Diagnostic performance of body mass index to detect obesity in patients with coronary artery disease

Abel Romero-Corral¹, Virend K. Somers¹, Justo Sierra-Johnson³, Michael D. Jensen², Randal J. Thomas¹, Ray W. Squires¹, Thomas G. Allison¹, Josef Korinek¹, and Francisco Lopez-Jimenez¹*

¹Division of Cardiovascular Diseases, Department of Internal Medicine, Gonda 5-368, 200 First Street SW, Rochester, MN 55905, USA; ²Endocrine Research Unit, Mayo Clinic College of Medicine, Mayo Foundation, Rochester, MN, USA; and ³Department of Medicine, Atherosclerosis Research Unit, Karolinska Institutet, Stockholm, Sweden

Received 26 January 2007; revised 30 April 2007; accepted 22 May 2007; online publish-ahead-of-print 10 July 2007

See page 2047 for the editorial comment on this article (doi:10.1093/eurheartj/ehm321)

Background Emerging evidence suggests that a mildly elevated body mass index (BMI), is related to improved survival and fewer cardiovascular events in patients with coronary artery disease (CAD). We hypothesize that these results are related to the poor diagnostic performance of BMI to detect adiposity, especially in the intermediate BMI ranges.

Methods and Results A cross-sectional study of 95 patients with CAD referred to phase II cardiac rehabilitation. Body fat (BF)% was estimated by air displacement plethysmography. Height, weight, BMI and waist circumference were measured the same day. We calculated the correlation between BMI and both, BF% and lean mass and assessed the diagnostic performance of BMI to detect obesity defined as a BF% (>25% in men and >35% in women). Although BMI had a good correlation with BF% ($r = 0.66, P < 0.0001$), it also had a good correlation with lean mass ($r = 0.41, P < 0.0001$), and BMI failed to discriminate between both (P-value = 0.72). A BMI ≥ 30 kg/m² had a good specificity (95%; 95% CI, 83–100) but a poor sensitivity (43%; 95% CI, 32–54) while a BMI ≥ 25 kg/m² had a good sensitivity (91%; 95% CI, 84–97) but a poor specificity (65%; 95% CI, 42–88) to detect BF%-obesity.

Conclusions In patients with CAD, BMI does not discriminate between BF% and lean mass, and a BMI ≥ 30 kg/m² is a poor index to diagnose obesity. These findings may explain the controversial findings that link mild elevations of BMI to better survival and fewer cardiovascular events in patients with CAD. Body composition techniques to accurately diagnose obesity in patients with CAD might be necessary.

KEYWORDS
Obesity; Body fat; Body mass index; Diagnostic performance; Cardiovascular risk factor

Introduction
Emerging evidence suggests that a mildly elevated body mass index (BMI), is related to better survival and fewer cardiovascular events in patients with coronary artery disease (CAD).¹,² This controversy known as the ‘obesity paradox’ has not been explained by adjustment for known confounders. Moreover, this paradox has been related not just to CAD, but to other diseases, such as congestive heart failure and renal disease.³,⁴ A possible explanation for the lack of the expected association between BMI and adverse cardiac outcomes in patients with CAD could be the poor diagnostic performance of BMI (especially for intermediate BMI ranges) to discriminate between body fatness and lean body mass factors each associated with opposite outcomes in cardiovascular disease.⁵,⁶

Even though the gold standard definition of obesity by the World Health Organization is an excess in body fatness ($>$25% in men and $>$35% in women),⁷ BMI is the commonest measure used to diagnose obesity in both clinical practice and epidemiological studies.⁸ However, BMI does not necessarily reflect the body fatness, and can be considerably different across gender, age, and race.⁹ Patients with CAD tend to be older, are more likely to be sedentary than patients without CAD and consequently have a lower lean body mass.¹⁰ Therefore, we hypothesized that BMI will not adequately discriminate between body fatness and lean body mass in patients with CAD, especially in those individuals in the normal and overweight BMI range.

Methods
Study design and patient population
We conducted a cross-sectional study of 95 patients with CAD enrolled in a phase II cardiac rehabilitation programme from February to December 2005 in whom body fat (BF) percentage was estimated using air displacement plethysmography (ADP). Inclusion criteria were age ≥18 years, Caucasian, established CAD, and authorization for use of medical records for research.
purposes. We did not include patients with cachexia and those enrolled in cardiac rehabilitation for reasons other than CAD, such as cardiac transplantation, valve or pericardial surgery, cardiomyopathies, significant left ventricular dysfunction (ejection fraction <30%), history of recent congestive heart failure decompensation, end-stage renal or liver disease, and myxedema, which would cause edematous-states, and could have affected the accuracy of body composition measurements. This study was approved by the Institutional Review Board at Mayo Clinic Rochester, MN, USA.

Definitions of variables
Obesity was defined using the World Health Organization criteria as BF percentage value of ≥25% in men and of ≥35% in women, and was used as the reference standard.\(^7\) CAD was defined as a history of myocardial infarction, percutaneous coronary intervention, or coronary artery bypass graft surgery. Hypertension was defined as a documented diagnosis in the medical records, or a systolic blood pressure of >139 mmHg and/or a diastolic blood pressure of >89 mmHg.\(^11\) We defined diabetes mellitus as having a clinical diagnosis of such or a fasting blood glucose value of ≥126 mg/dl or a hemoglobin A1c of >7% or taking any insulin or oral hypoglycemic agents.\(^12\) Dyslipidemia was defined as a total cholesterol value of ≥240 mg/dl or a low-density lipoprotein of ≥160 mg/dl, and included any patients who were taking lipid lowering therapy, or if the diagnosis of dyslipidemia was documented in the medical record.\(^13\) Patients were classified as having a recent episode of congestive heart failure if reported in the medical record within the month preceding the test. Smoking status was classified as never, former, and current.

Anthropometric measurements
Anthropometric measures and body composition were evaluated at the beginning of a phase II cardiac rehabilitation programme at Mayo Clinic in Rochester, MN, USA. We measured height in meters using an electronic calibrated scale and weight was measured using the air displacement plethysmography (ADP) calibrated electronic scale with 0.01 kg increments with patients wearing only a non-elastic tape. Height, weight, and waist circumference were measured midway between the lower rib margin and the iliac crest in standing subjects after normal expiration using a non-elastic tape. Height, weight, and waist circumference were measured within 2 h of BF% determination.

Body fat percentage
Body fat % was estimated by ADP using the Bod Pod\(^{14}\) (Life Measurement Instruments, Concorde, CA, USA).\(^14\) This two-component technique involves sitting in an air chamber while the volume of air displaced is measured. A standard two-point calibration was performed in the ADP chamber before every measure. The subject was asked to sit inside the chamber and to breathe normally. Generally, this procedure was performed once, but in some subjects two measurements were necessary because of excessive movement of the patient inside the chamber. The full test required 3-5 min. Body density as mass/volume, lean mass percentage and BF% were calculated automatically by computer software based on a two-compartment model (Siri model) for Caucasian populations.\(^15\) The average thoracic gas volume was predicted by the computer software from age and height according to the formulas developed by Crapo et al.\(^16\) Lean mass was obtained by multiplying lean mass percentage by weight in kilograms.

To assess the reliability of the measurements, we calculated the intraobserver and interobserver variability of ADP measurements by performing three measurements in six volunteers within 2 h, two by the same investigator and the third by a second investigator.

Statistical analysis
Data are presented as mean ± SD for continuous variables and as number and percentages for categorical variables. BMI was calculated as kilogram per meter squared. Owing to the non-linearity of BMI, BF%, and lean mass, we performed Spearman correlation coefficients between BMI and both BF% and lean mass for all patients and by gender and age groups (<65 and ≥65 years). Our hypothesis was that BMI would correlate similarly with both BF% as well as with lean mass, especially for patients with a BMI of <30 kg/m\(^2\). To further test this hypothesis, we performed statistical comparisons for the correlations between BMI and BF% vs. the correlation between BMI and lean mass. Using stepwise (forward, backward, and mixed) analyses, we assessed whether age, gender, waist circumference, and/or cardiovascular risk factors were significant predictors of BF% variability besides the BMI. We then incorporated these identified predictors to assess whether the correlation between BMI and BF% improved.

Finally, using the definition of obesity based on BF% as the reference standard (≥25% in men and ≥35% in women), we assessed the diagnostic performance of BMI to detect obesity by calculating sensitivity, specificity, and positive and negative predictive values with their 95% confidence intervals corrected for continuity using standard formulae.\(^17\) We performed these analyses using two cut-off points of BMI: ≥30 and ≥25 kg/m\(^2\). We also performed stratified analyses by gender and groups (<65 and ≥65 years). P-values of <0.05 were considered significant in advance. Statistical analyses were performed using JMP, version 6.0.\(^18\)

Results
After repeating the measure of BF% by ADP in six consecutive patients within 2 h of the measurements, we obtained a difference for BF% estimation in mean ± SE of −0.033 ± 0.36 for intraobserver variability and −0.035 ± 0.37 for interobserver variability.

Of the 116 possible participants who underwent ADP upon entry to a phase II cardiac rehabilitation programme from February to December 2005, 21 were excluded for not having CAD. The characteristics of the 95 subjects included in this study are presented in Table 1. Obesity was noted in 34.7% of patients according to a BMI value of ≥30 kg/m\(^2\), while 78.9% were obese as determined by BF%. Mean values of BF% were 32.1 ± 8% in men and 41.9 ± 9% in women. BMI was similar in men and women, 28.0 ± 6.5 kg/m\(^2\) vs. 28.8 ± 4.5 kg/m\(^2\) (P = 0.49), respectively. In patients ≥65 years, BF% was higher and BMI was lower compared with patients <65 years.

Figures 1 and 2 display the strong positive correlations between BMI and both BF% (p = 0.66, P < 0.0001) and lean mass (p = 0.41, P < 0.0001). Table 2 shows further details for correlations and comparison of correlations between BMI and both BF% and lean mass for all patients and by gender and age groups (<65 and ≥65 years). In all analyses, BMI correlated similarly with BF% and lean mass (all P > 0.20 for correlation comparisons). BMI of <30 kg/m\(^2\) did not discriminate between BF% and lean mass (p = 0.50, P < 0.0001 vs. p = 0.23, P = 0.04, respectively), P-value for correlation comparison = 0.24, whereas BMI of ≥30 kg/m\(^2\) showed a trend to do so (p = 0.68, P < 0.0001 vs. p = 0.17, P = 0.33, respectively), P-value for correlation comparison = 0.09.

Besides BMI, there were several variables that significantly predicted BF% (Table 3). Gender was found to be the most significant (P < 0.0001), but age and waist
circumference were also significant predictors (P = 0.001 and 0.01, respectively). Important to mention, none of the cardiovascular risk factors predicted the variability between BMI and BF%. After introducing gender, age and waist circumference into the model to predict BF% by BMI, the correlation coefficients improved from 0.96 in women (P < 0.0001 for model), and from 0.96 to 0.96 in men (P < 0.0001 for model).

The diagnostic performance of BMI using a cutoff of ≥30 kg/m² showed a sensitivity of 43% (95%CI, 32–54) and a specificity of 95% (95%CI, 83–100) to detect obesity (defined as an excess in BF%). When using a BMI cutoff of ≥25 kg/m², sensitivity was 91% (95%CI, 84–97) and specificity was 65% (95%CI, 42–88) to detect obesity. Table 4 presents the likelihood ratios of BMI to detect excess in BF% as well as other measures of diagnostic accuracy for all patients and by gender and age groups.

**Discussion**

This study shows that in patients with CAD, BMI was strongly correlated with BF%, but it failed to discriminate between BF% and lean mass, especially in patients with a BMI of < 30 kg/m². In addition, a BMI value of ≥30 kg/m² has an excellent specificity, but as a result of its poor sensitivity to detect obesity, it misses more than half of the patients with a true excess in body adiposity, diluting any possible association between mild elevations in BMI and adverse outcomes. Our results provide important information to understand the conflicting results of epidemiological studies assessing the association between BMI and adverse events in patients with CAD.

Furthermore, this poor diagnostic performance of BMI has also been found in other populations. Blew et al. showed that BMI values in the low range do not follow a linear relationship with BF% and therefore correlate poorly. Moreover, Wellens et al. showed that in a middle aged (20–45 years) population, BMI was a significant predictor of obesity defined as a BF% of ≥25% in men and ≥33% in women measured by densitometry. These results are similar to our 43% sensitivity for both genders using a lower cutoff for excess in BF% (> 35 years), supporting the notion that BMI has a poor sensitivity to detect obesity in women, and especially in elderly women. Blew et al. in agreement with our results reported that BMI values in the low range do not follow a linear relationship with BF% and therefore correlate poorly. Moreover, Wellens et al. showed that a BMI of ≥28 kg/m² had a sensitivity of ~48% for both genders to detect obesity defined as a BF% of ≥25% in men and ≥33% in women measured by densitometry. These results are similar to our 43% sensitivity for both genders using a BMI of ≥30 kg/m² and BF% cutoff of ≥25% in men and ≥35% in women to detect excess fatness, confirming that BMI is an uncertain diagnostic index for obesity.

An accurate diagnosis of obesity in patients with CAD is imperative. Excess body fat has been consistently linked to established cardiovascular disease mechanisms, and could be especially deleterious for patients with CAD. Obesity is associated with insulin resistance, increased sympathetic nervous activity, increase in the turnover of free fatty acids, and increased leptin levels. Moreover, obesity is also a causal factor for other cardiovascular risk factors, such as diabetes mellitus, hypertension, dyslipidemia, and obstructive sleep apnea. Therefore, it is biologically plausible that an excess in body fat will be deleterious in patients with CAD.

On the basis of these considerations, the following question then emerges: is BMI a good measure of obesity in patients with CAD? The results of our study suggest that...
the answer to this question is no, especially for patients with a BMI of $\geq 30$ kg/m$^2$. Only when BMI is high, is it able to differentiate between BF% and lean mass, explaining why prior studies have been more likely to show an association only in obese (BMI $\geq 30$ kg/m$^2$) and severely obese patients (BMI $\geq 35$ kg/m$^2$). Moreover, in our study BMI was positively and significantly correlated with lean mass, a measure which has been associated with better fitness and metabolic profiles and probably better prognosis in patients with cardiovascular diseases.

Because BMI relates not only to body fatness, but also to lean mass, patients with very low muscle mass with moderate amounts of BF will still fall in the normal range of BMI and therefore might be misclassified as having a `normal' weight. This was especially true in our study for patients $\geq 65$ years of age, where despite an increased BF% and lower lean mass (sarcopenic obesity) the BMI was significantly lower compared with patients $< 65$ years of age. Conversely, middle aged patients with CAD, particularly those who have engaged in an active lifestyle and have gained muscle mass and lost body fat, may be erroneously classified as overweight despite having a low BF%.

The strength of this study relies on the accepted validity and good reproducibility (similar to our intra- and inter-observer variability) of ADP to estimate BF%. In fact, previous studies have shown that there are no differences in BF% estimation by ADP compared with other techniques to measure BF%, such as dual X-ray absorptiometry or hydrostatic weighting. We decided not to use other methods to assess body composition, because ADP allows the inclusion of young and elderly patients, as well as those who are severely obese (BMI $\geq 35$ kg/m$^2$). In addition, ADP does not involve radiation and can be used in patients with pacemakers or implantable cardiac defibrillators.

Our study has some limitations to consider. First, we did not include consecutive patients referred to the cardiac rehabilitation programme; therefore, our sample was not randomized and selection bias may be present. However, the reason for not measuring BF% in every patient enrolled at the cardiac rehabilitation programme was due to the limited availability of personnel to measure BF% by ADP, and not due to investigator preferences or another systematic selection process. A second limitation is the relatively small sample of women included in the study, which limits the subgroup analyses by gender. Third, because patients entering cardiac rehabilitation programmes represent about 50% of the eligible patients with CAD, the possibility of participation bias is present in this study. Finally, other co-morbidities that could affect BF% variability such as metabolic syndrome were not considered in our study.
Implications

Patients with CAD and BMI (>30 kg/m²) require further assessment to accurately diagnose obesity. Measures of central obesity and even body composition techniques such as ADP, bioelectrical impedance, and dual X-ray absorptiometry might be necessary to further stratify patients according to levels and type of body fatness. Longitudinal studies will determine whether BF%, lean mass or the combination of both can reliably estimate the short- and long-term risk for adverse events in patients with CAD.

Conclusions

Although BMI has a good correlation with BF% in patients with CAD, it fails to discriminate between BF% and lean mass, especially in the intermediate BMI ranges. In addition, as a result of the low sensitivity of BMI (>30 kg/m²), >50% of the patients with a true excess in BF may be misclassified.
as ‘non-obese’. In patients with CAD and mildly elevated BMI, body composition techniques might be necessary to accurately diagnose obesity. These findings may help explain the controversial findings associating mild elevations of BMI in patients with CAD with better survival and fewer cardiovascular events.

Supplementary material
Supplementary material is available at European Heart Journal online.

Acknowledgements
V.K.S. was supported by NIH grants HL-65176, HL-70302, HL-73211, and M01-RR00585, J.S.-J. was partially supported by faculty funds from the Board of Post-Graduate Education of the Karolinska Institute (KID Award), and F.L.-J. was a recipient of a Clinical Scientist Development Award from the American Heart Association.

Conflict of interest: none declared.

References


Clinical vignette
doi:10.1093/eurheartj/ehl578
Online publish-ahead-of-print 29 March 2007

Congenital left main atresia in an adult diagnosed with multidetector computed tomography

Athanasios Kapetanopoulos1*, Domenic A. Zambuto2, and Charles A. Primiano1

1Henry Low Heart Center, Hartford Hospital, University of Connecticut, 80 Seymour Street, Hartford, CT 06102-5037, USA and 2Department of Interventional Radiology, Hartford Hospital, USA

*Corresponding author. Tel: +1 860 545 5596; fax: +1 860 545 5631. E-mail address: kthanos74@hotmail.com

A 53-year-old female underwent non-invasive coronary angiography with 64-slice multidetector computed tomography (MDCT) due to chest discomfort and an abnormal exercise treadmill test. Although there was no evidence of atherosclerotic coronary artery disease, MDCT demonstrated the absence of the left coronary ostium and left main trunk. The left anterior descending (LAD) and left circumflex (LCx) arteries were located at their normal position, but proximally ended blindly (arrows). Their blood supply was provided from the right coronary artery (RCA) via collaterals (arrowheads).

Specifically, the LAD appeared to fill principally by a large right ventricular marginal branch, which coursed anteriorly to the mid-vessel. The LAD segment proximal to the mid-vessel was of small caliper. The LCx was mainly supplied via a separate collateral branch arising from the right coronary artery (RCA) via collaterals (arrowheads).

Panel A. Three-dimensional volume-rendered MDCT image.
Panel B. Left anterior oblique angiographic view by computed tomography.
Panel C. Right anterior oblique angiographic view by computed tomography.
Panel D. Left anterior oblique angiographic view by invasive coronary angiography.
Panel E. Right anterior oblique angiographic view by invasive coronary angiography.

The authors wish to thank Gary Gillan, BSRT, 3D Lab Team Leader, Department of Radiology, Hartford Hospital, for his assistance with image reconstruction.