

Diagnostic criteria for metabolic syndrome: a comparative analysis in an unselected sample of adult male population

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Received 10 April 2007; accepted 16 October 2007

Abstract

This analysis compares the performance of 7 different diagnostic criteria of metabolic syndrome (MS) with regard to the prevalence of the syndrome, the characteristics of subjects with a positive diagnosis, and the ability to correctly identify individuals at high calculated cardiovascular (CV) risk or with signs of systemic inflammation or early organ damage. The diagnostic criteria proposed by the World Health Organization (1998); European Group for the Study of Insulin Resistance (EGIR) (1999); Adult Treatment Panel III (ATP III) (2001); American Association of Clinical Endocrinologists (AACE) (2003); ATP III (2004); International Diabetes Federation (IDF) (2005); and American Heart Association/National Heart, Lung, and Blood Institute (2005) were applied to the population of 933 men aged 59.5 years (range, 33–81 years) attending the 2002–2004 examination of the Olivetti Heart Study. Standardized measurements were available for body mass index, waist circumference, blood pressure, fasting serum total and high-density lipoprotein cholesterol, triglyceride, glucose, insulin, high-sensitivity C-reactive protein, and microalbuminuria. Insulin resistance was estimated by the homeostasis model assessment index; and CV risk, by the Prospective Cardiovascular Munster algorithm. The MS prevalence ranged from 8.6% (AACE) to 44.5% (IDF). Among MS-positive subjects, insulin resistance ranged from 94.8% (EGIR) to 49.2% (IDF), whereas type 2 diabetes mellitus (excluded by EGIR and AACE criteria) rated 59.9% by World Health Organization and 22% to 24% by ATP III, IDF, or American Heart Association/National Heart, Lung, and Blood Institute. By most criteria, MS-positive subjects had greater calculated CV risk than MS-negative subjects; but in general, the ability to correctly identify individuals at high CV risk was dampened by limited sensitivity (maximum 60%). Lowering the cutoff for abdominal adiposity (waist circumference <94 cm by IDF) did not improve the performance in this regard but identified a larger number of individuals with microalbuminuria (56%) and elevated C-reactive protein (53%).

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1. Introduction

Despite growing evidence that individuals with metabolic syndrome (MS) have increased cardiovascular risk [1–16], skepticism has been raised about the pathophysiological meaning and the clinical usefulness of the MS diagnosis [17–19]. This skepticism is partly shared by practicing physicians who are uneasy with the perhaps too frequent proposal of new diagnostic criteria for the syndrome. Since 1998, seven definitions have been proposed by authoritative

institutions and/or groups of experts [20–26]. In general, new definitions have been presented as a more valuable tool for clinicians to correctly identify individuals who are exposed to greater cardiovascular risk because of the aggregation of multiple interrelated abnormalities having their origin in a reduced sensitivity to insulin. Almost always, however, the new emerging criteria have not displaced the older ones; and thus, almost all of the different criteria proposed are still identified by various organisms and scientific societies as their operative definition.

Therefore, we compared these diagnostic criteria to highlight the result of using one or the other definition in clinical practice. We applied the 7 diagnostic criteria to a study

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Table 1
Different criteria proposed for clinical diagnosis of MS in men

Clinical measure	WHO (1998)	EGIR (1999)	ATP III (2001)	AACE (2003)	ATP III (2004)	IDF (2005)	AHA/NHLBI (2005)
Ins-R	IGT, IFG, T2DM, or lowered insulin sensitivity ^a plus any 2 of the following:	Plasma insulin >75th percentile plus any 2 of the following:	None, but any 3 of the following 5 features:	IGT or IFG plus any of the following based on clinical judgment:	None, but any 3 of the following 5 features:	None	None, but any 3 of following 5 features:
Body weight	Waist-to-hip ratio >0.90 and/or BMI >30 kg/m ²	WC ≥94 cm	WC ≥102 cm	BMI ≥25 kg/m ²	WC ≥102 cm	Increased WC >94 cm plus any 2 of the following:	WC ≥102 cm
Lipids	TG ≥ 1.7 mmol/L and/or HDL-C <0.91 mmol/L	TG ≥2.0 mmol/L and/or HDL-C <1.01 mmol/L or treated for dyslipidemia	TG ≥1.69 mmol/L, HDL-C <1.03 mmol/L	TG ≥1.69 mmol/L and HDL-C <1.03 mmol/L	TG ≥1.69 mmol/L, HDL-C <1.03 mmol/L	TG ≥1.7 mmol/L or on TG Rx, HDL-C <1.03 mmol/L or on HDL-C Rx	TG ≥1.69 mmol/L or on TG Rx, HDL-C <1.03 mmol/L or on HDL-C Rx
BP	≥160/90 mm Hg	≥140/90 mm Hg or on hypertension Rx	≥130/85 mm Hg	≥130/85 mm Hg	≥130/85 mm Hg	≥130 mm Hg systolic or ≥85 mm Hg diastolic or on hypertension Rx	≥130 mm Hg systolic or ≥85 mm Hg diastolic or on hypertension Rx
Glucose	IGT, IFG, or T2DM	IGT or IFG (but not diabetes)	>6.11 mmol/L (includes diabetes)	IGT or IFG (but not diabetes)	>5.6 mmol/L (includes diabetes)	≥5.6 mmol/L (includes diabetes)	≥ 5.6 mmol/L or on hypoglycemic
Other	mALB			Other features of Ins-R ^b			

T2DM indicates type 2 diabetes mellitus; WC, waist circumference; TG, triglycerides. All other abbreviations as in text.

^a Insulin sensitivity measured under hyperinsulinemic euglycemic conditions; glucose uptake below lowest quartile for background population under investigation.

^b Includes family history of type 2 diabetes mellitus, sedentary lifestyle, advancing age, and ethnic groups susceptible to type 2 diabetes mellitus.

population made up of the participants to the 2002–2004 follow-up examination of the Olivetti Heart Study (OHS). The specific aims of our analysis were (1) to detect the differences in prevalence and metabolic features associated with different definitions of MS; (2) to determine the extent to which subjects diagnosed as having MS by the different diagnostic criteria are actually insulin resistant using an objective albeit indirect measure of insulin sensitivity; (3) to evaluate the ability of the different diagnostic criteria to pick up individuals carrying abnormalities in recognized markers of inflammation and of early organ damage such as high-sensitivity C-reactive protein (hs-CRP) and microalbuminuria (mALB); and (4) to estimate the ability of the same criteria to correctly identify individuals at high cardiovascular risk as determined by an algorithm widely used in clinical practice.

2. Methods

2.1. Study population

The OHS protocol has been described previously [27,28]. The study was approved by the local ethics committee, and participants gave their informed consent to participate. The data used for the analysis were collected between January 2002 and May 2004 and derived from the examination of 997 unselected white adult male individuals who were or had been part of the Olivetti factory work force in Campania, a

region of Southern Italy. After the exclusion of 64 individuals due to an incomplete data set, 933 participants were included in the analysis.

2.2. Procedures

The participants underwent a physical examination and complete anthropometry. Body weight, height, waist circumference, and blood pressure (BP) were measured according to carefully standardized protocols [29]. A fasting venous blood sample was drawn, centrifuged, and stored at –70°C until analyzed. Serum total and high-density lipoprotein cholesterol (HDL-C), triglyceride, and glucose levels were measured by automated methods (Cobas-Mira, Roche, Milan, Italy); and serum insulin concentration, by an ultrasensitive enzyme-linked immunosorbent assay method (Mercodia, Uppsala, Sweden) on the ETISTAR analyzer (DiaSorin, Saluggia, Italy). Insulin resistance (Ins-R) was estimated by the homeostasis model assessment (HOMA) according to Matthews et al [30]. Serum hs-CRP (Roche Diagnostics, Indianapolis, IN) and albumin excretion rate in 24-hour urine collections (Horiba ABX Diagnostics, Rome, Italy) were measured by immunoturbidimetric assays on the Cobas-Mira autoanalyzer.

The Prospective Cardiovascular Munster (PROCAM) algorithm [31] was used to estimate a participant's risk of experiencing a myocardial infarction in 10 years. This estimate

Table 2

Prevalence of MS according to different diagnostic criteria and prevalence of selected cardiovascular risk factors among subjects with a positive diagnosis (data from the 2002–2004 examination of the OHS, n = 933)

	Prevalence of MS	Prevalence of selected cardiovascular risk factors among MS-positive participants							
		HPT	Overweight	Abd Obes	Low HDL	High TG	IFG	Ins-R	T2DM
WHO (1998) ^a	197 (21.1)	181 (91.9)	169 (85.8)	90 (45.7)	75 (38.1)	70 (35.7)	79 (40.1)	125 (63.5)	118 (59.9)
EGIR (1999) ^b	153 (16.4)	146 (95.4)	147 (96.1)	93 (60.8)	67 (43.8)	61 (39.9)	81 (52.9)	145 (94.8)	0
ATP III (2001)	270 (28.9)	261 (96.7)	248 (91.9)	175 (64.8)	187 (69.3)	175 (65.1)	88 (32.6)	147 (54.4)	76 (28.1)
AACE (2003) ^b	80 (8.6)	70 (87.5)	72 (90.0)	42 (52.5)	29 (36.3)	30 (37.5)	80 (100)	50 (62.5)	0
ATP III (2004)	320 (34.3)	309 (96.6)	296 (92.5)	201 (62.8)	200 (62.5)	188 (58.9)	138 (43.1)	167 (52.2)	78 (23.8)
IDF (2005)	415 (44.5)	400 (96.4)	394 (94.9)	209 (50.4)	200 (48.2)	190 (45.9)	176 (42.4)	204 (49.2)	91 (21.9)
AHA/NHLBI (2005)	332 (35.6)	321 (96.7)	307 (92.5)	209 (63.0)	209 (63.0)	194 (58.6)	140 (42.2)	170 (51.2)	77 (23.2)

n (%). Hypertension blood pressure $\geq 130/85$ mm Hg or Rx; overweight: BMI ≥ 25 ; abdominal obesity: waist ≥ 102 cm; low HDL-C: HDL-C < 1.03 mmol/L or Rx; hypertriglyceridemia (high TG): TG ≥ 1.69 mmol/L or Rx; IFG: serum glucose ≥ 5.6 and < 7.0 mmol/L; Ins-R: HOMA index ≥ 2.77 ; type 2 diabetes mellitus: serum glucose ≥ 7.0 mmol/L or Rx. HPT indicates hypertension; Abd Obes, abdominal obesity.

^a Impaired fasting glucose (serum glucose > 6.11 mmol/L) or positive diagnosis of type 2 diabetes mellitus (serum glucose ≥ 7.0 mmol/L or hypoglycemic Rx) was taken to indicate Ins-R (OGTT and hyperinsulinemic euglycemic clamp not available).

^b Impaired fasting glucose (serum glucose > 6.11 mmol/L) was used as glucose parameter (OGTT not available).

was possible only in a subgroup of 715 participants who fulfilled all the criteria for the use of the algorithm (age, 35–65 years; low-density lipoprotein cholesterol, 75–250 mg/dL; triglyceride, 50–400 mg/dL; glucose, 50–300 mg/dL; systolic BP, 100–225 mm Hg).

2.3. Diagnostic criteria for MS

The diagnostic criteria of MS that were the object of our comparison are reported in Table 1 [20–26]. Given the epidemiologic setting of our study, there were limitations concerning the evaluation of insulin sensitivity and glucose tolerance inasmuch as neither a euglycemic hyperinsulinemic clamp nor an oral glucose tolerance test (OGTT) was available. Therefore, the diagnosis of MS by the World Health Organization (WHO) criteria was limited to the use of impaired fasting glucose (IFG) or of type 2 diabetes mellitus based on fasting blood glucose only. Impaired fasting glucose and fasting serum insulin were used for the European Group for the Study of Insulin Resistance (EGIR) definition. With regard to the American Association of Clinical Endocrinologists (AACE) definition, in addition to IFG, other criteria adopted were a family history of type 2 diabetes mellitus, a sedentary lifestyle (ie, a reported physical activity in the lowest quintile for the OHS population), and advancing age (arbitrarily defined as 65 years or older). These limitations are very likely to lead to underestimation of the prevalence of MS using the WHO, AACE, and, to a lower extent, EGIR criteria in comparison with the one expected using the OGTT or the euglycemic hyperinsulinemic clamp.

Insulin resistance was defined as a HOMA index > 2.77 , corresponding to the 80th percentile of the HOMA index distribution in an Italian adult nonobese male population [32].

2.4. Evaluation of cardiovascular risk and target organ damage

A value $\geq 20\%$ in the PROCAM score was chosen as a threshold for high cardiovascular risk [31].

Microalbuminuria was defined as an albumin excretion rate of 30 to 300 mg/24 hours, and hs-CRP was considered elevated if it exceeded the 80th percentile value for the OHS population.

2.5. Statistical analysis

This was performed using SPSS 12.0 (SPSS, Chicago, IL). Results were expressed as means and 95% confidence intervals (CIs) unless otherwise indicated. Two-sided *P* values less than .05 were considered statistically significant. The prevalence of various metabolic and cardiovascular risk factors when using different definitions of MS was calculated by 2×2 contingency tables. The calculation of sensitivity, specificity, and area under receiver operating characteristic (ROC) curves was used to evaluate the ability of different diagnostic criteria of MS to correctly identify individuals bearing a high cardiovascular risk or having abnormal levels of hs-CRP or mALB.

3. Results

Mean age of the study population was 59.5 years (range, 33–81 years). The prevalence of *overweight* (ie, a body mass index [BMI] > 25) and *hypertension* (BP ≥ 140 and/or 90 mm Hg or current pharmacologic treatment) was 77% and 70%, respectively. The proportion of individuals with *abdominal obesity*, defined as a waist circumference greater than 94 cm, was more than 2-fold higher than that using the conventional 102-cm cutoff (68.2% vs 30.7%). The prevalence of IFG rose from 8.6% using the 110-mg/dL cutoff to 25.2% using the 100-mg/dL cutoff according to the recent American Diabetes Association recommendations [24–33].

Twenty-eight percent of participants were insulin resistant, nearly 13% were frankly diabetic, and 8.1% received medication for type 2 diabetes mellitus. Twelve percent of the study population was being treated for hypertriglyceridemia and/or low HDL-C, and one half of the hypertensive

Table 3

Ability of the different diagnostic criteria of MS to correctly identify participants with mALB (n = 117) or with elevated serum hs-CRP levels (n = 182) in subjects attending the 2002–2004 examination of the OHS (n = 933)

	No. of subjects with mALB (% detected)	No. of subjects with elevated hs-CRP (% detected)	mALB		hs-CRP	
			Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
WHO (1998) ^a	42 (35.9%)	44 (24.2%)	0.36 (0.27–0.45)	0.81 (0.78–0.84)	0.24 (0.18–0.30)	0.80 (0.77–0.83)
EGIR (1999) ^b	23 (19.7%)	35 (19.2%)	0.20 (0.12–0.27)	0.84 (0.82–0.87)	0.19 (0.14–0.25)	0.84 (0.82–0.87)
ATP III (2001)	45 (38.5%)	68 (37.4%)	0.38 (0.30–0.47)	0.72 (0.69–0.76)	0.37 (0.30–0.44)	0.73 (0.70–0.76)
AACE (2003) ^b	11 (9.4%)	19 (10.4%)	0.09 (0.04–0.15)	0.91 (0.90–0.93)	0.10 (0.06–0.15)	0.92 (0.90–0.94)
ATP III (2004)	54 (46.2%)	80 (44.0%)	0.46 (0.37–0.55)	0.67 (0.64–0.71)	0.44 (0.37–0.51)	0.68 (0.65–0.71)
IDF (2005)	65 (55.6%)	97 (53.3%)	0.56 (0.47–0.65)	0.58 (0.54–0.61)	0.53 (0.46–0.61)	0.57 (0.54–0.61)
AHA/NHLBI (2005)	56 (47.9%)	83 (45.6%)	0.48 (0.39–0.57)	0.66 (0.63–0.69)	0.46 (0.38–0.53)	0.67 (0.63–0.70)

See text for definitions of microalbuminuria and elevated hs-CRP.

^a Impaired fasting glucose (serum glucose >6.11 mmol/L) or positive diagnosis of type 2 diabetes mellitus (serum glucose ≥7.0 mmol/L or hypoglycemic Rx) was taken to indicate *insulin resistance* (OGTT and hyperinsulinemic euglycemic clamp not available).

^b Impaired fasting glucose (serum glucose >6.11 mmol/L) was used as *glucose* parameter (OGTT not available).

participants were on drug treatment. In all cases, these drugs had been prescribed by the participants' family physician.

The prevalence of MS using the different diagnostic criteria is shown in Table 2. Lower values were associated with the AACE, EGIR, and WHO definitions, whereas a much higher prevalence was produced by the use of the International Diabetes Federation (IDF); American Heart Association (AHA)/National Heart, Lung, and Blood Institute (NHLBI); and Adult Treatment Panel III (ATP III) criteria. Of the 515 subjects who had a positive diagnosis by at least one definition, approximately one third (35.4%) were positive by only 1 or 2 criteria, one third (31.5%) by 3 or 4, and one other third (33.2%) by 5 or more.

Table 2 also shows the prevalence of the cardiovascular risk factors relevant to MS in those who were MS positive by different criteria. Hypertension and overweight were extremely common by all criteria, whereas the occurrence of abdominal adiposity (if defined as a waist circumference of 102 cm or higher) was 45% using the WHO criteria for MS and nearly 65% by the ATP III (2001). Hypertriglyceridemia and low HDL-C were strictly interrelated: their occurrence was much lower using the EGIR, AACE, and WHO criteria as compared with both the ATP III and AHA/NHLBI definitions, with the values using the IDF criteria falling in between. Impaired fasting glucose occurred to a similar frequency (approximately 40%) by all criteria.

The occurrence of Ins-R ranged from 100% by the AACE criteria, which considered Ins-R a prerequisite for diagnosis, to much lower values by all other criteria, the lowest being that by IDF (50%). Finally, type 2 diabetes mellitus occurred in as many as 60% of MS-positive subjects according to the WHO criteria and in only 20% by IDF, and was excluded by definition when using the EGIR or AACE criteria.

The ability of the various diagnostic definitions of MS to pick up individuals with mALB or with elevated hs-CRP is illustrated in Table 3. There was a large variation in the performance of the 7 different criteria in this regard, with the IDF, AHA/NHLBI, and ATP III (2004) criteria having the best outcome (45% to more than 50%). At the other extreme, the EGIR definition identified only 20% of the carriers of mALB or elevated hs-CRP; and the AACE definition, just 10%. When these analyses were repeated after the exclusion of diabetic subjects, there was a sizable drop in the sensitivity of all the diagnostic criteria that include diabetes among the components of MS, particularly for mALB: WHO (from 0.36 to 0.13), ATP III 2001 (from 0.39 to 0.28), ATP III 2004 (from 0.46 to 0.38), IDF (from 0.56 to 0.45), and AHA/NHLBI 2005 (from 0.48 to 0.41).

The diagnosis of MS was also associated with a substantially higher level of PROCAM-predicted cardiovascular risk compared with a negative diagnosis using 5 different diagnostic criteria, namely, WHO (21.9% vs 14.1%, $P < .001$),

Table 4

Ability of the different diagnostic criteria of MS to correctly identify participants with a PROCAM risk value higher than 20% (n = 715)

	Sensitivity (95% CI)	Specificity (95% CI)	ROC AUC (95% CI)	Asymptotic significance (P)
WHO (1998)	0.31 (0.25–0.38)	0.85 (0.81–0.88)	0.579 (0.531–0.627)	.001
EGIR (1999)	0.16 (0.11–0.21)	0.83 (0.80–0.86)	0.492 (0.446–0.539)	.753
ATP III (2001)	0.48 (0.41–0.55)	0.80 (0.77–0.84)	0.642 (0.595–0.689)	<.001
AACE (2003)	0.11 (0.07–0.15)	0.92 (0.90–0.95)	0.515 (0.468–0.563)	.519
ATP III (2004)	0.53 (0.47–0.60)	0.75 (0.71–0.78)	0.641 (0.594–0.687)	<.001
IDF (2005)	0.60 (0.53–0.67)	0.64 (0.60–0.68)	0.619 (0.573–0.665)	<.001
AHA/NHLBI (2005)	0.55 (0.49–0.62)	0.74 (0.70–0.78)	0.647 (0.601–0.693)	<.001

AUC indicates area under ROC curve.

ATP III 2001 (21.8% vs 12.9%, $P < .001$), ATP III 2004 (21.5% vs 12.7%, $P < .001$), IDF (19.5% vs 12.7%, $P < .001$), and AHA/NHLBI (21.5% vs 12.6%, $P < .001$). On the other hand, the use of EGIR (15.7% vs 15.6%, $P = .94$) or AACE (18.2% vs 15.4%, $P = .12$) criteria was not associated with a significant difference in calculated cardiovascular risk.

In particular, the ability of the different criteria to correctly identify participants with a PROCAM risk value higher than 20% is illustrated in Table 4. Sensitivity was comprised between 11% (using AACE) and 60% (using IDF). The degree of specificity was in general much greater, with a minimum of 64% by IDF and a maximum of 92% by AACE. The highest values of the area under ROC curve were attained by the most recent AHA/NHLBI definition, but the ATP III and IDF definitions also achieved similar values. The WHO diagnostic criteria were less effective, whereas statistical significance was not reached by the EGIR and AACE criteria. There was no substantial difference in these results when the analysis was repeated after exclusion of the participants who reported to have already experienced a cardiovascular event (data not reported).

After the exclusion of diabetic participants from the analysis, the excess cardiovascular risk associated with a positive, compared with a negative, diagnosis of MS dropped to a variable extent for all the diagnostic criteria that include diabetes among the components of the syndrome: WHO (from 7.8% to 4.3%), ATP III 2001 (from 8.9% to 8.8%), ATP III 2004 (from 8.8% to 7.9%), IDF (from 6.8% to 6.2%), and AHA/NHLBI (from 8.9% to 8.0%).

4. Discussion

A 5-fold difference in the prevalence of MS resulted from the use of different diagnostic criteria. At the one end, the AACE and EGIR definitions led to a very conservative estimate by imposing Ins-R as a prerequisite for diagnosis but excluding diabetic individuals; at the other end, the IDF definition achieved the opposite result of a very high prevalence of the condition by eliminating Ins-R as a prerequisite, by adopting a 94-cm cutoff for abdominal obesity and 100 mg/dL for IFG, and by including diabetic individuals. The adoption of the 100-mg/dL cutoff for IFG by the ATP III (2004) in place of 110 mg/dL of ATP III (2001), all else being equal, produced an increase in prevalence from 29% to 34%. As described in Methods, given the unavailability of a 2-hour postglucose load glycemia, the prevalence of impaired glucose tolerance (IGT) and thus of MS was in all likelihood underestimated when using the WHO, AACE, and, to a lower extent, EGIR criteria. Indeed, in the Wandsworth Heart and Stroke Study, in a representative sample of 377 white subjects aged 40 to 59 years, 30 individuals were found to have an abnormal 2-hour response to OGTT and only 10% of these had IFG [34]. Assuming similar proportions for our study popula-

tion, the prevalence of MS could rise from 21.1% to a maximum of 27.4% using the WHO criteria and from 8.6% to a maximum of 15.7% using the AACE criteria. Smaller differences could also be observed with regard to the EGIR criteria. In all cases, however, the prevalence values obtained with these 3 definitions would remain definitely less than the rates observed using the ATP III (2004), IDF, and AHA/NHLBI criteria.

As a result of the heterogeneous diagnostic criteria, a quite small percentage of subjects had MS by all criteria; and as many as 25% of those affected were so by only one definition. This heterogeneity also resulted in a markedly different profile of the subjects identified as MS positive. Thus, remarkable differences were observed in the occurrence of dyslipidemia, IFG, Ins-R, and diabetes. Insulin resistance and IFG were typical features of patients with MS diagnosed by the AACE or EGIR criteria, which however excluded diabetic individuals. The same was true for the WHO criteria for which, however, diabetic individuals represented 60% of the total positive subjects. Noteworthy, when using the AACE definition, although all subjects with a positive diagnosis had IFG, only slightly more than 60% was found to be insulin resistant by HOMA index, compared with 95% observed by the EGIR definition that involved IFG in only half of the cases. An explanation for this apparent paradox is that EGIR used waist circumference as a measure of adiposity, a parameter more tightly associated with Ins-R, at variance with AACE, which used just overweight. It is also remarkable that, although the cutoffs used for defining hypertriglyceridemia and low HDL-C are practically common to all MS definitions, significant differences were observed in the occurrence of dyslipidemia using the different diagnostic criteria of the syndrome. Dyslipidemia was less common with those definitions (WHO, EGIR, and AACE) that are more focused on reduced insulin sensitivity. An explanation for this unexpected finding may again be found in the adoption by these 3 definitions of less effective indicators of abdominal adiposity (such as BMI or a cutoff for waist circumference of 94 in place of 102 cm) that include a large number of individuals with less abundant visceral fat depots.

It has been suggested that novel risk factors related to Ins-R might be useful additions to the syndrome definition [15,18]. Consideration was given in particular to CRP, in view of the role played by inflammation in atherogenesis [35], and to mALB, which is both an independent cardiovascular risk factor and a marker of early organ damage [36]. Our findings indicate that mALB and elevated serum hs-CRP levels are associated with the diagnosis of MS with variable strength depending on the diagnostic criteria adopted, but approximately to the same extent as is Ins-R. The criteria that picked up the largest number of subjects bearing these alterations were those of the IDF followed by the AHA/NHLBI.

It is often stated that the clinical usefulness of the concept of MS is to provide the practicing physician with an

instrument to easily identify individuals at high cardiovascular risk. Although our analysis was only based on cross-sectional data and as such could not evaluate the ability of MS as a predictor of cardiovascular risk, we considered it of interest to compare the average degree of calculated cardiovascular risk associated with the diagnosis of MS by different diagnostic criteria. In general, our analysis showed that the major drawback of all the proposed diagnostic criteria was indeed their limited ability to correctly detect individuals at high or very high cardiovascular risk. In fact, the top ranking criteria in this regard, namely, the AHA/NHLBI and IDF, had a 55% to 60% sensitivity. Thus, even using the most sensitive diagnostic criteria, a substantial number of high-risk individuals remain undetected. In particular, the criteria adopted by EGIR and AACE had a much lower discriminatory power. This last finding might be partly a consequence of the unavailability of OGTT in the OHS, which led to the underestimation of the number of individuals with IGT and then possibly with MS using the AACE, EGIR, and WHO criteria. Actually, several prospective studies have clearly shown that IGT is associated with greater risk of cardiovascular morbidity and mortality in comparison with IFG [37]. For instance, in the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe study, relative risks of mortality were 1.56 and 1.18, respectively, for subjects with IGT or IFG compared with normoglycemic individuals [38]. This notwithstanding, however, to some extent, the low predictive power of the EGIR and AACE criteria in this regard is also the result of the exclusion of diabetic individuals. This interpretation is supported by the finding of a much greater predictive power of the WHO criteria, for which there was a similar problem with the identification of IGT individuals but which did include diabetic patients. The relative weight of diabetes was further supported by the results of the analyses performed upon exclusion of diabetic patients. The ability of all the diagnostic criteria of MS that include diabetes among the components of the syndrome to identify individuals with mALB, elevated hs-CRP, or high estimated cardiovascular risk was more or less reduced by the exclusion of diabetic subjects. Furthermore, our finding is in keeping with the results of prospective investigations that also highlight the role of diabetes in the framework of MS. For instance, in elderly diabetic subjects followed for 8 years, MS was not an independent predictor of all-cause and cardiovascular mortality [39]. Also in another study in patients with long-lasting type 2 diabetes mellitus, the incremental risk attributable to high triglycerides or low HDL was blunted by the presence of diabetes itself [12]. Finally, in a study of patients with preexisting cardiovascular disease, the excess risk associated with MS was dependent on the inclusion of diabetes in the definition, and once diabetes was taken into account, MS was no longer a significant predictor of risk [40].

The OHS enrolled only white participants and lacked a female sample; thus, our study results and conclusions are generalizable only to other white male populations.

5. Conclusion

This comparative analysis of 7 different diagnostic criteria of MS, using the OHS 2002-2004 examination database, showed a 5-fold difference in the prevalence of MS depending on which diagnostic criteria were used. The analysis also highlighted remarkable differences in the biochemical and clinical profile of individuals with positive diagnoses implemented by different criteria, with particular regard to the occurrence of Ins-R, mALB, and elevated hs-CRP plasma levels. These differences could be only partly attributable to the underestimation of the occurrence of IGT due to the unavailability of an OGTT in our study population. Our study also showed that, although the diagnosis of MS is associated with a relatively high calculated cardiovascular risk by most (albeit not all) criteria, still a sizable proportion of individuals at high risk are left undetected.

On practical grounds, these results indicate the need to reach a consensus around a univocal definition of the diagnostic criteria for MS if this diagnosis has to be implemented in clinical practice. On the other hand, it is quite clear that the differences observed using the various proposed diagnostic criteria reflect different views of the proponents about the etiology and the pathophysiological bases of the syndrome. Thus, it is unlikely that a consensus on practical grounds could be reached until these different ideas are reconciled.

Acknowledgment

This work was funded in part by the Italian Ministry of University and Research (MIUR-FIRB n.RBNE01724C_005 and PRIN n. 2004069989).

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