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Impact of different metabolic syndrome classifications on the metabolic syndrome prevalence in a young Middle Eastern population

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Abstract

The metabolic syndrome (MetS) prevalence in a young Middle Eastern population has never been studied. We studied this prevalence in a randomly selected population of Lebanese students using different MetS classifications. Three hundred eighty-one subjects aged 18 to 30 years were included in the study. Anthropometric and biological parameters (waist circumference [WC], systolic and diastolic blood pressures, fasting plasma glucose, triglycerides, total cholesterol, high-density lipoprotein cholesterol, and homeostasis model assessment [HOMA] index to assess insulin resistance) were measured. Receiver operating characteristic (ROC) curves were generated to determine population-specific cutoff values for MetS parameters and HOMA index. The MetS prevalence was calculated using the National Cholesterol Education Program's Adult Treatment Panel III (ATP-III), the actualized ATP-III, and our cutoffs, either with or without HOMA index as an extra risk factor. The MetS prevalence using the ATP-III and the actualized ATP-III was, respectively, 5.25% and 5.28%. It increased to 9.19% when using our cutoff values and to 12.64% when HOMA index was added. This increase was significant only in men. The identified cutoff values are, for WC, 91 cm in women and 99.5 cm in men and, for HOMA index, 2.32. Among the MetS components, WC was the best MetS predictor, whereas fasting plasma glucose was the poorest. Our study shows that the MetS prevalence in Lebanon is comparable with other countries. In addition, we identified in our population new cutoff points for MetS parameters and HOMA index that allow the detection of a higher number of subjects with the MetS, mainly in the male population.

1. Introduction

The metabolic syndrome (MetS) was first described by Reaven [1] in 1988 as a cluster of risk factors for diabetes and cardiovascular disease such as obesity, dyslipidemia, hypertension, and impaired fasting plasma glucose (FPG). Subsequently, several definitions for this entity have been proposed [2-4]. The 2 mainly retained definitions are those of the World Health Organization [2] and the National Cholesterol Education Program's (NCEP's) Adult Treatment Panel III (ATP-III) [4]. The ATP-III is more commonly used because its criteria are easily measurable because they do not include insulin resistance, which is a nonreproducible measurement [5].

Worldwide, the prevalence of the MetS significantly increases with age [6-8] and can vary in the same population depending on the used definition [9,10]. This prevalence is also ethnic dependent [10-12], being much more prevalent in Hispanics compared with African Americans and Europeans [10]. In the Arab world, using the ATP-III panel criteria, the MetS prevalence was 24.3% in a population older than 40 years [13]. The prevalence of the MetS in populations younger than 30 years has been the subject of several publications [6-8,14-17]. Worldwide, this prevalence changes according to the study population and ranges from 2.9% [6] to 11.0% [7]. To our knowledge, no previous study looked at this prevalence in a Middle Eastern young population.

On the other hand, insulin resistance, which is not included in the ATP-III definition and which is commonly

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measured by the homeostatic model assessment (HOMA) index, predicts cardiovascular disease independently of the MetS [18].

The objective of this study is to assess the prevalence of the MetS according to the original and actualized ATP-III (ATP-IIIa) panel risk factors [4] in a representative sample of Lebanese students who are 18 to 30 years old. In addition, our study will define new cutoff values for the MetS parameters in our population and will look at the relation between MetS and HOMA index.

2. Materials and methods

2.1. Participants

Participants were students recruited from the Saint Joseph University Medical Sciences Campus located in Beirut. This private university, the second biggest one in Lebanon, admits students from all parts of the country that has an overall population of 4 million inhabitants. To obtain a sample representative of the young Lebanese population based on probability, approximately 400 subjects were needed, taking into account an error of 2%. Students were recruited randomly using a computerized database of 2082 registered names. An age- and sex-stratified population was selected by first dividing our database into 2 groups of men or women and then into 13 age subgroups, ranging from 18 to 30 years old, ending up with 26 subgroups. Fifteen names were randomly selected within each subgroup. Three hundred eighty-one randomly selected students of the 390 initially selected ones from both sexes accepted to participate in the study.

Every participant signed a written and informed consent that has been previously approved by our University Ethical Committee. Exclusion criteria were pregnancy, or use of contraceptive pills or drugs that may affect lipid profile and/or metabolic parameters.

The following anthropometric measures, performed using the same devices throughout this study, were taken by a registered nurse: height in meters, weight in kilograms using a manual scale, and waist circumference (WC) taken at the umbilicus in centimeters. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in millimeters of mercury in seated subjects after a rest of at least 15 minutes using a mercury tensiometer. Body mass index (BMI) was calculated as the weight in kilograms divided by the square of height in meters.

Subjects were classified as MetS positive (MetS[+]) according to the ATP-III criteria whenever at least 3 of the 5 following risk factors were found: increased WC of at least 102 cm in men and of at least 88 cm in women, elevated serum triglycerides of at least 150 mg/dL (or ≥1.70 mmol/L), reduced serum high-density lipoprotein (HDL) cholesterol of less than 40 mg/dL in men (or <1.04 mmol/L) and less than 50 mg/dL in women (or <1.30 mmol/L), FPG greater than 110 mg/dL (or >6.1 mmol/L), and elevated SBP of at least 130 mm Hg and/or DBP of at least 85 mm Hg. The American Heart Association/National Heart, Lung, and Blood Institute scientific statement, known as the *actualized ATP-III risk factor panel* (ATP-IIIa) [19], differs from the classic ATP-III by its lower cutoff values for FPG level (glucose ≥100 mg/dL).

2.2. Biological parameters

Peripheral blood was collected after a 12-hour fasting period. For all the measurements, blood was collected on plain tubes except for the glucose where an oxalate fluoride tube was used. In the hour after blood withdrawal, samples were centrifuged and serum was divided in several aliquots: some were stored at −80°C for later insulin measurement, and others were biochemically analyzed on an automated Cobas Integra 400 by Roche Diagnostics (Maizy, France).

Glycemia was measured using the GOD-PAP method (glucose oxydase, peroxidase, phenol, and 4-aminophenazone). Total cholesterol was measured using the CHOD PAP method (cholesterol esterase, cholesterol oxidase, peroxidase, phenol, and 4-aminoantipyrine). High-density lipoprotein cholesterol was measured using the phosphotungstic acid precipitant method; and triglycerides, using the glycerol-3-phosphate oxidase method. Low-density lipoprotein (LDL) cholesterol was then calculated using the Friedewald equation if triglycerides were found to be less than 4.6 mmol/L. Fasting insulin level was measured for all samples on the same run using a commercial chemiluminescent assay (Immulite; DPC, Los Angeles, CA). The sensitivity of the assay was 2 mIU/mL, the intraassay coefficient of variation was 6.4%, and the cross-reactivity with proinsulin was 8.5%. Insulin resistance was calculated using the *HOMA index* defined as (fasting immunoreactive insulin in microunits per liter × FPG in millimoles per liter)/22.5 [20]. The laboratory that did all measurements underwent a regular external quality control provided by Probioqual (Lequas, provided by Randox, Crumlin, UK).

2.3. Statistical analysis

Statistical analysis was performed using SPSS (Chicago, IL) version 13.0. Data are expressed as mean or as percentage ± SD. Univariate analysis was performed using the Pearson coefficient of correlation. Student *t* test was used to compare mean values between MetS(+) and MetS-negative (MetS[−]) subjects, and between men and women. A bilateral test of comparison of proportions was used to compare the percentages of men and women for each of the different MetS classifications and to compare the areas under the receiver operating characteristic (ROC) curves. Data were considered statistically significant if *P* values were less than .05.

To identify appropriate cutoff values for all the studied parameters, an ROC curve was generated for each studied parameter: BMI, SBP, DBP, FPG, triglycerides, and HOMA index. The WC and HDL cholesterol ROC curves were

Table 1
Clinical and biological data of the study population related to the MetS

	Total (N = 381)	Men (n = 201)	Women (n = 180)	P[b]
Clinical data (mean ± SD)				
BMI[a] (kg/m^2)	23.9 ± 4.1	25.5 ± 4.1	22.0 ± 3.3	<.0001
SBP (mm Hg)	111 ± 13	117 ± 10	104 ± 12	<.0001
DBP (mm Hg)	71 ± 10	74 ± 9	66 ± 9	<.0001
WC (cm)	82.7 ± 12.2	89.6 ± 11.0	75.0 ± 8.4	<.0001
Age[a]	23.9 ± 3.9	24.1 ± 3.9	23.8 ± 4.0	.39
Biological data				
FPG (mmol/L)	4.87 ± 0.27	4.93 ± 0.29	4.81 ± 0.23	<.0001
Triglycerides (mmol/L)	1.1 ± 0.7	1.2 ± 0.8	0.9 ± 0.5	<.0001
HDL cholesterol (mmol/L)	1.2 ± 0.3	1.1 ± 0.3	1.3 ± 0.3	<.0001
Total cholesterol (mmol/L)[a]	4.6 ± 1.0	4.5 ± 1.0	4.6 ± 1.1	.35
LDL cholesterol (mmol/L)[a]	2.8 ± 1.0	2.8 ± 0.9	2.8 ± 1.0	.94
HOMA index[a]	1.98 ± 1.1	2.11 ± 1.17	1.82 ± 0.99	.009

Data are expressed as mean ± SD.
[a] Risk factors not listed in the NCEP ATP-III panel.
[b] Comparison between men and women.

generated separately for men and women as defined in the ATP-III criteria. The optimal cutoff value of each tested parameter was chosen as being the point on the curve that maximizes the sum of squares of sensitivity and specificity ([sensitivity]^2 + [specificity]^2) to obtain the best sensitivity/specificity couple. The area under the ROC curve should be greater than 0.5. Area under the ROC curve equal to 1 would be the perfect test for a given cutoff value to discriminate the MetS risk, whereas area under the ROC curve equal to 0.5 is a test of probability of head or tails when tossing a coin.

3. Results

Three hundred eighty-one subjects were included in this cross-sectional study (201 men and 180 women). The population age ranges between 18 and 30 years, with a mean of 23.9. Baseline characteristics of the population (clinical and biological parameters) are shown in Table 1.

3.1. Prevalence of the MetS according to ATP-III and to ATP-IIIa

The overall frequency of the MetS is 5.25%, 7.47% in men and 2.78% in women, which correspond, respectively, to 15 men and 5 women (Fig. 1A). None of the tested male subjects has 5 risk factors, only 2 have 4 risk factors, and 13 have 3 risk factors. The 5 women have 3 risk factors. The difference in the MetS prevalence between men and women is statistically significant (P = .034). With the ATP-IIIa criteria, the MetS prevalence becomes 5.28% in the overall population, 7.00% in men and 3.35% in women.

3.2. Comparison of clinical and biological parameters in subjects with or without the MetS

The MetS(+) subjects have significantly higher age and BMI compared with the MetS(−) ones (P < .0001 for both variables); 4.2% of the MetS(−) population has a BMI greater than 30 kg/m^2, compared with 75% of the MetS(+) one. In addition, it was not surprising to find that SBP, DBP, WC, serum triglycerides, and FPG levels are all statistically higher in subjects with the MetS compared with those without the MetS, whereas HDL cholesterol is statistically lower (P < .001 for all variables). We then looked at the risk factors not included in the NCEP ATP-III panel. The MetS(+) subjects have statistically higher total cholesterol levels and HOMA index compared with the MetS(−) ones (P = .04 and P < .0001, respectively). However, LDL cholesterol level was not found to be statistically different between the 2 groups.

3.3. Definition of the best cutoff values of the MetS

To identify new cutoff values that better diagnose the MetS in our population, we assessed all the tested

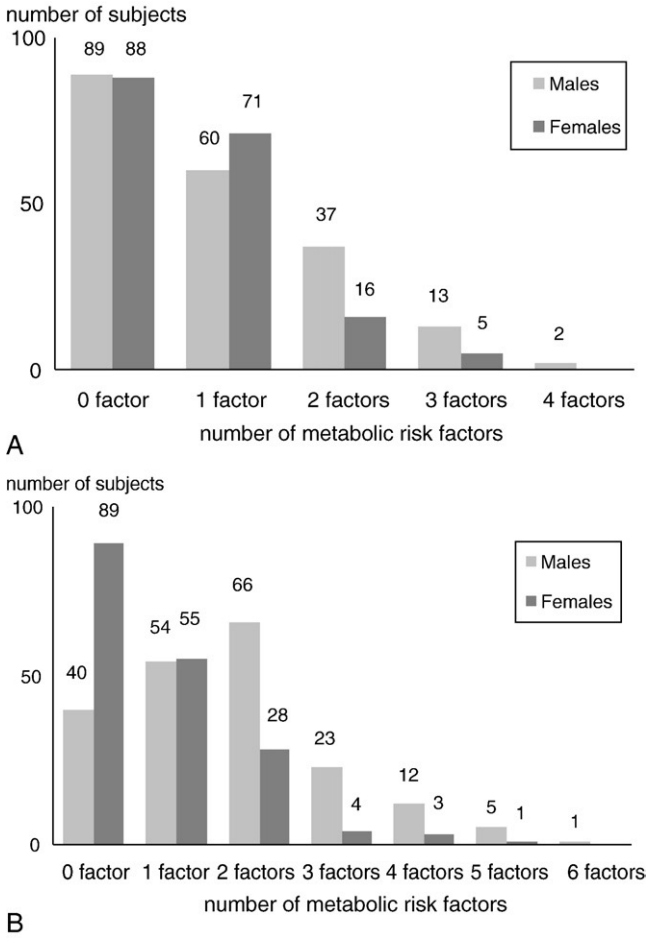

Fig. 1. Repartition of subjects according to the number of risk factors for the MetS using the original NCEP ATP-III classification (A) and our newly identified cutoff values including HOMA index as an extra risk factor in both men and women (B).

Table 2
Best cutoff deduced values from the ROC curves analysis, with best specificity and sensitivity of clinical and biological parameters for the occurrence of the MetS

Clinical data		Cutoff value	Sensitivity (%)	Specificity (%)	Area under ROC curve
BMI kg/m^2		27.5	95	89	0.95
SBP (mm Hg)[a]		125	85	90	0.87
DBP (mm Hg)[a]		77.5	90	73	0.86
WC (cm)[a,b]	Men	99.5	87	90	0.92
	Women	91	100	98	0.99
Biological data					
FPG (mmol/L)[a]		4.91	75	61	0.71
Triglycerides (mmol/L)[a]		1.64	80	91	0.89
HDL cholesterol (mmol/L)[a,b]	Men	0.85	88	45	0.75
	Women	1.08	82	57	0.71
HOMA index		2.32	85	84	0.88

[a] Risk factors of the NCEP ATP-III panel.
[b] The analysis was performed separately in men and women for WC and for HDL cholesterol because cutoff values are sex specific in the ATP-III definition.

parameters listed above using the ROC curves (Table 2, Figs. 2 and 3).

Waist circumference is the best predictor factor of the MetS, with a cutoff value of 99.5 cm in men and 91 cm in women. The respective sensitivity and specificity of these values in the MetS prediction are 87% and 90% for men and 100% and 98% for women. The area under the ROC curve for this parameter in the overall population is 0.94. Triglycerides and both SBP and DBP have lower area under the ROC curve values and respective cutoff values of 1.64 mmol/L, 125 mm Hg, and 77.5 mm Hg (Table 2). High-density lipoprotein cholesterol has a low area under the curve value and a cutoff value of 0.85 mmol/L in men and 1.08 mmol/L in women, compared with 1.04 mmol/L and 1.30 mmol/L, respectively, in the ATP-III panel criteria. Fasting plasma glucose has the smallest area under the curve value and a cutoff value of 4.91 mmol/L. Finally, the deduced cutoff value of HOMA index is 2.32; and the value of its area u8nder the curve is 0.88. We then performed a comparative analysis of the "area under the ROC curves" values. We found that both areas under the ROC curve values of WC and BMI (which are the highest values among all the variables) were statistically higher in comparison with each of SBP, DBP, FPG, HOMA index, and HDL cholesterol values ($P <$ .0001 for all variables), whereas the significance with triglycerides equals .0001.

3.4. Relation between NCEP ATP-III risk parameters and HOMA index

The HOMA index is strongly correlated with BMI, SBP, DBP, WC, FPG, and triglycerides ($r = 0.53$, $r = 0.28$, $r = 0.36$, $r = 0.61$ in men and 0.43 in women, $r = 0.34$, $r = 0.31$, respectively; with $P < .001$ for all variables), whereas the correlation with HDL cholesterol is weak in men ($r = -0.16$, $P < .05$) and nonsignificant in women ($r = -0.04$).

3.5. Prevalence of the MetS using the new cutoff values for the MetS with and without the HOMA index as an extra risk factor

Using our newly defined cutoff values, the MetS prevalence increases markedly in men (14.43% vs 7.47% for the ATP-III, $P = .03$), whereas the increase in women is not significant (3.34% vs 2.78%). Finally, when we add the

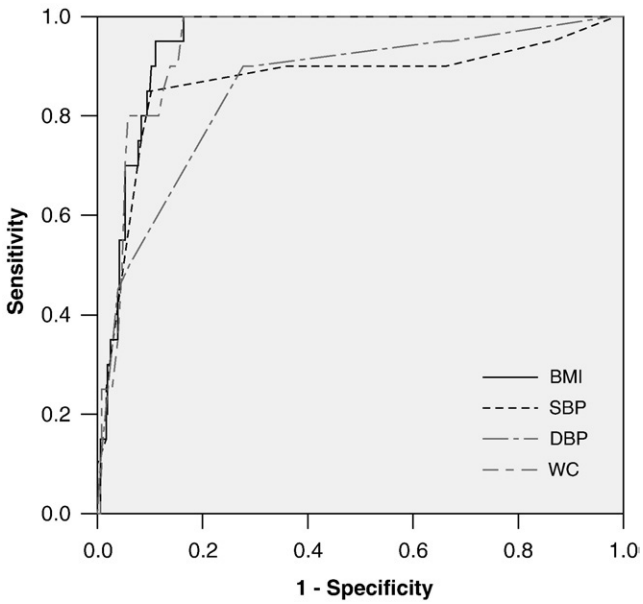

Fig. 2. The ROC curves of clinical parameters.

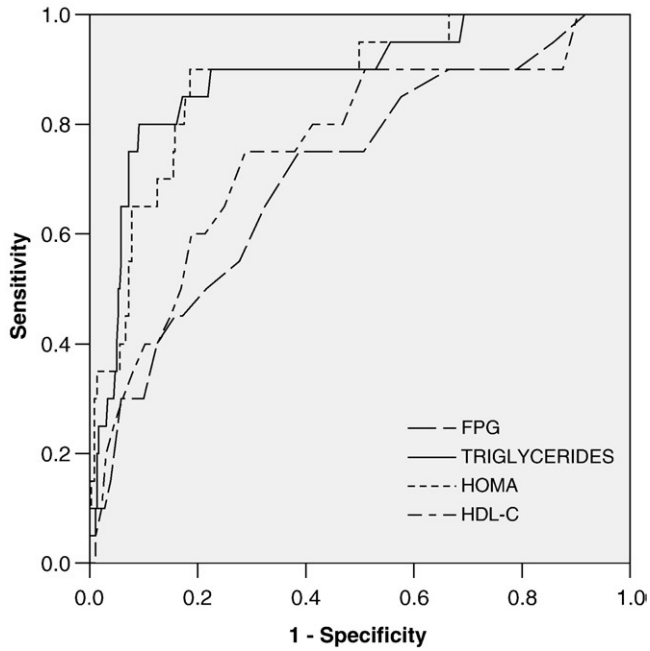

Fig. 3. The ROC curves of biological parameters.

Table 3
Prevalence of the MetS in the whole population and in men and women using the NCEP ATP-III panel, the ATP-IIIa, the ATP-III criteria with our own cutoff values, and our own cutoff values of ATP-III plus HOMA index

MetS definition	Total population	Men	Women	P [a]
ATP-III	5.25 ± 1.7	7.47 ± 1.8	2.78 ± 1.2	.034
ATP-IIIa	5.28 ± 1.1	7.00 ± 1.8	3.35 ± 1.3	.1
Our ATP-III cutoffs	9.19 ± 2.1	14.43 ± 2.5	3.34 ± 1.3	<.0001
Our ATP-III cutoffs + HOMA index	12.64 ± 2.5	20.40 ± 2.8	3.98 ± 1.5	<.0001

Data are expressed as percentage ± SD.
[a] Comparison between men and women.

HOMA index as the sixth risk factor, the *MetS prevalence* (defined as the presence of at least 3 of the overall 6 risk factors) increases to 20.40% (corresponding to 40 subjects) in men ($P < .001$ compared with the ATP-III prevalence) (Fig. 1B), whereas the increase in women is slight and non-significant (3.98%, corresponding to 8 subjects) (Table 3).

4. Discussion

Our results show that the prevalence of the MetS in a sample of the young Lebanese population is 5.25% using the ATP-III panel criteria. This prevalence is comparable with other published prevalences worldwide in the 18- to 30-year age range and using, similarly to our study, the ATP-III criteria. In the United States, in a 20- to 29-year-old population, this prevalence was 6.7% [14]. In European populations [7,15-17], the prevalence ranges from 3% to 11%; it is the lowest in Italy [16] and the highest in Norway [7]. Worldwide, the MetS prevalence is the lowest in Asian populations and varies between 2.9% and 3.1% [6,21]. Our study is the first one to be performed on a Middle Eastern population. The prevalence we observed is comparable with the Greek one, which is 4.8% in a population aged 19 to 29 years [17].

We found that MetS(+) subjects are significantly older than MetS(−) ones. This suggests that, despite the small age range in our population, the appearance of the MetS can occur early in life. Consistent with this finding, in the Arab Tunisian population older than 40 years [13], the MetS prevalence was 24.3%, which is much higher than what was found in our young population. In addition, the higher prevalence we observed in men has been described in studies performed on young populations [6,22]. This sex difference was also observed in the Tunisian study [13].

We recalculated the MetS prevalences using first the ATP-IIIa and then our newly identified cutoff values for the MetS risk factors. No statistical difference was observed in the MetS prevalence in both men and women using the ATP-III and ATP-IIIa criteria. However, when using our own cutoff values, a significant increase in the MetS prevalence in men but not in women was noticed. Similar results were obtained in a study conducted in Germany where the impact of changing MetS definitions was higher for men than women, hence widening the sex gap [23]. These results emphasize the importance of using, at least in our young male population, our own established cutoff values to identify a higher percentage of subjects at high risk for cardiovascular disease.

We then calculated this prevalence when HOMA index was added as an additional risk factor. This approach led to a significant increase in the MetS prevalence in our male population, which could be explained by the higher prevalence of cardiovascular risk factors in men. A similar approach, using an ROC curve, was done in a Spanish study performed on children. The identified HOMA index cut point was comparable with ours (2.28 vs 2.32) [24]. Another Korean study performed on nondiabetic adults and using also ROC curves adopted a HOMA index cutoff of 2.34 [25]. Finally, in a third study done on a white rural population, the HOMA cutoff value, determined as the 75th percentile, was 2.29 [26], as opposed to 2.45 in our population. The fact that quite similar cutoff values for HOMA index were found in populations of different age ranges may suggest ethnic differences because HOMA index increases with age [27]. The use of different commercial insulin assays could also explain these differences. However, in the 3 studies mentioned above, the authors did not compare different MetS classifications. Our study is the first one to compare in a same population a worldwide MetS classification using established cutoff values with new population-specific cutoff points.

Waist circumference represents a link between cardiovascular disease and the other MetS components [28]. In this study, it was found to be the most prevalent risk factor and the strongest predictor of the MetS, similarly to what was previously reported in Jordanian women [29]. Because, to date, there are still no available data in Middle Eastern Arab populations and because WC value is ethnic dependent, it was suggested to use WC European cutoff points until more specific data are available [10,28]. For the first time, we identified new cutoff values for WC with an excellent discriminating power that can be used as references for Middle Eastern populations. Comparable results were obtained for WC in a study done in Sweden [30]. The newly identified WC cutoffs in our study are, compared with those of ATP-III, lower in men (99.5 cm) and higher in women (91 cm), explaining probably the increase in the MetS prevalence in men but not in women, thus exacerbating the sex difference in the MetS prevalence. Similar approaches were done in Asian populations. In a Korean population [31], a modification of the NCEP ATP-III criteria by optimizing WC appropriately to Asians allowed an increase in the MetS prevalence from 16.0% to 29.0% in men and from 10.7% to 16.8% in women. Furthermore, in China [32], using ROC curves, a lowering of the WC cutoff values to 85 cm in men and 80 cm in women yielded an increase in the MetS prevalence. Because central obesity plays a major role in the development of the MetS and seems to precede the

appearance of the other MetS components [33,34], our new WC cutoff values could be used as a primary screening tool to identify subjects at high risk for developing type 2 diabetes mellitus or cardiovascular disease [35]. This approach is particularly interesting in our male population, where the newly identified WC cutoff is lower than that of ATP-III, thus allowing the detection of a higher number of subjects at MetS risk. This is also of utmost importance because the diabetes prevalence is very high in Lebanon (17.6% in our male population) [36].

We found that low HDL cholesterol, which is known to be a cardiovascular risk factor [37], is one of the poorest predictor of the MetS. Low HDL cholesterol was found to be the most common component of the MetS among Jordanian men [29] and Arab American of both sexes [38]. Similarly, in an Omani population, low HDL cholesterol was the most common component of the MetS followed by abdominal obesity (75.4% vs 24.6%) [39]. The difference with our results could be explained by the older age of these populations and/or by environmental factors.

Finally, we found that, in our population, FPG was the least predictive factor of the MetS. This finding has been previously described in Portuguese adults [40]. Fasting plasma glucose level was also found to be the least prevalent component of the MetS in young Turkish adults [8]. Despite these facts, in the new ATP-IIIa criteria, the cutoff value of FPG level has been lowered to greater than or equal to 100 mg/mL [12] because it can be used as an indicator of increased risk of type 2 diabetes mellitus. A prospective Israeli study that followed young subjects [41] shows a progressive increase in risk of type 2 diabetes mellitus when FPG level is greater than 87 mg/mL (4.83 mmol/L), which represents 51.5% of our population. The fact that HDL cholesterol and FPG are the least predictive factors of the MetS could be explained by the later variations of these 2 parameters during life.

In addition, we found that 4.2% of the overall population we studied has a BMI greater than 30 kg/m^2, vs 75% in the MetS(+) subjects. This strong association is expected because no significant difference between WC and BMI was found [42]. It is also consistent with the figures found in the US population where MetS prevalence is 4.6% in normal-weight subjects and 59.6% in obese ones [43] and consistent with the results of a study conducted on adolescents in Belgium where MetS prevalence was significantly higher in obese students (39.1%) as compared with overweight (2.8%) and normal-weight ones (0.3%) [44].

Our study may present certain limitations because the participants were recruited from a medical sciences private university campus. Thus, they probably do not represent all social classes of the Lebanese population. In addition, these subjects might be more aware of health problems compared with the overall Lebanese population. This is why it is possible that the MetS prevalence is underestimated. In addition, our study was not designed to detect a sex difference. Thus, it is possible that an increase in the sample size would lead to a significant sex difference using the ATP-IIIa classification.

In conclusion, our results show that the MetS prevalence in the young Lebanese population is close to what has been previously published in worldwide populations. Using the ATP-IIIa definition, this prevalence did not change. However, using our newly identified cutoff values, this prevalence increased markedly in men but not in women. Our results allowed, for the first time, the identification of new cutoff values that could be applicable to other Middle Eastern populations. These new cutoff values require further validation in other groups of the Lebanese population because it might differ with age and socioeconomic status. In our population, the best predictor of MetS is an elevated WC, whereas HDL cholesterol and FPG level are the poorest predictors. Finally, following prospectively these subjects will clarify how the use of these new cutoff values could lead to a better identification of subjects at high risk for cardiovascular disease and, subsequently, to the implementation of lifestyle modifications at an early age where the benefits are greater.

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