as physically inactive (ie, physical activity <1 time per week), whereas physically active subjects had a lower %BF. Moreover, when physical activity increased, %BF decreased independently of BMI. This effect was more evident in men than women.

This study has some limitations. The first one is the low number of subjects. Therefore, it was not possible to compare groups of subjects with discordance between BMI and %BF (eg "normal BMI and high %BF" or "high BMI and normal %BF"), which have shown differences in CV risk factors in other studies. Second, we may have had potential bias for recruitment, since the individuals included in the study were those presenting to a preventive cardiovascular health program. Third, inflammatory markers such as C-reactive protein and insulinemia were not measured. These factors are closely associated with adiposity (mainly visceral adiposity) and could have further clarified the role of WC and %BF in measuring cardiovascular risk. Finally, physical activity was determined by self-report. This approach could have overestimated actual rates of physical activity in the study population. Although, the measurement of %BF could be seen as a limitation, as it was measured using skinfold thicknesses and not DXA, this paper was intended to underline the use of %BF as an easy bedside marker. In this regard the head to head comparison with other proven anthropometric parameters, such as WC and BMI supports our findings.

The main strength of this paper is that we demonstrated in a fairly young and low CV risk population that an easy and ready-to-use anthropometric parameter included in the nutritional assessment, as it is %BF, could be as good as BMI and WC, especially in those in whom overweight or obesity is not evident. These results also emphasize the role of the dietitian in the primary care team.

Aknowledgements

Disclosures

The authors report no conflict of interest in this work.

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