



## Indexes of adiposity and body composition in the prediction of metabolic syndrome in obese children and adolescents: Which is the best?



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**Abstract** *Background and aim:* There is no agreement about which index of adiposity and/or body composition is the most accurate in identifying the metabolic syndrome (METS). The aim of our study was to compare the accuracy of the different indexes in order to recognize the most reliable.

*Methods and results:* We evaluated 1332 obese children and adolescents (778 females and 554 males), aged  $14.4 \pm 1.8$  yrs, Body Mass Index (BMI) standard deviation scores (SDS)  $2.99 \pm 0.55$ , followed at the Istituto Auxologico Italiano, a tertiary center for childhood obesity. For each subject the following indexes were assessed: BMI, BMI SDS, Fat-Free Mass Index (FFMI), Fat Mass Index (FMI), Tri-Ponderal Mass Index (TMI), Waist-to-Height ratio (WtHR) and a new one, the Body Mass Fat Index (BMFI), which normalizes the BMI for percentage of body fat and the waist circumference. Thereafter we calculated for each index a threshold value for age and sex, in order to compare their accuracy, sensitivity and specificity in identifying the METS. There was a good correlation among indexes ( $p < 0.0001$  for all). However, when the area under the curve (AUC) was compared, some of them, in particular the BMFI and the BMI, performed better than the other ones, although the differences were small.

*Conclusions:* BMI, which neither considers body composition nor fat distribution, performs as good as other indexes, and should therefore be the preferred one, also because of the easiness of its calculation.

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### Introduction

Obesity is closely associated with the metabolic syndrome (METS), which is a strong risk factor for atherosclerotic cardiovascular disease and type 2 diabetes mellitus

(T2DM). As a result, the increase in the prevalence of obesity worldwide has led to a considerable increase in its economic consequence. The raising number of obese children and adults has solicited in recent years the creation of indexes able to accurately define weight excess, body composition and in particular visceral obesity, because the latter is a marker for a higher risk of cardio-metabolic diseases [1]. These surrogate indexes of adiposity and/or visceral adiposity are routinely used in clinical practice as objective measurements of fat mass and

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visceral adiposity require expensive machinery, such as dual energy X-ray absorptiometry (DEXA) and Magnetic Resonance/Computed Tomography, whose availability is limited. Other techniques, such as bioelectrical impedance (BIA) and skinfold measurements, provide only information on overall adiposity and subcutaneous fat mass respectively. Moreover, the resulting data are inaccurate and/or poorly reproducible.

Body Mass Index ( $BMI = kg/cm^2$ ) is by far the oldest and most commonly surrogate index used [2], but does not allow to discriminate fat mass from fat-free mass. As a matter of fact, a body builder may show the same BMI as a sedentary TV watcher. Furthermore, in pediatric age BMI varies with age and sex, requiring specific cutoff points. Thus, BMI standard deviation scores (SDS) are commonly used for growing children and adolescents. Since nowadays it has been recognized that the amount of fat mass and its distribution are the most important metabolic risk factors [3], other indexes have been developed subsequently, which also take into account these parameters. This is the case of adiposity indexes such as Fat Mass Index (FMI) [4] and Tri-Ponderal Mass Index (TMI) [5], as well as for indexes of body fat distribution as Waist Circumference (WC) [6], Model of Adipose Distribution (MOAD) and Visceral Adiposity Index (VAI) [7] and Waist-to-Height ratio (WtHR) [8], all built up with the aim to assess body fatness and its relationship with cardiovascular and metabolic comorbidities. Indexes of visceral adiposity seem to have greater clinical utility than BMI in predicting disease and mortality [9,10]. Similarly, anthropometric markers of adiposity have proved to be useful for predicting the METS in youth [11,12]. In addition, the Fat-free Mass Index (FFMI) [13] is considered an indicator of nutritional status in healthy and ill subjects, different from measures of body fat or body fat distribution, and has been previously used as predictor of components of the METS [14]. Despite a number of publications, however, no agreement has been reached on which index should be used to date, both in children and adolescents as well as in adults [15].

In order to close this gap, in the present study we calculated, in a large group of obese children and adolescents, a new index, the Body Mass Fat Index (BMFI), which also adjusts the BMI for the body composition and for the WC. The objective of this study was to test the hypothesis that BMFI, the most comprehensive index, would perform better than the others in identifying METS. For this purpose, we evaluated for this index as well as for indexes of adiposity (BMI, BMI SDS, FMI, TMI), body fat distribution (WtHR) and body composition (FFMI), the age- and sex-adjusted threshold that allows to identify or exclude the presence of METS, comparing then the sensitivity and specificity of all indexes to predict METS.

## Methods

### Study population

Between June 2013 and June 2017 we evaluated 1332 obese children and adolescents [778 females, 554 males,

aged  $14.4 \pm 1.8$  (range 10–17) years, height standard deviation score (SDS)  $0.28 \pm 1.05$  (range  $-3.38$ – $4.35$ ), and BMI SDS  $2.99 \pm 0.55$  ( $2.01$ – $5.06$ )], consecutively enrolled in the obesity inpatient clinic of the Istituto Auxologico Italiano, Piancavallo, Verbania, Italy. All but 27 patients were Caucasian. All the subjects were born full-term and suffered from simple obesity, other genetic, organic and hormonal causes having been excluded. None of them had received treatment with any drug known to interfere with metabolism such as oral contraceptives or insulin sensitizers for the previous 12 months. Pubertal development was assessed according to Tanner classification [16]. One hundred and twenty-seven patients were prepubertal (stage 1), 683 pubertal (stage 2–4) and 522 fully developed (stage 5).

The study protocol was approved by the Ethical Committee of the Istituto Auxologico Italiano (ref. no. 01C822). Written informed consent was obtained for all procedures from parents or legal guardians and written assent from children and adolescents were obtained before enrollment.

### Anthropometric data

All subjects underwent body measurements wearing light underwear, in fasting conditions after voiding. Physical examination was carried out by the same investigators specifically trained.

Standing height was determined by a Harpenden Stadiometer (Holtain Limited, Crymch, Dyfed, UK). Body weight was measured to the nearest 0.1 kg, using standard equipment. Height and BMI, through the text and tables, were expressed as SDS, according to Cacciari et al. [17] in order to normalize the values for age and sex. Waist circumference (WC) was measured midway between the lowest rib and the top of the iliac crest after gentle expiration with a non-elastic flexible tape measure.

### Blood pressure measurements and instrumental examination

Diastolic and systolic blood pressure (BP) were measured to the nearest 2 mmHg in the supine position after 5 min rest, using a standard mercury sphygmomanometer with appropriately sized cuff. The average of three measurements on different days was used.

Body composition: fat mass (FM), fat mass percentage (FM%), fat-free mass (FFM) and fat-free mass percentage (FFM%), were assessed by bioelectrical impedance analysis (BIA) using a tetrapolar impedance meter (Human-IM Scan; DS-Medigroup, Milan, Italy). For this purpose, we have employed a cross-validate prediction equations of body composition from BIA measurements using DEXA as the reference method, developed by Lazzero et al. in obese children and adolescents [18]. Measurements were performed according to the method of Lukaski et al. [19], after 20-min rest in a supine position with relaxed arms and legs.

### Laboratory analyses

Baseline blood samples were drawn by venipuncture for determination of glycemia, high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG). Routine laboratory data were measured by enzymatic methods (Roche Diagnostics, Mannheim, Germany). In all patients, a standard oral glucose tolerance test (1.75 g of glucose/kg body weight up to 75 g with blood samples taken at 0, 30, 60, 90, 120 min) was then performed to evaluate glucose homeostasis.

### Definitions

We defined as obese those patients with a BMI higher than the centile curve that at age 18 passed through the cut-off point of 30 for adult obesity [17].

The following indexes have been calculated according to the respective formulas:

- (1) BMFI:  $\text{BMI} \times \text{FM} (\%) \times \text{WC} (\text{cm})$ ;
- (2) FFMI [13]: fat-free mass in kg/height in  $\text{m}^2$ ;
- (3) FMI [4]: fat mass in kg/height in  $\text{m}^2$ ;
- (4) TMI [5]: mass in kg/height in  $\text{m}^3$ ;
- (5) WtHR [8]:  $\text{WC} (\text{cm})/\text{height} (\text{cm})$ .
- (6) BMI SDS [17]:  $(\text{BMI} - \text{mean BMI (for age and sex)})/\text{SD}$

Diagnosis of altered glucose metabolism was determined according to the American Diabetes Association criteria [20]. Hypertension was defined as values of systolic or diastolic BP > 95th percentile for age, sex, and height or when any antihypertensive drug was being used [21]. According to the IDF criteria for METS diagnosis in children and adolescents [22], our patients were considered to have the METS if they had abdominal obesity [ $\text{WC} \geq 90$ th percentile for ages <16 years [23], and  $\geq 94$  cm for males and  $\geq 80$  cm for female for ages >16 years] plus two or more of the following factors [1]: raised TG level:  $\geq 150$  mg/dL (1.7 mmol/L) for ages <16 years and the same cutoff or specific treatment for this lipid abnormality for ages >16 years [2]; reduced HDL-C: <40 mg/dL (1.03 mmol/L) for males and females for ages <16 years, and <40 mg/dL for males and <50 mg/dL (1.29 mmol/L) for females, or specific treatment for this lipid abnormality for ages >16 years [3]; raised BP: systolic BP  $\geq 130$  mmHg or diastolic BP  $\geq 85$  mmHg for ages <16 years, and same cutoff or treatment of previously diagnosed hypertension for ages >16 years [4]; raised fasting plasma glucose (FPG) concentration  $\geq 100$  mg/dL (5.6 mmol/L) or previously diagnosed T2DM for all ages [5].

### Statistical analysis

The data were first scrutinized for outliers, using a cutoff of 4.5 standard deviation score. No data was excluded on this basis. To explore the data, preliminary analyses were performed. Continuous data are presented as mean (SD) or with 95% CIs. Mean values were tested for statistical significance using 2-tailed t tests. Pearson correlation

coefficients were calculated to assess the relationship between body-composition indexes. Correlation analyses were used to assess the associations between each body-composition index and each metabolic risk factor component. Fisher's transformation, changing  $r$  to a Z-score, was used to compare correlated correlations.

To calculate the growth pattern of body-composition indexes, a quantile regression was used [24] as alternative of LMS Method [25]. The logarithm of each body composition index is used as response, fitted with a parametric model which involves inverse of age and square root of age. The standardized residuals were retained to represent age-adjusted values.

Receiver operating characteristic (ROC) curves were then generated to obtain the values of area under the curve (AUC) with 95% CI, and also sensitivity and specificity, for each age-adjusted standardized body composition index as predictor of METS [26]. Assuming the BMI as the "A" standard method for diagnosing METS and the BMFI method as the new method to be tested (method "B"), considering the already demonstrated prevalence of METS in our obese population, a sample consisting of 300 children and adolescents with metabolic syndrome (METS+) and 1000 children without the metabolic syndrome (METS-), for a total of 1300 children, allows to estimate a difference of 0.05 in the area under the ROC curve (ROC-AUC) of a diagnostic test with a ROCAUC of 0.80 (standard method "A") and one with a ROC-AUC of 0.85 (new method "B") with a power of 94% at an alpha level = 0.05, using a two-tailed test with a continuous variable and a correlation between the two diagnostic tests equal to 0.6 in both METS+ and METS- children and adolescents. In addition, the likelihood ratio (LR+ and LR-), and positive and negative predictive values (+PV and -PV respectively), were examined.

To identify the optimal cutoff the Youden index [27] was calculated. The corresponding percentile value for each cutoff was used in the quantile regression to identify the age-specific body composition cutoff. A median regression with the waist circumference as response and the predicted value of the body composition index at the identified percentile level was used to calculate the corresponding waist circumference for the optimal cutoff. A within-subjects ANOVA analysis was performed to compare the waist circumference means for each index within the subjects.

The significance threshold was set at  $P < 0.05$ . The data were analyzed using SAS Enterprise Guide 4.3 (SAS Institute Inc., Cary, NC USA).

### Results

The clinical and laboratory characteristics of the study population are reported in Table 1. At the time of the study, the entire group of 1332 subjects fulfilled the criteria for obesity and all of them except two (males) had abdominal obesity according to the IDF criteria for METS.

High triglycerides values were present in 141 patients (67 males) (10.6%), while 521 (232 males) had reduced

**Table 1** Clinical characteristics of the subjects.

	Females	Males	All
<b>Number of subjects</b>	<b>778</b>	<b>554</b>	<b>1332</b>
Age yrs	14.5 ± 1.8	14.2 ± 1.9*	14.4 ± 1.8
BMI	37.2 ± 5.7	37.5 ± 5.9	37.3 ± 5.8
BMI SDS	2.96 ± 0.50	3.02 ± 0.61	2.99 ± 0.55
TMI	23.3 ± 3.6	22.6 ± 3.4°	23.0 ± 3.5
BMFI	22.6 ± 8.1	22.9 ± 8.6	22.7 ± 8.3
FMI	20.1 ± 4.9	19.2 ± 5.0°	19.7 ± 4.9
WtHR	0.69 ± 0.08	0.70 ± 0.07°	0.69 ± 0.08
FFMI	17.1 ± 1.9	18.3 ± 2.3&	17.6 ± 2.2
WC (cm)	109.9 ± 13.7	116.9 ± 13.9&	112.8 ± 14.2
SBP (mm/Hg)	122.7 ± 11.4	127.0 ± 12.7&	124.5 ± 12.1
DBP (mm/Hg)	77.2 ± 7.5	78.3 ± 8.1*	77.7 ± 7.8
HDL-C (mg/dl)	45.7 ± 10.6	42.4 ± 11.2&	44.3 ± 11.0
TG (mg/dl)	93.5 ± 42.1	100.9 ± 43.1*	96.6 ± 42.6
glycemia (mmol/L)	4.3 ± 0.4	4.4 ± 0.4°	4.4 ± 0.4

For significance: \*p < 0.01; °p < 0.001; &p < 0.0001.

HDL-C levels (39.1%). Five hundred fifty-one subjects (286 males) suffered from hypertension (41.4%), and only 4 of them was receiving treatment. Raised FPG was detected in 7 patients (3 males) (0.5%), while T2DM was present in 6 individuals (2 males) (0.45%). Altogether, the presence of METS was found in 309 patients (23.2%).

According to sex, we found that males were younger (p < 0.01), had lower TMI (p < 0.001), lower FMI (p < 0.001), higher FFMI (p < 0.0001), greater WC (p < 0.0001), greater WtHR (p < 0.001), higher systolic (p < 0.0001) and diastolic BP (p < 0.01), lower HDL-C (p < 0.0001), higher triglycerides (p < 0.01) and glycemia (p < 0.001) than females (Table 1).

METS was more frequent in males than in females (29.6% vs 18.6%; p < 0.0001). As expected, all parameters were significantly higher in the subjects with METS than in those without METS, both in males and in females, except glycemia (Table 2).

Figure 1 shows the threshold, which identify the risk of METS, for each index, according to sex and chronological age.

## Correlations

In Table 3, the AUC and the pairwise comparison of AUC of the different indexes are reported. BMFI performs better among females than TMI (p < 0.05), FMI and FFMI (both p < 0.01). BMFI performs better among males than TMI, FMI and WtHR (p < 0.05). BMI also performs better than TMI (females and males p < 0.01) and FFMI (females, p < 0.01). BMI and BMI SDS show the same performance.

In Table 4, the sensitivity, the specificity, the positive and negative predictive values together with the likelihood ratio for each index are reported. NPV showed high values for all indexes, as compared to PPV, even if sensitivity was higher than specificity.

In females BMI and BMFI showed the higher sensitivity (p < 0.05) while in males BMI and TMI were the most sensitive (p < 0.05).

WC and WtHR showed the highest specificity among females, while in males, BMFI, FMI, FFMI, WC and WtHR were superior in specificity to BMI and TMI (p < 0.05).

In Table 5 the results of the Pearson partial (age) correlation analysis. The Fisher's z transformation coefficients (95% CI) are reported, showing the relative influence and the correlations of the different parameters of METS on each adiposity index adjusted for age. The parameters of Mets are significantly associated with the different indexes, (p < 0.01) but triglycerides among males (all indexes) and glycemia vs FFMI.

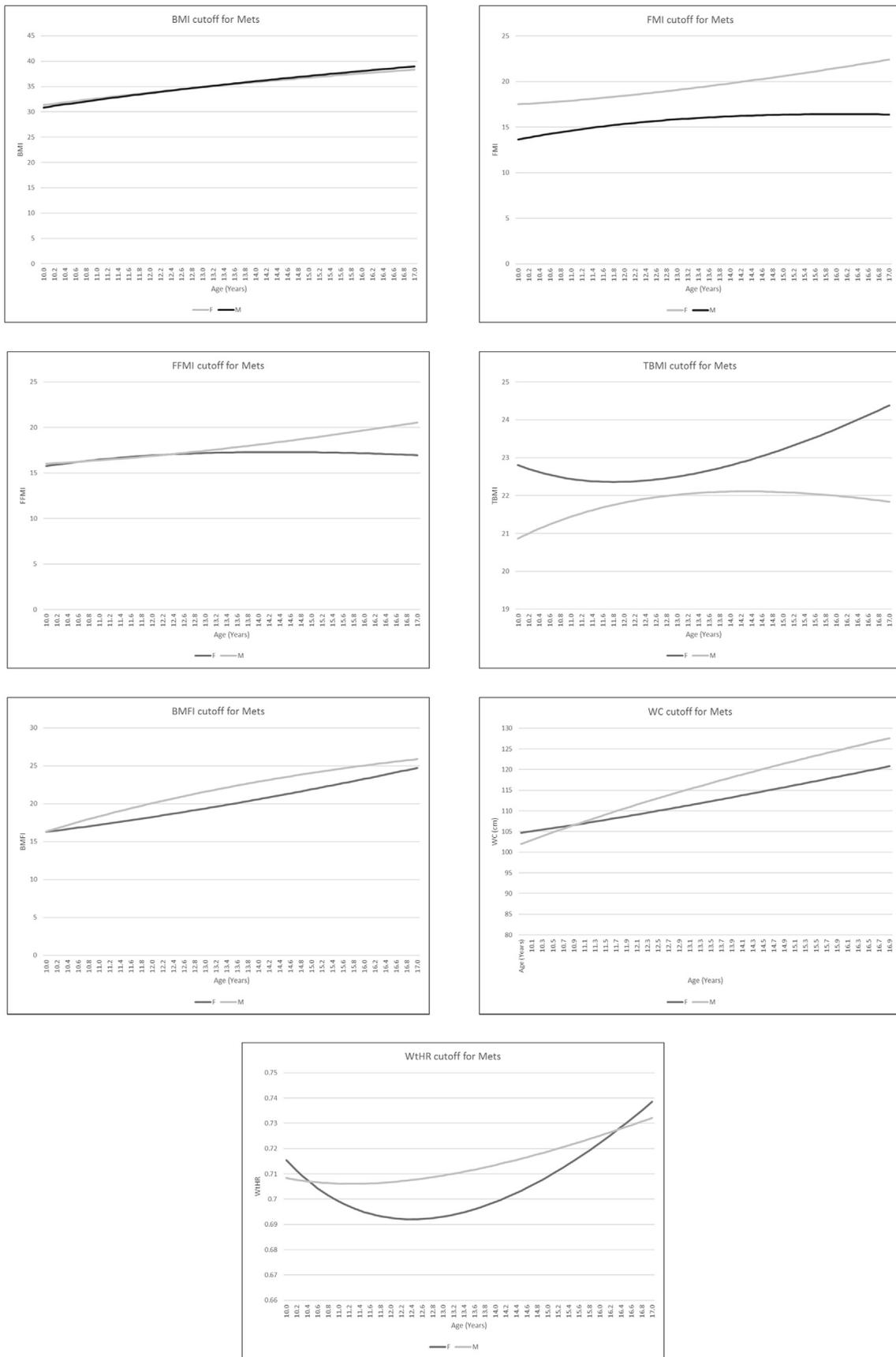
## Discussion

METS is specifically associated with increased risk for coronary heart disease, stroke and T2DM [28]. There is evidence that the prevalence of METS in children and adolescents has increased over the last 20 years, simultaneously with the epidemic development of obesity in this age group [29]. In this context, it is interesting to note that the prevalence of METS in this study was similar to our

**Table 2** Measurements of subjects subdivided according to sex and the absence or presence of METS.

	No METS		METS	
	Females	Males	Females	Males
<b>Number of subjects</b>	<b>633</b>	<b>390</b>	<b>145</b>	<b>164</b>
Age yr	14.4 ± 1.8	13.9 ± 1.8	14.9 ± 1.8 <sup>§</sup>	15.0 ± 1.7 <sup>&amp;</sup>
BMI	36.5 ± 5.4	36.6 ± 5.4	40.3 ± 6.1 <sup>&amp;</sup>	39.6 ± 6.6 <sup>&amp;</sup>
BMI SDS	2.90 ± 0.50	2.93 ± 0.57	3.22 ± 0.45 <sup>&amp;</sup>	3.25 ± 0.64*
TMI	22.9 ± 3.4	22.3 ± 3.2	25.0 ± 3.8 <sup>&amp;</sup>	23.2 ± 3.8 <sup>§</sup>
BMFI	21.5 ± 7.3	21.7 ± 7.3	27.2 ± 9.5 <sup>&amp;</sup>	26.0 ± 10.5 <sup>&amp;</sup>
FMI	19.5 ± 4.6	18.6 ± 4.5	22.6 ± 5.3 <sup>&amp;</sup>	20.6 ± 5.7 <sup>&amp;</sup>
WtHR	0.68 ± 0.08	0.70 ± 0.07	0.73 ± 0.08 <sup>&amp;</sup>	0.72 ± 0.08 <sup>&amp;</sup>
FFMI	17.0 ± 1.9	18.0 ± 2.3	17.7 ± 1.9 <sup>&amp;</sup>	18.9 ± 2.3 <sup>&amp;</sup>
WC (cm)	108.0 ± 12.7	114.4 ± 12.6	117.9 ± 14.7 <sup>&amp;</sup>	122.7 ± 14.9 <sup>&amp;</sup>
SBP (mm/Hg)	120.3 ± 9.9	124.0 ± 12.1	132.9 ± 11.8 <sup>&amp;</sup>	134.0 ± 11.3 <sup>&amp;</sup>
DBP (mm/Hg)	76.3 ± 7.2	77.2 ± 7.6	80.8 ± 7.9 <sup>&amp;</sup>	81.0 ± 8.7 <sup>&amp;</sup>
HDL-C (mg/dl)	47.9 ± 10.2	46.0 ± 11.1	36.0 ± 5.6 <sup>&amp;</sup>	33.9 ± 5.5 <sup>&amp;</sup>
TG (mg/dl)	83.7 ± 29.7	88.6 ± 30.5	136.1 ± 58.6 <sup>&amp;</sup>	130.2 ± 53.4 <sup>&amp;</sup>
glycemia (mmol/L)	4.3 ± 0.4	4.4 ± 0.4	4.4 ± 0.5	4.5 ± 0.4

For significance: <sup>§</sup>p < 0.01 for the difference vs subjects of the same sex without METS; \*p < 0.001 for the difference vs subjects of the same sex without METS; <sup>&</sup>p < 0.0001 for the difference vs subjects of the same sex without METS.



**Figure 1** Threshold for METS for each index in females and males.

**Table 3** The AUC and the pairwise comparison of AUC of the different indexes among females and males.

	BMFI	BMI	TMI	FMI	FFMI	WtHR	BMI SDS
<b>Females</b>							
AUC	0.69	0.68	0.66	0.67	0.61	0.68	0.68
BMFI	–	0.50	0.03	0.001	0.006	0.35	0.36
BMI		–	0.002	0.08	0.001	0.67	0.32
TPMI			–	0.55	0.03	0.42	0.01
FMI				–	0.05	0.71	0.15
FFMI					–	0.01	0.001
WtHR						–	0.77
<b>Males</b>							
AUC	0.59	0.58	0.55	0.58	0.55	0.56	0.58
BMFI	–	0.54	0.01	0.049	0.31	0.03	0.74
BMI		–	0.001	0.73	0.30	0.16	0.42
TPMI			–	0.05	0.97	0.78	0.001
FMI				–	0.49	0.22	0.56
FFMI					–	0.92	0.26
WtHR						–	0.12

previous observation, using the same definition criteria [30], remaining practically unchanged over the past decade. We found a higher prevalence of METS in males than in females, as previously reported both in pediatric age [31] and in adult patients [32]. Furthermore, we have detected a low prevalence of T2DM in our study group, at variance with what observed in other populations but in accordance with the incidence rates commonly observed in European countries [33]. The reliability of these findings derives from the large group of obese children assessed in a single center and by the same operators, which is the strength of our study.

The objective of this investigation was to compare different indexes, in order to identify in the most complete way which of these could be more reliable in discovering the METS presence, thus allowing to prevent cardiovascular diseases and T2DM. In the past an adiposity index was mostly considered a tool to assess the amount of weight excess, however in recent years it became clear that we do not need an index which simply evaluates weight excess, but we need an index which informs us whether an obese patient is already at risk for cardiovascular and metabolic diseases. Considering the limits of BMI [34], which only establishes the weight excess of a patient for his/her height, other indexes which also consider body composition (FFMI), body fat and body fat distribution

(FMI, TMI, WtHR) have been subsequently developed. In this light, we tested a new index, the BMFI, which in addition to the body composition also takes into consideration the WC, the latter considered a very accurate marker of cardiovascular risk [35].

In the present study we have calculated for each index a threshold value for age and sex, comparing thereafter all indexes each other, in order to check their accuracy, sensitivity and specificity predictive values and likelihood in identifying the METS. In particular, we were interested to verify which index might identify more accurately the METS. For this purpose, we have chosen waist circumference as the discriminating factor, i.e. we have evaluated which index identified METS at the smallest waist circumference.

As a matter of fact, there was a very good correlation among indexes ( $p < 0.0001$  for all), and no index performs clearly better than all the other ones. Correlation analysis shows that triglycerides are not associated with any index (among males) and that glycemia is not associated with FFMI.

As to the predictive value, NPV showed high values for all indexes, as compared to PPV, even if sensitivity was higher than specificity. This suggests that these indexes are more suitable to exclude than to identify METS. Furthermore, BMI SDS gave the same results as the BMI.

Two other studies, which similarly compared different adiposity indexes, showed a discriminatory power for TMI and FMI [12] and for WC and abdominal volume index [36], respectively, in identifying METS. The results were obtained however in a population of Colombian and Spanish children, and therefore we do not know whether they are applicable to our population.

Strength of this study is the large number of children and adolescents evaluated in the same obesity center, by the same personnel with the same modalities, which surely increases the reliability of the data. The major limitation of this study, on the other hand, is not having evaluated the percentage of body fat by DEXA, which however would have been impractical and too expensive to perform in such a large number of subjects. DEXA and BIA are not interchangeable for the assessment of body composition in obese subjects, as the former is considered the gold standard for assessing body fat. In this respect, however, we have used a validated prediction equation, able to give a satisfactory estimation of body composition

**Table 4** Sensitivity and specificity, positive and negative predictive value and the likelihood ratio for each index.

	Female						Male					
	Sensitivity	Specificity	PPV	NPV	LR+	LR–	Sensitivity	Specificity	PPV	NPV	LR+	LR–
BMI	0.80	0.55	0.29	0.92	1.76	0.37	0.63	0.51	0.35	0.77	1.28	0.73
TMI	0.66	0.60	0.27	0.88	1.64	0.57	0.57	0.51	0.33	0.74	1.18	0.83
BMFI	0.74	0.57	0.29	0.91	1.75	0.44	0.52	0.63	0.37	0.76	1.40	0.76
FMI	0.66	0.63	0.29	0.89	1.78	0.54	0.55	0.57	0.35	0.75	1.29	0.79
FFMI	0.65	0.56	0.25	0.87	1.48	0.63	0.55	0.60	0.37	0.76	1.38	0.75
WC	0.57	0.70	0.31	0.88	1.93	0.61	0.55	0.63	0.38	0.77	1.48	0.72
WtHR	0.61	0.67	0.30	0.88	1.86	0.58	0.49	0.63	0.36	0.75	1.32	0.81
BMI SDS	0.81	0.55	0.29	0.92	1.77	0.36	0.67	0.47	0.35	0.77	1.27	0.70

**Table 5** Pearson partial<sup>a</sup> correlations statistics (Fisher's z transformation). All results are shown as: Fisher's z (95% CI).

	SPB	DBP	HDL_C	Glycemia	TG
<b>Females (n = 778)</b>					
BMI	0.32 (0.25, 0.38)	0.25 (0.18, 0.31)	-0.18 (-0.25, -0.11)	0.10 (0.03, 0.17) (0.17, 0.24)	0.17 (0.10, 0.24)
TMI	0.25 (0.19, 0.32)	0.21 (0.14, 0.27)	-0.16 (-0.23, -0.09)	0.10 (0.03, 0.17) (0.17, 0.24)	0.17 (0.10, 0.24)
BMFI	0.31 (0.25, 0.37)	0.27 (0.20, 0.33)	-0.18 (-0.25, -0.11)	0.11 (0.04, 0.18) (0.18, 0.24)	0.17 (0.10, 0.24)
Fat Mass Index	0.30 (0.23, 0.36)	0.25 (0.18, 0.31)	-0.16 (-0.22, -0.09)	0.11 (0.04, 0.18) (0.18, 0.22)	0.15 (0.08, 0.22)
Fat Free Mass Index	0.19 (0.12, 0.26)	0.12 (0.05, 0.19)	-0.15 (-0.22, -0.08)	0.02 (-0.05, 0.09) <sup>o</sup>	0.13 (0.06, 0.20)
WtHR	0.21 (0.14, 0.28)	0.22 (0.15, 0.28)	-0.20 (-0.26, -0.13)	0.11 (0.04, 0.17) (0.17, 0.28)	0.21 (0.14, 0.28)
BMI SDS	0.30 (0.24, 0.36)	0.24 (0.17, 0.31)	-0.20 (-0.26, -0.13)	0.10 (0.03, 0.17) (0.17, 0.26)	0.19 (0.12, 0.26)
<b>Males (n = 554)</b>					
BMI	0.44 (0.37, 0.50)	0.31 (0.24, 0.39)	-0.22 (-0.30, -0.14)	0.18 (0.09, 0.25) (-0.05, 0.11) <sup>o</sup>	0.03 (-0.05, 0.11) <sup>o</sup>
TMI	0.28 (0.21, 0.36)	0.24 (0.16, 0.32)	-0.13 (-0.21, -0.04)	0.21 (0.13, 0.29) (0.29, 0.08) <sup>o</sup>	0.00 (-0.09, 0.08) <sup>o</sup>
BMFI	0.39 (0.32, 0.46)	0.31 (0.23, 0.38)	-0.21 (-0.29, -0.13)	0.23 (0.15, 0.31) (-0.05, 0.11) <sup>o</sup>	0.03 (-0.05, 0.11) <sup>o</sup>
Fat Mass Index	0.36 (0.29, 0.43)	0.29 (0.21, 0.37)	-0.17 (-0.25, -0.09)	0.23 (0.15, 0.31) (-0.08, 0.09) <sup>o</sup>	0.01 (-0.08, 0.09) <sup>o</sup>
Fat Free Mass Index	0.33 (0.26, 0.41)	0.17 (0.09, 0.25)	-0.20 (-0.27, -0.11)	-0.06 (-0.14, 0.03) <sup>o</sup>	0.06 (-0.02, 0.14) <sup>o</sup>
WtHR	0.22 (0.14, 0.30)	0.23 (0.15, 0.31)	-0.16 (-0.24, -0.08)	0.23 (0.15, 0.31) (-0.05, 0.12) <sup>o</sup>	0.03 (-0.05, 0.12) <sup>o</sup>
BMI SDS	0.45 (0.39, 0.52)	0.31 (0.23, 0.38)	-0.23 (-0.31, -0.15)	0.15 (0.07, 0.23) (0.23, -0.05, 0.12) <sup>o</sup>	0.04 (-0.05, 0.12) <sup>o</sup>

For significance: all parameters showed a p value of <0.01, except glycemia vs FFMI (>0.05) and TG for all indexes in males only (<sup>o</sup>p > 0.05).

<sup>a</sup> Partial variable: age.

in obese children and adolescents from measurements of stature and body impedance [13].

Furthermore, since our investigation is a cross-sectional study, aimed at identifying the most sensible index that recognizes the presence of METS, we are unable to predict whether the METS will persist in our patients or will appear in the future in those patients who are borderline or presenting some of the criteria for defining METS. Altogether, contrary to our initial hypothesis, in obese children and adolescents we have demonstrated that the first developed, simplest and most commonly used index, the BMI, performs as good as other indexes which also consider body composition and fat distribution, in turn

considered as more reliable in predicting the risk of cardio-metabolic disease in recent years. We believe that our results represent a good information for the clinicians since the BMI can be easily and quickly calculated in out-patients. Furthermore, the use of BMI also allows a reduction of the costs because it does not need the assessment of body composition.

## Disclosure statement

The authors have nothing to disclose.

## References

- [1] Borrueal S, Moltó JF, Alpañés M, Fernández-Durán E, Álvarez-Blasco F, Luque-Ramírez M, et al. Surrogate markers of visceral adiposity in young adults: waist circumference and body mass index are more accurate than waist hip ratio, model of adipose distribution and visceral adiposity index. *PLoS One* 2014;9(12): e114112. <https://doi.org/10.1371/journal.pone.0114112>.
- [2] World Health Organization. Obesity and overweight. 2011. <http://www.who.int/mediacentre/factsheets/fs311/en/>.
- [3] Kim SH, Després JP, Koh KK. Obesity and cardiovascular disease: friend or foe? *Eur Heart J* 2016;37(48):3560–8. <https://doi.org/10.1093/eurheartj/ehv509>.
- [4] Allison DB, Zhu SK, Plankey M, Faith MS, Heo M. Differential associations of body mass index and adiposity with all cause mortality among men in the first and second National Health and Nutrition Examination Surveys (NHANES I and NHANES II) follow-up studies. *Int J Obes Relat Metab Disord* 2002;26(3):410–6.
- [5] Peterson CM, Su H, Thomas DM, Heo M, Golnabi AH, Pietrobello A, et al. Tri-ponderal mass index vs body mass index in estimating body fat during adolescence. *JAMA Pediatr* 2017;171(7):629–36. <https://doi.org/10.1001/jamapediatrics.2017.0460>.
- [6] Rankinen T, Kim SY, Perusse L, Després JP, Bouchard C. The prediction of abdominal visceral fat level from body composition and anthropometry: ROC analysis. *Int J Obes Relat Metab Disord* 1999; 23:801–9.
- [7] Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, et al. (2010) Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. *Diabetes Care* 2010;33(4):920–2. <https://doi.org/10.2337/dc09-1825>.
- [8] Maffei C, Banzato C, Talamini G. Obesity Study Group of the Italian Society of Pediatric Endocrinology and Diabetology. Waist-to-height ratio, a useful index to identify high metabolic risk in overweight children. *J Pediatr* 2008;152(2):207–13. <https://doi.org/10.1016/j.jpeds.2007.09.021>.
- [9] Chen Z, Klimentidis YC, Bea JW, Ernst KC, Hu C, Jackson R, et al. Body mass index, waist circumference, and mortality in a large multi-ethnic postmenopausal cohort—results from the women's health initiative. *J Am Geriatr Soc* 2017 Sep;65(9):1907–15. <https://doi.org/10.1111/jgs.14790>.
- [10] Mohammadreza B, Farzad H, Davoud K, Fereidoun AF. Prognostic significance of the complex "Visceral Adiposity Index" vs. simple anthropometric measures: tehran lipid and glucose study. *Cardiovasc Diabetol* 2012;11:20. <https://doi.org/10.1186/1475-2840-11-20>.
- [11] Gomes TN, Nevill A, Katzmarzyk PT, Pereira S, Dos Santos MM, Buranarugs R, et al. Identifying the best body-weight-status index associated with metabolic risk in youth. *Scand J Med Sci Sports* 2018 Nov;28(11):2375–83. <https://doi.org/10.1111/sms.13249>. Epub 2018 Jul 16.
- [12] Ramírez-Vélez R, Correa-Bautista JE, Carrillo HA, González-Jiménez E, Schmidt-RíoValle J, Correa-Rodríguez M, et al. Tri-ponderal mass index vs. Fat mass/height<sup>3</sup> as a screening tool for metabolic syndrome prediction in Colombian children and young people. *Nutrients* 2018 Mar 27;10(4). <https://doi.org/10.3390/nu10040412>. pii: E412.
- [13] VanItallie TB, Yang MU, Heymsfield SB, Funk RC, Boileau RA. Height-normalized indices of the body's fat-free mass and fat mass: potentially useful indicators of nutritional status. *Am J Clin Nutr* 1990;52(6):953–9.

- [14] Mooney SJ, Baecker A, Rundle AG. Comparison of anthropometric and body composition measures as predictors of components of the metabolic syndrome in a clinical setting. *Obes Res Clin Pract* 2013;7(1):e55–66. <https://doi.org/10.1016/j.orcp.2012.10.004>.
- [15] Abbasi F, Blasey C, Reaven GM. Cardiometabolic risk factors and obesity: does it matter whether BMI or waist circumference is the index of obesity? *Am J Clin Nutr* 2013;98(3):637–40. <https://doi.org/10.3945/ajcn.112.047506>.
- [16] Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity and stages of puberty. *Arch Dis Child* 1976;51:170–9.
- [17] Cacciari E, Milani S, Balsamo A, Spada E, Bona G, Cavallo L, et al. Italian cross-sectional growth charts for height, weight and BMI (2 to 20 yr). *J Endocrinol Invest* 2006;29(7):581–93.
- [18] Lazzer S, Bedogni G, Agosti F, De Col A, Mornati D, Sartorio A. Comparison of dual-energy X-ray absorptiometry, air displacement plethysmography and bioelectrical impedance analysis for the assessment of body composition in severely obese Caucasian children and adolescents. *Br J Nutr* 2008;100(4):918–24. <https://doi.org/10.1017/S0007114508922558>.
- [19] Lukaski HC, Bolonchuk WW, Hall CB, Siders WA. Validation of tetrapolar bioelectrical impedance method to assess human body composition. *J Appl Physiol* 1986 Apr;60(4):1327–32.
- [20] Kurian MJ, Carracher AM, Close KL. American diabetes association 78th scientific sessions. *J Diabetes* 2018. <https://doi.org/10.1111/1753-0407.12830>.
- [21] National, Heart, Lung and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics* 2011; 128(Suppl 5):S213–56. <https://doi.org/10.1542/peds.2009-2107C>.
- [22] Zimmet P, Alberti KG, Kaufmann F, Tajima N, Silink M, Arslanian S, et al. IDF consensus group. The metabolic syndrome in children and adolescents - an IDF consensus report. *Pediatr Diabetes* 2007; 8(5):299–306.
- [23] McCharty HD, Jarret KV, Crawley HF. The development of waist circumference percentiles in British children aged 5.0 ± 16.9 y. *Eur J Clin Nutr* 2001;55:902–7.
- [24] Chen C. Growth charts of body mass index (BMI) with quantile regression. In: Proceedings of international conference on algorithmic mathematics and computer science. Las Vegas; 2005. p. 1–7.
- [25] Cole TJ, Freeman JV, Preece MA. British 1990 growth reference centiles for weight, height, body mass index and head circumference fitted by maximum penalized likelihood. *Stat Med* 1998 28;17(4):407–29.
- [26] Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, Berenson GS. Body mass index, waist circumference, and clustering of cardiovascular disease risk factors in a biracial sample of children and adolescents. *Pediatrics* 2004;114(2):e198–205.
- [27] Youden WJ. Index for rating diagnostic tests. *Cancer* 1950;3(1): 32–5.
- [28] Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. *J Am Coll Cardiol* 2010;56(14):1113–32. <https://doi.org/10.1016/j.jacc.2010.05.034>.
- [29] Bussler S, Penke M, Flemming G, Elhassan YS, Kratzsch J, Sergeev E, et al. Novel insights in the metabolic syndrome in childhood and adolescence. *Horm Res Paediatr* 2017;88(3–4): 181–93. <https://doi.org/10.1159/000479510>.
- [30] Lafortuna CL, Adorni F, Agosti F, De Col A, Sievert K, Siegfried W, et al. Prevalence of the metabolic syndrome among extremely obese adolescents in Italy and Germany. *Diabetes Res Clin Pract* 2010;88(1):14–21. <https://doi.org/10.1016/j.diabres.2010.01.008>.
- [31] Lee AM, Gurka MJ, DeBoer MD. Trends in metabolic syndrome severity and lifestyle factors among adolescents. *Pediatrics* 2016; 137(3). <https://doi.org/10.1542/peds.2015-3177>. e20153177.
- [32] Lafortuna CL, Agosti F, De Col A, Pera F, Adorni F, Sartorio A. Prevalence of the metabolic syndrome and its components among obese men and women in Italy. *Obes Facts* 2012;5(1):127–37. <https://doi.org/10.1159/000336700>.
- [33] Fazeli Farsani S, van der Aa MP, van der Vorst MM, Knibbe CA, de Boer A. Global trends in the incidence and prevalence of type 2 diabetes in children and adolescents: a systematic review and evaluation of methodological approaches. *Diabetologia* 2013; 56(7):1471–88. <https://doi.org/10.1007/s00125-013-2915-z>.
- [34] Demerath EW, Schubert CM, Maynard LM, Sun SS, Chumlea WC, Pickoff A, et al. Do changes in body mass index percentile reflect changes in body composition in children? Data from the Fels Longitudinal Study. *Pediatrics* 2006;117(3):e487–95.
- [35] Hirschler V, Aranda C, Calcagno Mde L, Maccalini G, Jadzinsky M. Can waist circumference identify children with the metabolic syndrome? *Arch Pediatr Adolesc Med* 2005;159(8):740–4.
- [36] Perona JS, Schmidt Rio-Valle J, Ramírez-Vélez R, Correa-Rodríguez M, Fernández-Aparicio Á, González-Jiménez E. Waist circumference and abdominal volume index are the strongest anthropometric discriminators of metabolic syndrome in Spanish adolescents. *Eur J Clin Invest* 2019 Mar;49(3):e13060. <https://doi.org/10.1111/eci.13060>.