Relative fat mass is a better predictor of dyslipidemia and metabolic syndrome than body mass index

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Background Relative fat mass (RFM) had been recently developed. We aimed to examine RFM predictability to various cardiometabolic risk factors, compared to BMI.

Methods Observational, cohort study, among patients who visited the Rambam Periodic Examinations Institute (RPEI). We compared the correlation of BMI and RFM to hypertension, impaired fasting glucose, high LDL, low HDL and metabolic syndrome, by gender.

Results During study years, 20167 patients visited the RPEI and included in the trial. Compared to BMI, RFM showed significantly better predictability (odds ratio [OR], [95% confidence interval (CI), *P* value]) of high LDL [1.618 (1.441–1.816, *P*<0.001) vs. 0.732 (0.67–0.8, *P*<0.001) in men; 1.572 (1.377–1.794, *P*<0.001) vs. 0.938 (0.849–1.163, *P*=0.94) in women], low HDL [2.944 (2.569–3.373, *P*<0.001) vs. 2.177 (2–2.369, *P*<0.001) in men, 2.947 (2.519–3.448, *P*<0.001) vs. 1.9 (1.658–2.176, *P*<0.001) in women], high triglycerides [4.019 (3.332–4.847, *P*<0.001) vs. 1.994 (1.823–2.181, *P*<0.001) in men, 3.93

(2.943–5.247, *P*<0.001) vs. 2.24 (1.887–2.62, *P*<0.001) in women] and metabolic syndrome [7.479, (4.876–11.47, *P*<0.001) vs. 3.263 (2.944–3.616, *P*<0.001) in men, 16.247 (8.348–31.619, *P*<0.001) vs. 5.995 (5.099–7.048, *P*<0.001) in women]. There was no significant difference in the predictability of BMI and RFM to hypertension and diabetes mellitus.

Conclusion RFM provides high predictability for dyslipidemias and metabolic syndrome. *Cardiovasc Endocrinol Metab* 8: 77–81 Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

In the past decades, the increasing prevalence of obesity is becoming a greater public health and health economic issue [1]. Obesity is a recognized risk factor for various cardiometabolic diseases and several indices are used clinically to assess the overall cardiometabolic risk [2]. BMI is traditionally the most widely used measure of obesity. Abnormal BMI is an independent predictor of mortality, and BMI is also used by some as part of the criteria for metabolic syndrome [3,4]. The main advantage of BMI is its simplicity to use both by clinicians and patients. It can also effectively rule out metabolic syndrome in certain populations [5]; however, the BMI is unable to differentiate between lean mass and fat mass, nor to consider body fat distribution.

Other measures of adiposity consider body fat distribution, like waist circumference, waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR), and more recently developed body adiposity index (BAI), none proved overall superiority [6–9].

In the light of the conflicting data, the best adiposity measure to help predict cardiovascular risk factors has remained controversial. Relative fat mass (RFM) had been recently developed as a new estimator of whole

body fat percentages among American adult individuals of Mexican, European or African ethnicity. RFM is calculated using the equation: $64 - (20 \times \text{height} / \text{waist circumference}) + (12 \times \text{sex})$; sex = 0 for men and 1 for women. Abnormal RFM (above 33.9 for women and 22.8 for men) showed promising results in its validation study. Compared with BMI, RFM better predicted abdominal obesity among men using dual energy x-ray absorptiometry as the gold standard; RFM was also found to be superior to BMI as a predictor of diabetes [10]. Only a few later studies were conducted using RFM as an obesity indicator. In a small trial, RFM was validated to estimate fat percentage among men and women with and without Down's syndrome [11]. One study found RFM to be a better predictor of severe liver disease and mortality than BMI [12]. Our earlier reported results suggest RFM may be used instead of waist circumference to define metabolic syndrome [5]. Up to date, to the best of our knowledge, no further studies were published and the question whether RFM correlates better than BMI to metabolic disturbances is yet to be determined.

The aim of this study, therefore, was to add to the body of evidence regarding the clinical applicability of RFM and to examine whether RFM is superior to BMI and correlates better with various cardiometabolic risk factors.

Methods

A retrospective, observational, cohort-based, cross-sectional study performed at the Rambam Health Care Campus (RHCC) Periodic Examinations Institute between the years 2008 and 2016. RHCC is a primary and tertiary care university-affiliated hospital in northern Israel and operates an outpatients' periodic examinations institute. 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 who underwent medical testing at the RPEI. Patients are instructed to fast prior to their visit to the periodic examinations institute; hence, all blood tests done during the visit are fasting blood tests. Patients were identified using RHCC electronic patient data file. RHCC operates a full electronic patient register that includes clinical, laboratory and radiological data. It also has access to medical summary reports and diagnoses from other healthcare providers. Patients who did not have the required measurement for BMI or RFM calculation were excluded from the study.

Abnormal RFM was defined as above 33.9 for women and 22.8 for men, as defined previously [9], abnormal BMI was defined as above 25, as commonly accepted.

Metabolic syndrome was defined by the ATP III criteria – at least three of the five conditions – central obesity (as defined by men waist circumference >40 inch or women waist circumference >35 inch), hypertriglyceridemia (above 150 mg/dl or on treatment), reduce HDL (below 40 mg/dl for men or 50 mg/dl for women), hypertension (above 130/85 mmHg or on treatment) and abnormal fasting plasma glucose (above 110 mg/dl or on treatment) [13].

Hypertriglyceridemia, reduced HDL and impaired fasting glucose were assessed by the blood test results during the visit, or the presence of appropriate diagnosis or treatment in the patient history.

Hypertension was assessed by the blood pressure measurement during the examination at RPEI, a confirmed diagnosis of hypertension or chronic use of antihypertensive medications.

Statistical analysis

Descriptive statistics in terms of mean, SD and ranges were presented to the all parameters in the study. We compared the associations of BMI and RFM to various categorical variables (presence of cardiometabolic risk factors) using the Fisher exact test and continuous variables were compared using the *t*-test.

Diagnostic parameters such as sensitivity, specificity, positive predicted variable and negative predicted variable were calculated related to occurrence of metabolic syndrome.

A receiver operating characteristic (ROC) curve with area under the curve and 95% confidence interval (CI) was demonstrated to describe the relationship between the sensitivity and the false positive rate for different values of BMI in identification of patients at risk for metabolic Syndrome. The Youden index was used for describing the best cutoff for identification.

$P < 0.05$ was consider as significant. SPSS version 25 was used for the statistical analysis.

Results

During the study period, 20167 patients underwent medical examination at the RPEI and were included in the study. The mean age of participants was 52.3 years. Patients with abnormal RFM were older had higher BMI and more comorbidities (see Table 1).

RFM and BMI showed high level of correlation both among men ($R^2 = 0.858$, $P < 0.001$) and women ($R^2 = 0.825$, $P < 0.001$) (Fig. 1).

We tried to identify the correlation between BMI and RFM to cardiometabolic risk factors. When compared to BMI, RFM showed significantly better predictability [odds ratio (OR), 95% CI] to low HDL [2.944 (2.569–3.373, $P < 0.001$) vs. 2.177 (2–2.369, $P < 0.001$) in men, 2.947 (2.519–3.448, $P < 0.001$) vs. 1.9 (1.658–2.176, $P < 0.001$) in women] and high triglycerides [4.019 (3.332–4.847, $P < 0.001$) vs. 1.994 (1.823–2.181, $P < 0.001$) in men, 3.93 (2.943–5.247, $P < 0.001$) vs. 2.24 (1.887–2.62, $P < 0.001$) in women] among both men and women, with no overlap in CIs of ORs. RFM correlated with high LDL, among men and women, while BMI did not show significant correlation to high LDL among women and showed reverse ratio correlation among men [1.618 (1.441–1.816, $P < 0.001$) vs. 0.732 (0.67–0.8, $P < 0.001$) in men; 1.572 (1.377–1.794, $P < 0.001$) vs. 0.938 (0.849–1.163, $P = 0.94$) in women]. Both BMI and RFM showed statistically significant correlation with hypertension and diabetes mellitus/impaired fasting glucose. Among men, BMI performed slightly better, while among women, RFM showed superiority, but with overlap in the CIs (Table 2).

When diagnostic accuracy of BMI and RFM for metabolic syndrome is examined, the negative and positive predictive values of RFM among women (99.4 and 18.2%, respectively) were higher than among men (98.9 and 15.9%, respectively). Compared to BMI (96 and 18% among women; 98 and 24% among men), RFM showed better negative predictive value in both genders and slightly lower positive predictive value among men. Bivariant analysis for metabolic syndrome showed higher OR (95% CI, P value) of RFM compared to BMI for

Table 1 Demographics and past medical history of patients with normal and abnormal relative fat mass, by gender

	Women (n=6246)				Men (n=13921)		
	Overall (N=20 167)	Normal RFM (n=1584)	High RFM (n=4662)	P value	Normal RFM (n=1703)	High RFM (n=12 218)	P value
Age, years	52.3±10.5	47.1±9.5	52.6±9.4	<0.0001	45.2±9.7	53.8±10.5	<0.0001
BMI, mean	27.0±4.2	21.6±2.0	27.7±4.4	<0.0001	22.7±1.8	28.1±3.6	<0.0001
DM, n (%)	6707 (33.3%)	105 (6.6%)	1225 (26.3%)	<0.0001	264 (15.5%)	5113 (41.8%)	<0.0001
Hypertension, n (%)	3480 (17.3%)	34 (2.1%)	568 (12.2%)	<0.0001	67 (3.9%)	2811 (23.0%)	<0.0001
Dyslipidemia, n (%)	9293 (46.1%)	349 (22.0%)	1986 (42.6%)	<0.0001	473 (27.8%)	6485 (53.1%)	<0.0001
Hypertriglyceridemia, n (%)	4162 (20.8%)	55 (3.5%)	765 (16.7%)	<0.0001	132 (7.8%)	3210 (26.4%)	<0.0001
Metabolic Syndrome, %	2827 (14.0%)	9 (0.6%)	850 (18.2%)	<0.0001	22 (1.3%)	1946 (15.9%)	<0.0001
Beta blockers use	1799 (8.9%)	24 (1.5%)	351 (7.5%)	<0.0001	25 (1.5%)	1399 (11.5%)	<0.0001
ACE/ARB use	3291 (16.3%)	36 (2.3%)	525 (11.3%)	<0.0001	75 (4.4%)	2655 (21.7%)	<0.0001
Statins use	4991 (24.7%)	106 (6.7%)	944 (20.2%)	<0.0001	136 (8.0%)	3805 (31.1%)	<0.0001

ACE, angiotensin converting enzyme inhibitors; ARB, angiotensin II receptor blockers; DM, diabetes mellitus; RFM, relative fat mass.

Table 2 Odds ratios (95% confidence interval, *P*) for relative fat mass and BMI to various cardiometabolic conditions among men and women

	Men		Women	
	RFM	BMI	RFM	BMI
Hypertension	2.807 (2.226–3.539, <i>P</i> <0.001)	2.71 (2.456–2.989, <i>P</i> <0.001)	2.619 (1.9–3.611, <i>P</i> <0.001)	3.376 (2.826–4.033, <i>P</i> <0.001)
Diabetes mellitus/impaired fasting glucose	2.827 (1.893–4.221, <i>P</i> <0.001)	2.409 (2.118–2.739, <i>P</i> <0.001)	3.456 (1.661–7.194, <i>P</i> <0.001)	4.581 (3.428–6.122, <i>P</i> <0.001)
Hypertriglyceridemia	4.019 (3.332–4.847, <i>P</i> <0.001)	1.994 (1.823–2.181, <i>P</i> <0.001)	3.93 (2.943–5.247, <i>P</i> <0.001)	2.24 (1.887–2.62, <i>P</i> <0.001)
Low HDL	2.944 (2.569–3.373, <i>P</i> <0.001)	2.177 (2–2.369, <i>P</i> <0.001)	2.947 (2.519–3.448, <i>P</i> <0.001)	1.9 (1.658–2.176, <i>P</i> <0.001)
High LDL	1.618 (1.441–1.816, <i>P</i> <0.001)	0.732 (0.67–0.8, <i>P</i> <0.001)	1.572 (1.377–1.794, <i>P</i> <0.001)	0.938 (0.849–1.163, <i>P</i> =0.94)

RFM, relative fat mass.

women (16.247 [8.348–31.619, *P*<0.001 vs. 5.995 [5.099–7.048, *P*<0.001]), and for men (7.479, [4.876–11.47, *P*<0.001] vs. 3.263 [2.944–3.616, *P*<0.001]); again, there was no overlap in the ORs' CIs.

Using ROC curves, we described the relationship between the sensitivity and the false positive rate for different values of RFM in identification of patients at risk for metabolic syndrome. Using the Youden index, RFM of 39.8 was found to be the ideal value for identification of metabolic syndrome in women with area under the curve (AUC) of 0.864 (95% CI 0.852–0.857, *P*<0.001), not significantly different from the AUC of the ideal BMI that was found, 27.4 (AUC: 0.845, 95% CI: 0.833–0.857, *P*<0.001). For men, the ideal RFM was found to be 27.72 with AUC of 0.739 (95% CI: 0.728–0.75, *P*<0.001) similar to that of ideal BMI that was found 27.4, same as for women (AUC: 0.727, 95% CI: 0.716–0.738, *P*<0.001) (Fig. 2).

Discussion

The question of which obesity marker should be used by the primary physician is still open. Nowadays, BMI is the most commonly and widely used obesity marker. Other markers such as waist circumference, WHtR, WHR and BAI are also used by physicians [2,6–9]. Recently, RFM was proposed and showed promising results in its validation trail and few later trials [5,10–12]. We aimed to examine whether RFM provides better predictability than BMI to various cardiometabolic endpoints.

In our cohort, when compared to BMI, RFM was a significantly better predictor of high LDL, low HDL, high triglyceride and metabolic syndrome, both in men and women. RFM also showed better negative predictive value to rule out metabolic syndrome in both genders. BMI provided slightly better predictability for hypertension and diabetes mellitus in women (RFM among men), but these findings were not statistically significant. In our cohort, high BMI in men was associated to normal LDL, suggesting a protective effect. This finding requires further research.

The cutoff values of abnormal RFM were to be 33.9 for women and 22.8 for men [9]. In our trial, using ROC curve, we tried to identify the ideal RFM for identification of metabolic syndrome, as a signal of higher cardiometabolic risk. RFM of 39.8 was found to be the ideal value for identification of metabolic syndrome in women with AUC of 0.864 (95% CI: 0.852–0.857, *P*<0.001), while for men, the ideal RFM was found to be 27.72 with AUC of 0.739 (95% CI: 0.728–0.75, *P*<0.001). These values are higher than the suggested cutoff values previously used [9], and further studies should be performed in order to determine the ideal cutoff values.

Our study, however, has some limitations; first, it was done on a specific group, Israeli adults who visited the RPEI during study years. Patients who attend periodic medical examination institute are assumingly more aware to preventive health issues than the general

Fig. 1

population. On the other hand, the large number of patients allowed us to achieve statistical significance to most of our findings. The characteristics of our cohort may also cause bias, as most of the cohort had obesity and abnormal RFM (vast majority among men). Second,

the character of our study did not enable us to use endpoints as mortality, myocardial infarction or stroke. Longer follow-up or prospective trials may be done to examine whether RFM is a better predictor for these endpoints as well.

Fig. 2

ROC curves for identification of metabolic syndrome for BMI and RFM, by gender. (a) Men and (b) Women. RFM, relative fat mass; ROC, receiver operating characteristic curve.

In conclusion, understanding of the advantages of different adiposity measures as predictor of cardiometabolic risk is important in maintaining and promoting health. The newly suggested obesity marker, RFM carries diagnostic benefits. When compared to BMI, RFM provides better predictability of various dyslipidemias (high LDL, low HDL and high triglycerides) and metabolic syndrome, which is an independent risk factor for coronary heart disease, peripheral artery disease, stroke and total mortality. A higher than previously suggested cutoff values of RFM may be used in men and women to predict metabolic syndrome. Further prospective studies are required in order to fully reveal the long-term clinical significance of RFM.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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