Obesity *vs.* Whole-body-fat and myocardial infarction risk prediction. Body fat percentage is better indicator

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Summary

Objective: Our aim was to realize an anthropometric analysis to identify both the association and plausibility of measurements and indicators of general obesity and whole-body fat on the risk prediction for myocardial infarction (MI) in men.
Material and method: A case-control study in 244 European men aged 30-74 years was conducted. We measured weight, height, waist and hip perimeters and skinfolds: triceps, subscapular and supraspinale, according to standardized protocols. We calculated the areas under the ROC curves, the odds ratios and correlations for indicators.
Results: Body mass index (BMI) [AUC: 0.687, 95% CI (0.619-0.715); OR: 3.5]. Waist circumference (WC) [AUC: 0.742, 95% CI (0.679-0.805); OR: 5.9]. Waist-to-height ratio (WHtR) [AUC: 0.780, 95% CI (0.721-0.839); OR: 8.4]. Endomorphy [AUC: 0.721, 95% CI (0.656-0.785); OR: 2.4]. Body fat percentage (%BF) [AUC: 0.774, 95% CI (0.714-0.834); OR: 10.2]. Lean body mass (LBM) [AUC: 0.490, 95% CI (0.413-0.568); OR: 1]. BMI correlated with %BF (0.84), endomorphy (0.80), WC (0.69), WHtR (0.72) and LBM (0.65). WHtR correlated with WC (0.97), %BF (0.92), endomorphy (0.62) and LBM (0.32). %BF correlated with WC (0.86) and endomorphy (0.78). The correlations between WHtR and body fat-associated indicators were strong (all $r \geq 0.62$, $p < 0.001$).
Conclusions: In MI men, body fat-associated indicators show different discriminative ability. BMI-defined obesity presents moderate discrimination and anthropometric association bias that do not lent support their suitability as risk predictor. Abdominal adiposity and whole-body fat percentage show the highest discriminative abilities and robust anthropometric reasons related with the true biological risk. We defend the use of WHtR as concept of risk volume and individual visceral adiposity for the early identification of adult men at risk of myocardial infarction.

Key words:
Obesity. Myocardial infarction. Anthropometric indicator. Body fat. Cardiometabolic risk. Risk prediction.

Obesidad *vs.* grasa corporal total y predicción de riesgo de infarto. El porcentaje de grasa corporal es mejor indicador

Resumen

Introducción: Nuestro objetivo era realizar un análisis por antropometría para identificar la asociación y plausibilidad de mediciones e indicadores de obesidad general y grasa corporal total en la predicción de riesgo de infarto en varones.
Material y método: estudio caso-control en 244 varones de 30 a 74 años de edad. Medimos peso y talla, perímetros de cintura y cadera, y pliegues de triceps, subescapular y supraespinal, según protocolos estandarizados. Obtuvimos las áreas bajo la curva ROC y las *odds ratios* para la asociación de indicadores.
Resultados: índice de masa corporal (IMC) [ABC: 0,687, 95% CI (0,619-0,715); OR: 3,5]. Circunferencia de cintura (CC) [ABC: 0,742, 95% CI (0,679-0,805); OR: 5,9]. Índice cintura-talla (ICT) [ABC: 0,780, 95% CI (0,721-0,839); OR: 8.4]. Endomorfia [ABC: 0,721, 95% CI (0,656-0,785); OR: 2,4]. Porcentaje de grasa corporal (GC%) [ABC: 0,774, 95% CI (0,714-0,834); OR: 10,2]. Masa magra (MM) [ABC: 0,490, 95% CI (0,413-0,568); OR: 1]. IMC correlacionó con GC% (0,84), endomorfia (0,80), CC (0,69), ICT (0,72) y MM (0,65). ICT correlacionó con CC (0,97), GC% (0,92), endomorfia (0,62) y MM (0,32). GC% correlacionó con CC (0,86) y endomorfia (0,78). Las correlaciones entre ICT y los indicadores asociados a la grasa corporal fueron fuertes (todas $r \geq 0,62$, $p < 0,001$).
Conclusiones: En los varones infartados, los indicadores asociados a la grasa corporal muestran diferente capacidad discriminativa. El IMC presenta moderada discriminación y sesgos de asociación antropométrica que no avalan su idoneidad como predictor de riesgo. La obesidad abdominal y el porcentaje de grasa corporal muestran las mayores capacidades discriminativas y robustas razones antropométricas relacionadas con el verdadero riesgo biológico. Nosotros defendemos el uso del índice cintura-talla como concepto de volumen de riesgo y adiposidad visceral individual para la temprana identificación de varones adultos en riesgo de infarto de miocardio.

Palabras clave:
Obesidad. Infarto de miocardio. Indicador antropométrico. Grasa corporal. Riesgo cardiometabólico. Predicción de riesgo.

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Introduction

Obesity is a public health problem with high prevalence in Spain and worldwide[1,2]. Adiposity is associated with several diseases, including cardiovascular disease as the leading cause of morbidity and mortality worldwide[2]. Coronary heart disease represents 31.2% of cardiovascular mortality in Spanish men[3]. Body mass index (BMI) has been associated with myocardial infarction (MI) in Europe and worlwide[4-7] but in spite of its wide use does not provide accurate information on the whole-body fat percentage (%BF) and fat distribution. Thus, accurate estimation of the body fat distribution is highly relevant from a public health perspective, an aspect that has been endorsed by the American Heart Association Obesity Committee[8]. Technological methods for assessing whole-body fat such as dual-energy X-ray absorptiometry (DXA) can support the criterion of a more accurate evaluation; however, it is impractical in clinical settings. The diagnosis of BMI-defined obesity is the failure to considerer the impact of real adiposity on MI risk prediction[5-7]. Further, BMI has been found as a worse index than %BF to diagnose obesity in patients with coronary disease or acute coronary syndrome[9,10]. Evidence is accumulating in support of the anatomical distribution of adipose tissue as strong indicator of coronary heart disease and mortality[11-13]. Equally, our study previously published supports the anatomical distribution of adipose tissue as strong indicator of risk in proving the different biological risk for both visceral and subcutaneous adipose tissue[14]. From the INTERHEART and Norwegian studies, waist-to-hip ratio (WHR) is confirmed as a strong indicator to explain MI and risk attributable to obesity[5,6]. However, we have revealed statistical error bias for WHR-associated risk if the cutoff were not biologically equivalents with other indicators such as waist circumference (WC) and waist-to-height ratio (WHtR)[14]. Equally, we have described the anthropometric reasons that do not lent support WHR-associated risk unlike WHtR[7,10,14]. Additionally, in the same study of body composition by somatotyping we have warned about the spurious risk attributed to both BMI and WHR, being very important to know that in the MI-associated risk the role of each component as metabolic mediator is well different for each one[14].

Although a wide variety of anthropometric methods to estimate body composition in adults has been developed without taking into account hip dimension[15], WHR derived from cross-sectional and prospective larger studies[5,6] is still very considered even without keeping in mind our revelations[7,14]. In addition, WHtR has been described as the best predictor of %BF and visceral adipose tissue mass (by DXA) in Caucasian individuals[16], and in a recent study, relative fat mass (RFM) as new indicator of %BF, foundated on WHtR inverse, also has been validated by DXA in European-American adult individuals[17]. We know that BMI-defined obesity is associated to MI beyond other cardiovascular risk factors but provide poor discriminative performance[5-7,14]. Maybe this indicator used as proxies of obesity may not have the validity relative to use of a standard method of reference to assess real adiposity of risk.

Our aim was to assess the relative importance of measurements, general obesity, relative fatness, %BF and other classic indicators on the MI risk prediction in a sample of European men. We evaluated the discriminative ability by comparing the Receiver Operating Curves (ROC). Furthermore, we determined the correlations between anthropometric indicators in differentiating those that estimate body fat-associated risk by measuring total body weight, subcutaneous and visceral adipose tissue, and %BF.

Material and method

Study participants were recruited from a Hospital Complex in the Health Area of Caceres in Spain. Cases were selected from a post-myocardial infarction Cardiac Rehabilitation Program. The minimum sample size for calculating was of 91 cases and at least 1 control per case, with an obesity exposition for adult population of 22%, a level of safety of 0.99 and a statistical power of 0.99. The odds ratio (OR) to detect was of 3. A sample of 244 subjects, men of Europid ethnicity, aged 30-74 years, from 2012 database and new additions during 2018 was evaluated. Cases data were collected in the first fitting days after hospital diagnosis. Exclusion criteria were nonage, physical disability or any chronic disease. One control age-matched (± 5 years) was recruited per case at two Health Centers (60%), a wellness center (20%) and a department of workers of the State General Administration (20%). Exclusion criteria for controls were identical to those described for cases, with the additional criterion that controls had no previous diagnosis of coronary disease or history of exertional chest pain.

All subjects signed an informed consent approved by the Ethical Committee of the Hospital, according to the principles of the Declaration of Helsinki and Data Protection.

Anthropometric measures

Measurements were made according to standard international protocols[18,19]. Weight was measured (kg) wearing light underwear. Height was measured (cm) without shoes and the head was positioned in the Frankfort plane. Skinfolds (mm): triceps, subscapular and supraspinale were measured on the right side. WC and hip circumference were measured to the nearest 0.1 cm. WC was determined in a horizontal plane in the perimeter passing through the navel and just above the uppermost lateral border of the right iliac crest at the midaxillary line, and at the end of a normal expiration. HC was measured at the maximum perimeter around the buttocks with feet together and without gluteus contraction. Technical error of measurement for each dimension with an anthropometric tolerance for skinfolds about 5%, for perimeters 1%, and for height and weight 0.5%, was calculated.

BMI dividing body weight by square height (kg/m^2), WHR and WHtR (waist, hip and height in cm) were calculated. BMI ≥25-29.9 was defined as overweight and ≥30 as general obesity. Endomorphy rating was calculated according to the Heath-Carter Instruction Manual[20]. The equation to calculate endomorphy was:

Endomorphy = - 0.7182 + 0.1451 (X) - 0.00068 (X^2) + 0.0000014 (X^3).

Where X = (sum of triceps, subscapular and supraspinale skinfolds) x (170.18/height).

Rating on endomorphy component of 0.5 to 2.5 was considered low, 3 to 5 were moderate, and 5.5 to 7 were high. RFM as %BF was calculated according to the formula from Woolcott and Bergman for men: 64 - (20 * height (m)/WC (m))[17]. Lean body mass (LBM) was calculated by subtracting body fat mass (BFM) of total body weight: LBM= weight – BFM (kg). BFM is the transformation from %BF to unit of mass = RFM*100/weight (kg).

Statistical analysis

Data were computed using SPSS® software (version 20.0 IBM for Windows). Descriptive statistics as means, standard deviations are provided. Normal distributions were assessed using Kolmogorov Smirnov test. Student -test as parametric and Chi-square as no parametric test were applied to establish differences. Bivariate analysis was used for calculating Pearson´s correlation coefficients (r). Sensitivity and specificity by ROC analysis were assessed. The total area under the curve (AUC) was tested with no parametric differences and their values were used for identifying the strength of association for each indicator. The cutoff were defined there where sensitivity plus specificity was the highest. The odds ratio (OR) of prevalence of indicators according to different cutoff was calculated by using contingency tables and binary logistic regression analysis. The confidence interval was set at 95% in all cases. A value of p <0.01 was considered significant.

Table 2. Analysis ROC for the association of anthropometric indicators in myocardial infarction men.

Anthropometric variables	AUC	Error	95% CI	p
BMI	0.687	0.034	0.619-0.715	<0.001
BFM	0.721	0.033	0.657-0.785	<0.001
WC	0.742	0.033	0.679-0.805	<0.001
WHtR	0.780	0.030	0.721-0.839	<0.001
Inverse WHtR	0.220	0.030	0.161-0.279	<0.001
LBM	0.490	0.039	0.413-0.568	0.808
Endomorphy	0.721	0.033	0.656-0.785	<0.001
%BF	0.774	0.030	0.714-0.834	<0.001

AUC: Area under the curve; BF: Body fat; BFM: Body fat mass; BMI: Body mass index; LBM: lean body mass; WC: waist circumference; WHtR: Waist-to-height ratio. p: Significance level.

Results

Baseline anthropometric indicators are shown in Table 1. The main anthropometric indicators present significant differences. Both indicators of general obesity and abdominal obesity show strongly differences with level of significance. Indicators measured by skinfolds (endomorphy) as well as %BF also show significant differences. Only LBM and HC do no show anthropometric differences (p = 0.8, *p*= 0.2 respectively).

The AUC to establish the differences between groups were calculated according to sensitivity and specificity at each point of the ROC curve (Table 2). It is worth noting that an inferior limit less than 0.5 included in the confidence interval would indicate lack of association.

The cut-off point, sensitivity, specificity, OR and confidence interval for risk indicators are shown (Table 3). The different ROC curve patterns are plotted in Figure 1 and 2. The correlation coefficients for the main variables in MI men are given in Table 4. BMI correlated with endomorphy, LBM and %BF (0.80, 0.65 and 0.84 respectively). The correlations for WHtR with WC, endomorphy, LBM and %BF were 0.97, 0.62, 0.32 and 0.92 respectively. WHtR was notably correlated with body fat-associated risk indicators. LBM correlated strongly with BMI and weakly with both skinfold and central obesity variables (all r <0.5).

Discussion

Our study shows that indicators proxies of adiposity are associated to MI men with different discriminative ability. Previous studies have shown the association of both general and abdominal obesity with MI although BMI-defined obesity and WHR have presented statistical error bias on their predictive ability[4-7,14]. In addition, statistical association for any indicator is not the same as epidemiological causality and implicit risk. Therefore, some anthropometric indicators could show confusing in its true putative risk[14]. To our knowledge, the anthropometric risk associated to MI would depend on body fat-associated risk rather than the indicators may be responsible for all or much of the statistical association. In this line, BMI does not discriminate between musculoskeletal

Table 1. Baseline anthropometric indicators of the study participants.

Variable	MI (n=122)	95% CI	Control (n=122)	95% CI	p
Age (years)	53.8 ± 9.8	52.07 – 55.5	51.7 ± 9.5	50.1– 53.5	0.09
Height (cm)	169.4±7.3	168.1 – 170.7	173.5 ± 6.8	172.3 – 174.8	<0.01
HC (cm)	99.1 ± 13.1	96.8 – 101.5	97.5 ± 6.4	96.3 – 98.6	0.21
BMI (kg/m^2)	28.5 ± 4.0	27.7 – 29.2	25.2 ± 3.4	25.6 – 26.8	<0.01
WC (cm)	101.6 ± 20.7	97.9 – 105.3	91.3 ± 10.2	89.4 – 93.1	<0.01
WHR	1.02 ± 0.13	0.9 – 1.04	0.93 ± 0.06	0.92 – 0.95	<0.01
WHtR	0.60 ± 0.12	0.57 – 0.62	0.52 ± 0.06	0.51 – 0.53	<0.01
Endomorphy	4.6 ± 1.2	4.3 – 4.8	3.6 ± 0.9	3.4 – 3.8	<0.01
%BF	29.8±4.6	28.9¬ – 30.6	25.5±4.0	24.8 – 26.3	<0.01
BFM (kg)	36.8±5.1	35.8 – 37.7	32.6 – 4.8	31.7 – 33.4	<0.01
LBM (kg)	45.0±16.4	42.1 – 48.0	46.4±14.5	43.8 – 49	0.8

Abbreviations: BF: Body fat; BFM: Body fat mass; BMI: Body mass index; HC: Hip circumference; LBM: Lean body mass; MI: Myocardial infarction; WC: waist circumference; WHR: Waist-to-hip ratio; WHtR: Waist-to-height ratio. p: Significance level.

Table 3. Cut-off points, sensitivity, specificity and odds ratio for the association between anthropometric indicators and myocardial infarction men.

Variables	Cut-off point	Sensitivity	Specificity	OR	95% CI	p
BMI (kg/m^2)	≥30	0.322	0.918	3.5	2.3-10.3	<0.001
WC (cm)	≥94.4	0.711	0.605	5.9	3.4-10.3	<0.001
WHtR	≥0.54	0.777	0.746	8.4	4.7-15.1	<0.001
LBM	45.5	0.492	0.459	1	0.6-1.2	<0.001
%BF	27.2	0.769	0.754	10.2	5.7-18.5	0.8
Endomorphy	≥3.9	0.682	0.581	2.4	1.4-4.2	<0.001
BFM	33.3	0.694	0.607	3.9	2.3-6.8	<0.001

BF: Body fat; BFM: Body fat mass; BMI: Body mass index; LBM: Lean body mass; WC: Waist circumference; WHtR: Waist-to-height ratio; p: significance level.

Table 4. Correlations between anthropometric variables of European men with myocardial infarction (N = 122).

Variables	BMI	WC	WHR	WHtR	Endo	%BF	LBM
BMI	1	0.69(*)	0.69(*)	0.72(*)	0.80(*)	0.84(*)	0.65(*)
WC	0.69(*)	1	1	0.97(*)	0.59 (*)	0.86(*)	0.49(*)
WHR	0.52(*)	0.76(*)	0.76(*)	0.75(*)	0.48 (*)	0.79(*)	0.24(*)
WHtR	0.72(*)	0.97(*)	0.97(*)	1	0.62(*)	0.92(*)	0.32(*)
Endo	0.80(*)	0.59 (*)	0.59 (*)	0.62(*)	1	0.78(*)	0.45(*)
%BF	0.84(*)	0.86(*)	0.86(*)	0.92(*)	0.78(*)	1	0.30(*)
LBM	0.65(*)	0.49(*)	0.49(*)	0.32(*)	0.45(*)	0.30(*)	1

Data are correlation coefficients.
BF: Body fat; BMI: Body mass index; Endo: Endomorphy; LBM: Lean body mass; WC: Waist circumference; WHR: Waist-to-hip ratio; WHtR: Waist-to-height ratio;
*Correlation is significant at the .01 level.

Figure 1. Graph representing of the ROC curves for calculated indicators. AUC denotes area under the curve, BF body fat, BMI body mass index, LBM lean body mass and WHtR waist-to-height ratio.

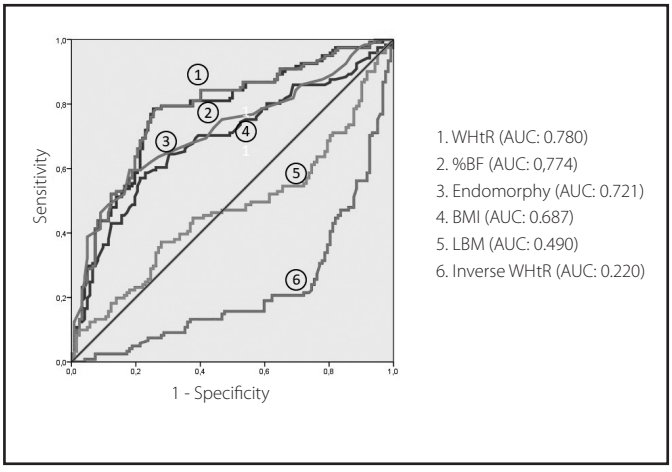
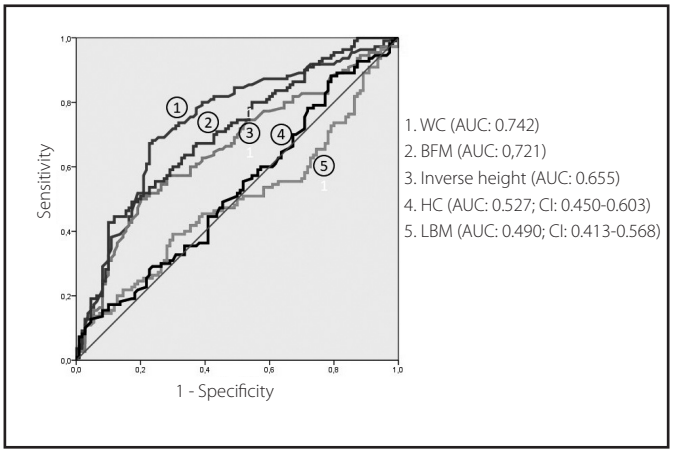


Figure 2. Graph representing of the ROC curves for simple indicators and others represented by units of mass. AUC denotes area under the curve, BFM body fat mass, LBM lean body mass, HC hip circumference and WC waist circumference.



component and body fatness in attributing partially a spurious risk to mesomorphy component[14]. Thus, BMI in depending on various components (muscle, bone, fat and residual mass) it underestimates abdominal obesity risk. Moreover, whether LBM does not show discriminative ability BMI provides an association bias beyond of BFM-associated risk. Our study is in agreement with previous study about body composition by somatotyping[14], and we can prove the different discriminative association between BMI-defined obesity and %BF by measuring WC and height. Equally, relative body fatness (expressed by endomorphy) in measuring three skinfolds, shows moderate discrimination according to somatotype of MI patients[7,14]. These observations could confirm the different biological risk for both visceral and subcutaneous fat depots what is in agreement with body composition and high prevalence of %BF-defined obesity in coronary disease men[9,10,14]. Additionally, in the Spanish thesis from the Complutense University of Madrid[10], %BF estimated from four skinfold thickness (method of Durnin-Womersley)[15] presented clear higher prevalence than BMI-defined obesity. In this study, %BF mean value (27.4 ±4.5) was lesser than RFM mean of the present study. This is important, since subcutaneous adipose tissue is less deleterious than intra-abdominal fat accumulation, which influences cardiometabolic processes and atherosclerotic coronary events risk[5-7,9,11-14,21-25].

Our study supports the anatomical distribution of adipose tissue as notable risk predictor although all variables with WC measurements shown higher discrimination than indicators with skinfolds distribution or body fat associated to body weight. In strict anthropometric sense WC as proxy of abdominal obesity is the true focal component of risk to relate adiposity and coronary risk and mortality in European men[11-14,21,23-28]. At time, in a recent research, WC has been found as the only metabolic syndrome component independently associated with left ventricular global longitudinal strain impairment[29]. Strain by echocardiography is an advanced cardiological technique that seems to be an independent predictor long-term risk of cardiovascular morbidity and mortality[30]. In this line, we have exposed the role of WC and height as physical dimensions in relation to a body volume index through WHtR[7,14]. Thus, our data strengthen the ability of WHtR to predict MI risk actually being WC and height measurements the foundated anthropometric basis for estimating %BF[17]. In our results, %BF shows the same discriminative power as WHtR actually drawing inverse WHtR the same reciprocal ROC curve as %BF but associated to status of healthy controls. The question is the scientific deduction, %BF comes from equations of statistical models and WHtR provides an index of biological risk volume by unit of height, with too little - too much dependence on LBM – visceral adiposity[7,14]. To our knowledge, this is the first time that anthropometrically-predicted %BF provide a clear discriminative association by using ROC analysis.

On the other hand, the differences of associated risk between simple measurements or unit of measure (e.g. length, mass) such as WC, height, HC, and body weight, BFM and LBM are the fundamental anthropometric key for the understanding of the true risk for each compound indicator. Our findings are in agreement with previous studies[7,14] and it strengthen statistical bias in research for BMI and WHR. Both indicators depend at time on peripheral body fat (with lesser discriminative risk) and LBM (without associated risk) in underestimating abdominal obesity. Anthropometric evidence supports that HC does not influence body composition but vice versa and WHR in showing a spurious risk would be misleading on the risk association[14].

According to our reasoning, the validity for any indicator depends on strength of their formula to reflect body fat-associated risk although keeping in mind the discriminative ability as well as epidemiological causality and real risk equivalence from each biological measurement[14]. Therefore, anthropometric evaluation will have more strength with those formulas that properly may translate a higher, verifiable, and plausible biological risk. In our results, WHtR and %BF show the highest real discriminative abilities although conceptually are different. We have proposed WHtR as risk volume concept where WC and inverse height (associated risk factors) always would be proportional to the individual biological risk[14]. However, %BF in spite of being a more intuitive concept, in depending on other statistical numerical variables could not translate the whole and true biological risk.

Lastly, our results provide critical perspectives on cardiovascular research related with obesity classification criteria. In MI risk prediction, we defend WHtR-associated risk as the best classification criteria, at least in adult men. Anyway, a pending question in research is to determine validated geographic region-specific and ethnicity-specific cutoff values for both WHtR and anthropometrically predicted %BF.

One limitation of our study is that the cross-sectional design did not allow showing long-term epidemiological causality between MI and associated risk indicators. Another limitation is that our results cannot be generalized by the sample size. Despite this, thousands of subjects are not needed for the interpretation about an anthropometric profile similar to those of other from large studies. The new data referenced help to better understanding a profile related with obesity and %BF on MI risk prediction. The relevance of these results extends the knowledge for the large number of infarcted people whose degree of BMI-defined obesity or %BF measured by anthropometry could be very close to our values. Future studies should confirm this possibility.

Conclusions

In MI men, body fat-associated indicators show different discriminative ability. BMI-defined obesity presents moderate discrimination and anthropometric association bias that do not lent support their suitability as risk predictor. Abdominal adiposity and whole-body fat percentage show the highest discriminative abilities and robust anthropometric reasons related with the true biological risk. We defend the use of WHtR as concept of biological risk volume and individual visceral adiposity for the early identification of men at risk of myocardial infarction.

Conflict of interest

The authors do not declare a conflict of interest.

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