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Letter to the Editor

Relative fat mass (RFM) as abdominal obesity criterion for metabolic syndrome

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Obesity is a recognized risk factor for various cardio-metabolic diseases and several indices are used clinically to assess overall cardio-metabolic risk [1]. The metabolic syndrome, which is an independent risk factor for coronary heart disease, peripheral artery disease, stroke and total mortality [2–5], was defined by the Adult Treatment Panel III (ATP III) as at least three of the five conditions – central obesity (as defined by men waist circumference > 40 in. or women waist circumference > 35 in.), raised triglycerides (above 150 mg/DL or on treatment), reduce HDL (below 40 mg/DL for men or 50 mg/DL for women), raised blood pressure (above 130/85mmHG or on treatment) and abnormal fasting plasma glucose (above 110 mg/DL or on treatment) [6].

The definition of increased waist circumference (WC), as part of metabolic syndrome diagnosis, requires the use of gender and ethnic specific values and is less intuitive- hence not commonly used in common practice [7,8]. Due to WC disadvantages, the best adiposity measure to help predict cardiovascular risk factors has remained controversial. Body Mass Index (BMI) is traditionally the most widely used measure of obesity, it is a simple to use both by clinicians and patients; however, the BMI is unable to differentiate between lean mass and fat mass, nor to consider body fat distribution.

Other measures of adiposity, which consider body fat distribution, like waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) have been developed. WHtR seems to be a good predictor for cardiometabolic risk, mainly in the Asian population [9]. In Western populations, however, WC tends to serve as a better predictor of cardiovascular risk [10]. Body Adiposity Index (BAI), which estimates the total body fat, is calculated using hip circumference and height was proposed but was not consistently proved as a better clinical predictor [11,12].

Relative fat mass (RFM), calculated as $64 - (20 \times \text{height/waist circumference}) + (12 \times \text{sex})$; sex = 0 for men and 1 for women, has recently been developed as a new estimator of whole-body fat percentages. Compare with abnormal BMI, abnormal RFM (above 33.9 for women and 22.8 for men) better predicted obesity among men using dual energy X-ray absorptiometry (DXA) as the gold standard; it was also found to be superior to BMI as a predictor of diabetes [13]. Recently, a few studies were conducted using RFM as an obesity indicator. In a small study, RFM was validated to estimate fat percentage among men and women with and without Down syndrome [14] and was found to be a better predictor of severe liver disease and mortality than BMI [15]. Up to date, no comparison between RFM and waist circumference was published.

In our study, we aimed to compare between RFM and waist circumference as the obesity criterion for the definition of metabolic syndrome.

A retrospective, observational, cohort-based study, performed at the Rambam Health Care Campus (RHCC) Periodic Examinations Institute between the years 2008–2016. The study was approved by the hospital's ethics committee, with a waiver of consent.

The Rambam Periodic Examinations Institute (RPEI) is an independent institute which operates within RHCC. It provides service of comprehensive medical examination for patients, including physical examination, blood tests, exercise test (when indicated) etc.

We included any adult patient underwent medical testing at the RPEI, we excluded patients whose file was lacking the needed anthropometric indices.

Descriptive statistics in terms of mean, SD, and ranges were presented to the whole parameters in the study. Categorical variables were compared using the Fisher exact test and continuous variables were compared using the *t*-test. Diagnostic parameters (sensitivity, specificity, positive predicted variable and negative predicted variable were calculated related to occurrence of metabolic syndrome. $P < .05$ was consider as significant. SPSS version 25 was used for the statistical analysis.

During the study period 20,167 patients underwent medical examination at the RPEI and were included in the study. The mean age of participants was 52.3 years. We identified metabolic syndrome among 2827 patients (14%), with slightly higher proportion among men than among women (14.1% vs 13.7%). The baseline characteristics of men and women with metabolic syndrome were significantly different. While there was no significant difference in the mean age of men and women with metabolic syndrome, women with metabolic syndrome had higher proportions of abnormal waist circumferences (89.9% vs. 52.6%, $p < .001$). Men had significantly higher proportions of all four non-obesity parameters (hypertension [59.1% vs. 43.6%, $p < .001$], impaired fasting glucose/diabetes mellitus [92.4% vs. 77.1%, $p < .001$], hypertriglyceridemia [76.9% vs. 59.9%, $p < .001$] and low HDL [89.3% vs. 79.8%, $p < .001$), see Table 1.

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Table 1
Characteristics of patients with metabolic syndrome and 'new metabolic syndrome', by gender.

	Metabolic syndrome			'New metabolic syndrome'		
	Women N = 859	Men N = 1968	P	Women N = 1122	Men N = 4894	P
Age, years	56.1 ± 8.68	56.9 ± 9.4	0.32	55.6 ± 8.8	55.9 ± 10.1	0.35
Obesity (WC\RFM as appropriate)	772 (89.9%)	1035 (52.6%)	< 0.001	1113 (99.2%)	4872 (99.5%)	0.16
Hypertension	374 (43.6%)	1163 (59.1%)	< 0.001	431 (38.4%)	2244 (45.8%)	< 0.001
Hypertriglyceridemia	514 (59.9%)	1513 (76.9%)	< 0.001	623 (55.5%)	2753 (56.3%)	0.66
Low-HDL	685 (79.8%)	1757 (89.3%)	< 0.001	883 (78.7%)	3542 (72.3%)	< 0.001
DM\Impaired fasting Glucose	662 (77.1%)	1818 (92.4%)	< 0.001	797 (71.0%)	3545 (72.4%)	0.35

Table 2
Predictability of RFM and Waist circumference for metabolic syndrome.

	Negative predictive value	Positive predictive value	Sensitivity	Specificity
Waist men	89%	30%	85%	36%
Waist women	89%	35%	91%	29%
RFM men	98%	16%	99%	14%
RFM women	99%	18%	99%	27%

We also examined the correlations between RFM and WC, which was higher among women ($r = 0.84$, $p < .001$ Vs $r = 0.67$, $p < .001$). When compared the predictability of RFM and waist circumferences to metabolic syndrome, RFM provided higher negative predicative value and sensitivity among men and women, with lower specificity and positive predictive value (Table 2).

We defined a population of 'new metabolic syndrome' using abnormal RFM as the obesity criteria of metabolic syndrome instead of abnormal WC. The prevalence of 'new metabolic syndrome' was 29.8%, (35% among men, 17.9% among women). Nevertheless, when compared the characteristics of patients with 'new metabolic syndrome', the differences between men and women are much subtler than observed in metabolic syndrome. Nearly all patients, regardless of gender, fulfill the obesity criteria (99.5% of men, 99.2% of women, p = .16). There was no significant difference in the age of men and women with 'new metabolic syndrome' (55.9 ± 10.1 Vs. 55.6 ± 8.8, respectively, p = .35) nor in the proportions of diabetes mellitus/impaired fasting glucose (72.4% of men, 71% of women, p = .35) and hypertriglyceridemia (56.3% of men, 55.5% of women, p = .66). Low HDL was more common among women (78.7% Vs. 72.3% of men, p < .001) and hypertension among men (45.8% Vs. 38.4% of women, p < .001), but the absolute difference was much smaller than observed in metabolic syndrome (Table 1).

The question of which obesity marker should be used as part of the cardiometabolic risk assessment is still open. Recently, a new obesity marker, RFM, was developed and show high correlation with abdominal obesity [13]. Previous studies compared RFM to BMI [13–15], but not to waist circumference. We aim to assess the effect of RFM as a potential obesity criterion for metabolic syndrome. When we used the ATP III criteria to define metabolic syndrome, we identified metabolic syndrome among 14% of our cohort. The characteristics of men and women with metabolic syndrome were different, except the prevalence and age of patients, that was similar among men and women. Women had significantly higher prevalence of obesity (measured by waist circumference) and significantly lower prevalence of dyslipidemias, impaired fasting glucose and hypertension. The difference in characteristics of metabolic syndrome in men and women was previously published. Using RFM instead of waist circumference defined more than twice of patients in our cohort to suffer from metabolic syndrome (29.8% compared to 14% using ATPIII definition), with much higher prevalence among men (35% vs. 17.9%). Despite the substantial difference in the prevalence of newly defined metabolic syndrome among men and women, the characteristics of the two populations were similar in the mean age, the prevalence of hypertriglyceridemia and impaired fasting glucose. There was still a statistically significate difference in the prevalence of hypertension which was more common in men (45.8% of men, 38.4% of women, p < .001) and low HDL which was more common in women (78.7% vs 72.3%, p < .001), but the differences were much smaller than observed using the traditional definition.

Bearing in mind that men are known to have increased cardiometabolic risk, our finding raise the question whether RFM may be a more accurate criteria for metabolic syndrome and to reflect more accurately the cardio-metabolic risk. This hypothesis will need to be examined in a prospective trial.

We also examine the correlation of RFM and waist circumferences, which was stronger among women; and the predictability of RFM for metabolic syndrome by the accepted definition. RFM provided excellent negative predictive value and sensitivity to metabolic syndrome (99% sensitivity in men and women; NPPV 99% in women, 98% in men), higher than waist circumferences (sensitivity 91% in women, 85% in men, NPPV 89% in men and women). Hence, may be also used as a test to rule out metabolic syndrome.

Our study, however, have some limitations, first, due to the retrospective character of our trial we cannot conclude regarding the long-term predictability of RFM as the obesity criterion of metabolic syndrome, and this will be needed to assed in a prospective trial. Second, our study was done on a specific group, Israeli adults who visited the RPEI during study years. On the other hand, the large number of patients allowed us to achieve statistical significance for our findings.

In conclusion, RFM as the obesity criterion of metabolic syndrome define a larger proportion of the population as suffering from metabolic syndrome, with much higher prevalence among men than women. However, the metabolic characteristics of men and women defined using RFM are much more similar and there is less gender-based bias in these characteristics. Further studies are needed to determine whether it reflect better the population in high cardiometabolic risk.

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