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The hypertriglyceridemic waist phenotype versus the National Cholesterol Education Program–Adult Treatment Panel III and International Diabetes Federation clinical criteria to identify high-risk men with an altered cardiometabolic risk profile

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Abstract

The hypertriglyceridemic waist phenotype, the National Cholesterol Education Program–Adult Treatment Panel III (NCEP-ATP III) criteria, and the International Diabetes Federation (IDF) criteria have been proposed as screening tools to identify subjects with features of the metabolic syndrome and therefore at increased cardiometabolic risk. The aim of the present study was to compare the ability of these 3 clinical approaches to identify individuals at increased cardiometabolic risk as suggested by the presence of deteriorated markers such as hyperinsulinemia, elevated apolipoprotein B levels, small low-density lipoprotein particles, high C-reactive protein concentrations, and low adiponectin levels. For that purpose, physical and cardiometabolic characteristics of a sample of 272 white men recruited for various metabolic investigations were studied. The hypertriglyceridemic waist phenotype was defined as having both a high waist circumference (≥90 cm) and increased fasting triglyceride levels (≥2.0 mmol/L). Having at least 3 of the 5 NCEP-ATP III criteria or waist circumference of at least 94 cm plus any 2 of the 4 additional IDF criteria was also used to identify individuals at increased cardiometabolic risk. A large proportion of men with the hypertriglyceridemic waist phenotype also met the NCEP-ATP III (82.7%) or IDF (89.2%) criteria. Men with the hypertriglyceridemic waist phenotype were characterized by alterations in their lipoprotein-lipid profile that included small low-density lipoprotein particles, increased apolipoprotein B and insulin levels, as well as reduced adiponectin concentrations, which were similar to individuals meeting the NCEP-ATP III or the IDF criteria. Moreover, the Framingham risk score of men meeting any of the 3 screening tools criteria was higher and was similar across the 3 approaches (4.2, 3.8, and 3.7, respectively). These results suggest that hypertriglyceridemic waist may be as discriminant as the NCEP-ATP III or the IDF criteria and could be used as an initial screening approach to identify individuals with deteriorated cardiometabolic risk markers.

1. Introduction

The metabolic syndrome is recognized as a cluster of cardiometabolic risk factors that includes an atherogenic dyslipidemic state, insulin resistance, elevated blood pressure, impaired fibrinolysis, and a prothrombotic profile and an inflammatory state [1]. The association between these cardiometabolic risk markers and cardiovascular disease (CVD) or cardiovascular mortality is well recognized [2-4]. However, controversy remains around the underlying pathophysiologic processes leading to the development of the metabolic syndrome (insulin resistance and/or hyperinsulinemia vs abdominal obesity) [5].

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Guidelines encouraged identification of patients with features of the metabolic syndrome in clinical practice [6-8]. In this regard, several clinical criteria to aid detection of individuals characterized by features of the metabolic syndrome have been developed [1,6,8-12]. However, it is very important to point out that clinical criteria are not the definition of the metabolic syndrome per se but that they are proposed as screening tools with the hope that they will help physicians to identify patients with a cluster of atherogenic cardiometabolic risk abnormalities largely resulting from the presence of abdominal obesity [13].

The criteria of the National Cholesterol Education Program–Adult Treatment Panel III (NCEP-ATP III) guidelines are widely used in clinical practice to identify subjects likely to have the metabolic syndrome [1]. With the NCEP-ATP III clinical criteria, a diagnosis of the metabolic syndrome is made when 3 or more of 5 criteria are met: (1) enlarged waist circumference, (2) elevated triglycerides (TG), (3) low high-density lipoprotein (HDL) cholesterol, (4) impaired fasting glucose, and (5) elevated blood pressure [1,11]. More recently, the International Diabetes Federation (IDF) has attempted to provide a global approach to identify men and women characterized by the metabolic syndrome worldwide [8]. The IDF criteria have been built upon the NCEP-ATP III 5 screening tools but differ in 2 aspects. First, the waist circumference cutoff has been lowered (102 to 94 cm); and the cutoff is also population specific. Second, an elevated waist circumference is a mandatory clinical criterion and must be present along with 2 additional criteria to diagnose the metabolic syndrome [8]. Both the NCEP-ATP III and IDF criteria have been associated with similar relative increase in the risk of CVD [14].

We have also been interested in the development of a simple screening approach to identify men at increased cardiometabolic risk. In 2000, Lemieux et al [12] proposed that the hypertriglyceridemic waist phenotype (waist girth ≥90 cm combined with fasting plasma TG levels ≥2.0 mmol/L) was predictive of a very high probability for men to be characterized by the simultaneous presence of some cardiometabolic risk markers. It has also been suggested that the hypertriglyceridemic waist phenotype could be helpful in the assessment of risk of coronary artery disease and type 2 diabetes mellitus [12,15].

More recently, Tankó and colleagues [16] have compared the ability of the hypertriglyceridemic waist phenotype and of the NCEP-ATP III clinical criteria to estimate cardiovascular risk in postmenopausal women. They found that the combined presence of an elevated waist circumference (≥88 cm) and increased TG levels (≥1.45 mmol/L) was the best indicator of progression rate of aortic calcification over an 8.5-year follow-up period [16]. However, although many prevalence studies have been published comparing numbers obtained with the NCEP-ATP III and IDF criteria, no study has simultaneously compared the ability of hypertriglyceridemic waist, NCEP-ATP III, and IDF screening tools to identify men characterized by deteriorated cardiometabolic risk markers such as hyperinsulinemia, elevated apolipoprotein B levels, small low-density lipoprotein (LDL) particles, increased C-reactive protein (CRP) concentrations, and low adiponectin levels.

2. Methods

2.1. Study sample and measurements

Two hundred seventy-two men, aged 25 to 63 years (mean age ± SD, 44.9 ± 7.6 years), were recruited from the Québec City metropolitan area by solicitation through the media. Participants were selected to cover a wide range of body mass index values (18.7-39.1 kg/m^2). Subjects gave their written consent to participate in the study, which was approved by the Medical Ethics Committee of Université Laval. All subjects were sedentary but healthy, nonsmoking, and nondiabetic volunteers; and they were not under treatment of coronary heart disease, diabetes, dyslipidemias, or endocrine disorders.

Body weight, height [17], and waist circumference [18] were measured following standardized procedures. For the waist circumference measurement, the subject had to stand with his feet shoulder-width apart, the arms hanging on each side of the body. The measurement was taken at the end of a normal expiration while ensuring that the participant did not contract his abdominal muscles. The person performing the waist measurement marked with a pencil the right and left last ribs, the right and left iliac crests, as well as the mid-distance between the last rib and the top of the iliac crest of the 2 sides. The tape was placed horizontally directly on the skin with respect to both mid-distance landmarks.

Abdominal adipose tissue accumulation was assessed by computed tomography, which was performed on a Siemens Somatom DRH scanner (Erlangen, Germany) using previously described procedures [19]. Briefly, computed tomography scan was performed at the level corresponding to the disk between the fourth and fifth vertebrae. The attenuation range used for adipose tissue calculations was −190 to −30 Hounsfield units. Total and visceral fat areas were measured by drawing a line with a graph pen within the middle of the muscle wall surrounding the abdominal cavity. Subcutaneous fat was calculated by subtracting the visceral fat area from the total abdominal fat area.

Three supine blood pressure measurements were taken 3 minutes apart on the nondominant arm with an appropriate cuff size measured after the subject had been resting in the supine position for 5 minutes. The measurements were performed using a mercury sphygmomanometer and have been averaged.

Blood samples were drawn in the morning from an antecubital vein into Vacutainer tubes containing EDTA (Miles Pharmaceuticals, Rexdale, Ontario, Canada) after a 12-hour overnight fast. Plasma TG [20] and cholesterol [21] concentrations were measured with a Technicon RA-500 analyzer (Bayer Corp, Tarrytown, NY). The HDL fraction was obtained after precipitation of LDL in the infranatant

(d >1.006 g/L) with heparin and $MnCl_2$ [22]. Total apolipoprotein B concentrations were measured in the fasting plasma by the rocket immunoelectrophoretic method of Laurell [23] as previously described [24]. The LDL peak particle diameter was assessed with nondenaturing 2% to 16% polyacrylamide gradient gel electrophoresis of plasma as previously described [25]. Plasma glucose was measured enzymatically [26], whereas fasting plasma insulin was measured by radioimmunoassay with polyethylene glycol separation [27].

The CRP levels were measured in a subsample of 164 men in frozen plasma samples (−80°C) with a highly sensitive immunoassay that used a monoclonal antibody coated with polystyrene particles; the assay was performed on a Dade Behring BN ProSpec nephelometer (Dade Behring, Marburg, Germany) according to the methods described by the manufacturer [28]. Fasting plasma adiponectin concentrations were determined by an enzyme-linked immunosorbent assay (B-Bridge International, San Jose, CA) on plasma kept at −80°C on a subsample of 223 men.

2.2. Screening tools for the metabolic syndrome

The NCEP-ATP III criteria [1,11], the IDF criteria [8], and the hypertriglyceridemic waist phenotype [12] were used to identify individuals with or without the metabolic syndrome. To meet the NCEP-ATP III criteria, men had to be characterized by 3 or more of the following risk variables: waist circumference greater than 102 cm, TG levels of at least 1.69 mmol/L, HDL cholesterol less than 1.03 mmol/L, blood pressure of at least 130/at least 85 mm Hg, and fasting glucose of at least 5.6 mmol/L [1,11]. To meet the IDF criteria, subjects must have abdominal obesity (waist circumference ≥94 cm for white population) plus any 2 of the 4 following factors: TG levels of at least 1.7 mmol/L, HDL cholesterol less than 1.0 mmol/L, blood pressure of at least 130/at least 85 mm Hg, and fasting glucose of at least 5.6 mmol/L [8]. The hypertriglyceridemic waist phenotype was defined as having both a high waist circumference (≥90 cm) and elevated fasting TG levels (≥2.0 mmol/L) [12].

2.3. Framingham risk score

The Framingham risk score was calculated for each subject [29]. With the Framingham algorithm, a global risk score was calculated based on categorical values of age, total cholesterol, HDL cholesterol, blood pressure, smoking, and diabetes. The scoring sheet is available in the original article [29] and online at www.nhlbi.nih.gov/about/framingham/riskabs.htm. Because subjects with diabetes were excluded from the present study, this criterion (diabetes) was not considered in the Framingham risk score. In addition, our subjects were nonsmoking volunteers.

2.4. Statistical analyses

Data are expressed as mean ± SD in the table and as mean ± SE in the figures. Group differences for continuous variables were examined using Student unpaired t tests. As values were not normally distributed, fasting TG levels were log transformed. In all analyses, a P value equal to or less than .05 was considered significant. The data were analyzed using the statistical package program SAS v8.1 (SAS Institute, Cary, NC).

3. Results

In the present sample, the prevalence of men with the NCEP-ATP III criteria, IDF criteria, or hypertriglyceridemic waist phenotype was 59.2%, 64.0%, and 51.1%, respectively. A large proportion of men having the hypertriglyceridemic waist phenotype also met the NCEP-ATP III (82.7%) or the IDF (89.2%) criteria. Physical characteristics and fasting cardiometabolic risk profile of men with or without the NCEP-ATP III, the IDF, or the hypertriglyceridemic waist criteria are presented in Table 1. Adiposity indices (body mass index, waist circumference, and visceral adipose tissue accumulation) were higher in men meeting the metabolic syndrome clinical criteria, irrespective of the screening approach used (P < .0001). As expected, men with the hypertriglyceridemic waist phenotype displayed a more deteriorated fasting plasma lipoprotein-lipid profile including lower HDL cholesterol levels, elevated TG and fasting glucose concentrations, and higher cholesterol to HDL cholesterol ratio than men without this phenotype (P < .05). Similar results were obtained in men with the NCEP-ATP III (P < .0001) or the IDF (P < .0001) criteria. Interestingly, the plasma lipoprotein-lipid profile was similar in men who met the NCEP-ATP III, the IDF, or the hypertriglyceridemic waist phenotype criteria.

Fig. 1 presents features of the atherogenic metabolic triad (apolipoprotein B and insulin levels as well as LDL peak particle size) among men with or without the NCEP-ATP III, the IDF, or the hypertriglyceridemic waist criteria. Men with the hypertriglyceridemic waist phenotype were characterized by alterations in their LDL particle size and insulin levels that were comparable to individuals meeting the NCEP-ATP III or the IDF criteria. However, apolipoprotein B concentrations were only significantly increased among men with the IDF and hypertriglyceridemic waist screening tools. Fig. 2 shows CRP and adiponectin concentrations among men who were positive/negative for the 3 clinical tools. This figure illustrates that only men with the NCEP-ATP III or IDF criteria presented higher CRP levels compared with men without these clinical criteria (P < .05). However, only subjects characterized by the presence of the NCEP-ATP III criteria or the hypertriglyceridemic waist phenotype were characterized by significantly decreased adiponectin concentrations (P < .03), whereas only a trend was observed for men meeting the IDF criteria (P = .056).

Finally, the Framingham risk score has been quantified among men with or without the NCEP-ATP III, IDF, or hypertriglyceridemic waist criteria. Fig. 3 shows that men

Table 1
Physical characteristics and fasting cardiometabolic risk profile in a sample of 272 men with or without the NCEP-ATP III, IDF, and hypertriglyceridemic waist criteria

Variables	NCEP-ATP III criteria		IDF criteria		Hypertriglyceridemic waist phenotype	
	Without	With	Without	With	Without	With
No. of subjects (%)	111 (40.8)	161 (59.2)	98 (36.0)	174 (64.0)	133 (48.9)	139 (51.1)
Age (y)	44.8 ± 7.4	44.9 ± 7.7	45.2 ± 7.5	44.7 ± 7.7	45.3 ± 7.6	44.4 ± 7.6
Body mass index (kg/m^2)	26.6 ± 3.6	31.3 ± 3.4*	26.0 ± 3.7	31.3 ± 3.1†	27.8 ± 4.4	31.0 ± 3.2‡
Waist circumference (cm)	93.7 ± 9.9	107.3 ± 9.0*	91.8 ± 10.3	107.3 ± 7.9†	97.0 ± 12.2	106.3 ± 8.8‡
Abdominal adipose tissue areas (cm^2)						
Total	372.3 ± 129.9	533.8 ± 128.7*	346.7 ± 131.2	537.1 ± 114.5†	408.3 ± 154.4	525.9 ± 124.1‡
Visceral	135.5 ± 50.3	204.6 ± 66.2*	131.3 ± 52.0	202.2 ± 64.3†	151.3 ± 65.7	200.9 ± 63.5‡
Subcutaneous	236.7 ± 100.7	329.2 ± 100.4*	215.4 ± 97.8	334.8 ± 92.0†	257.0 ± 114.2	325.1 ± 95.2‡
Systolic blood pressure (mm Hg)	113.5 ± 11.0	118.7 ± 11.2*	114.4 ± 11.5	117.8 ± 11.1†	115.1 ± 11.6	118.0 ± 10.9‡
Diastolic blood pressure (mm Hg)	78.5 ± 7.0	82.7 ± 9.4*	79.9 ± 8.4	81.7 ± 8.9	80.9 ± 8.9	81.3 ± 8.7
Cholesterol (mmol/L)	5.06 ± 0.86	5.06 ± 0.67	5.02 ± 0.87	5.08 ± 0.68	4.88 ± 0.79	5.23 ± 0.67‡
LDL cholesterol (mmol/L)	3.42 ± 0.77	3.16 ± 0.69*	3.34 ± 0.75	3.23 ± 0.72	3.32 ± 0.73	3.22 ± 0.73
HDL cholesterol (mmol/L)	1.03 ± 0.24	0.85 ± 0.12*	1.06 ± 0.24	0.85 ± 0.12†	1.01 ± 0.22	0.84 ± 0.13‡
Cholesterol to HDL cholesterol ratio	5.15 ± 1.49	6.03 ± 1.05*	4.95 ± 1.36	6.08 ± 1.11†	5.01 ± 1.21	6.31 ± 1.09‡
Triglycerides (mmol/L)	1.55 ± 0.76	2.53 ± 0.89*	1.53 ± 0.80	2.47 ± 0.89†	1.41 ± 0.50	2.82 ± 0.79‡
Fasting glucose (mmol/L)	5.38 ± 0.46	5.81 ± 0.51*	5.43 ± 0.49	5.75 ± 0.52†	5.57 ± 0.54	5.69 ± 0.51‡

Data are means ± SD unless otherwise indicated. The significant difference with the corresponding subgroup is indicated as follows: *different from men without the NCEP-ATP III criteria ($P < .03$); †different from men without the IDF criteria ($P < .02$); ‡different from men without the hypertriglyceridemic waist phenotype ($P < .05$).

meeting the NCEP-ATP III, IDF, or hypertriglyceridemic waist criteria were all characterized by a higher Framingham risk score compared with men not meeting these clinical criteria ($P < .002$). In addition, differences observed in the Framingham risk score were similar between men who were positive/negative for these screening tools irrespective of the clinical criteria used to diagnose the condition.

4. Discussion

The NCEP-ATP III guidelines have recognized the metabolic syndrome as a cluster of abnormalities increasing the risk of CVD and type 2 diabetes mellitus [1]. Indeed, studies have shown that the risk of CVD is increased by about 2-fold, whereas the risk of type 2 diabetes mellitus could be increased by about 3- to 5-fold among subjects diagnosed with the clinical markers of the metabolic syndrome [2,30-32]. Because the metabolic syndrome is a prevalent condition [33], it is important to develop simple screening tools to identify in clinical practice individuals characterized by this "multiplex risk factor for CVD and/or type 2 diabetes mellitus." In this regard, several expert groups have proposed diagnostic criteria to detect subjects likely to have cardiometabolic risk markers of the metabolic syndrome [1,6,8-11]. In this regard, the hypertriglyceridemic waist phenotype represents a novel concept first introduced in the literature by Lemieux et al [12]. This previous study had shown that the simultaneous presence of high waist circumference and high TG levels was associated with a high probability of finding individuals characterized by a cluster of abnormalities predictive of an increased CVD risk [12]. The ability of the hypertriglyceridemic waist phenotype to identify high-risk patients has also been investigated in other studies, and similar conclusions were reached [16,34-45].

The different approaches to screen for the presence of cardiometabolic risk abnormalities have previously been compared in their ability to predict CVD and/or type 2 diabetes mellitus. Using both the NCEP-ATP III and the IDF clinical tools, Katzmarzyk et al [14] found that the predictive ability for CVD mortality of these 2 clinical criteria was comparable. Another recent analysis from the Hoorn Study also reported minimal differences across metabolic syndrome screening tools in the prediction of CVD [31]. These data are concordant with our results, as we found that hypertriglyceridemic waist may be as discriminant as the NCEP-ATP III and IDF criteria to identify men with an altered cardiometabolic risk profile.

Other studies have compared the ability of the hypertriglyceridemic waist phenotype to identify high-risk subjects with other screening tools [16,32,34]. The Insulin Resistance Atherosclerosis Study examined the ability of various metabolic syndrome screening tools to predict the 5-year incidence of type 2 diabetes mellitus [32]. Impaired glucose tolerance was the strongest predictor of future development of diabetes at follow-up and was followed closely by the World Health Organization, NCEP-ATP III, and IDF criteria [32]. Although hypertriglyceridemic waist has been associated with an increased risk of developing type 2 diabetes mellitus, this association is of moderate magnitude; and this phenotype has been shown to be significantly less predictive of type 2 diabetes mellitus than impaired glucose tolerance [32]. Tankó et al [16] investigated the relevance of the hypertriglyceridemic waist phenotype (waist circumference

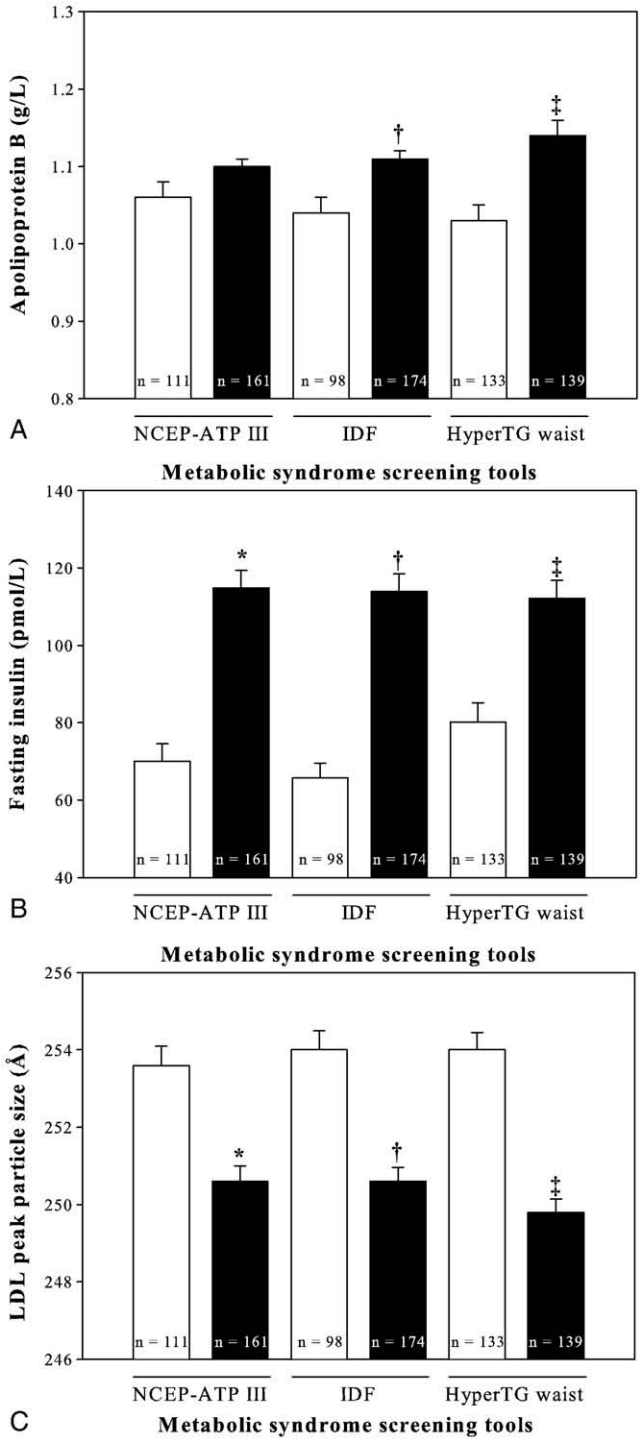

Fig. 1. Apolipoprotein B levels (A), fasting insulin concentrations (B), and LDL peak particle size (C) among men without (□) and with (■) the NCEP-ATP III, the IDF, or the hypertriglyceridemic waist phenotype criteria. Numbers below each bar represent the frequency of men in each subgroup. *$P < .0001$, different from men without the NCEP-ATP III criteria; †$P = .008$, different from men without the IDF criteria; and ‡$P < .0001$, different from men without the hypertriglyceridemic waist phenotype. HyperTG indicates hypertriglyceridemic.

≥88 cm and TG ≥1.45 mmol/L) compared with the NCEP-ATP III criteria in estimating future risk of cardiovascular mortality and the annual progression rate of aortic calcification in a large cohort of postmenopausal women. At baseline, women with the hypertriglyceridemic waist phenotype had a deteriorated fasting cardiometabolic risk profile, which was of similar magnitude than in women who had NCEP-ATP III criteria [16]. However, the presence of the hypertriglyceridemic waist phenotype was associated with the highest risk for fatal cardiovascular events over the 8.5-year follow-up [16]. Moreover, women characterized by the hypertriglyceridemic waist phenotype also had a higher annual progression rate of aortic calcification compared with those who had the NCEP-ATP III criteria [16]. These results suggest that hypertriglyceridemic waist could be a better indicator of cardiovascular risk in postmenopausal women than the NCEP-ATP III criteria. However, prospective studies are clearly needed to further compare the cardiovascular risk associated with the hypertriglyceridemic waist phenotype vs other metabolic syndrome screening tools in men. Kahn and Valdez [34] have compared the ability of enlarged waist with elevated TG (EWET) and NCEP-ATP III to identify high-risk subjects. They found that EWET alone identified more persons with high-risk concentrations of LDL cholesterol and apolipoprotein B than did NCEP-ATP III alone. However, HDL cholesterol, fasting glucose, blood pressure, fasting insulin, insulin resistance, and glycated hemoglobin levels were more likely to be deteriorated in the group with the NCEP-ATP III criteria alone. The waist circumference and TG levels thresholds (≥95 cm and ≥1.45 mmol/L, respectively) used in the EWET study were slightly different to the thresholds used in the present study.

The central role of abdominal obesity in the development of an atherogenic/diabetogenic cardiometabolic risk profile has been underlined in the NCEP-ATP III guidelines [1]. Ford et al [33] have also suggested that increases in the prevalence of abdominal obesity and high blood pressure, and to a lesser degree hypertriglyceridemia, most likely accounted for much of the increased prevalence of the metabolic syndrome. However, it has been suggested that a high waist circumference value in the absence of risk factors was not sufficient to be associated with a substantially increased risk of CVD [12,14]. In this regard, to properly estimate risks associated with an elevated waist circumference, clinicians must combine a metabolic marker suggestive of the presence of high-risk abdominal obesity. Hypertriglyceridemic waist and IDF criteria are screening approaches based on this concept. Indeed, waist circumference is a mandatory criterion of the metabolic syndrome under these 2 clinical screening tools, whereas an elevated waist is not required under the NCEP-ATP III criteria. In addition, the waist circumference threshold for men proposed by the NCEP-ATP III (>102 cm) is higher compared with the cutoff proposed by the hypertriglyceridemic waist phenotype (≥90 cm) and IDF criteria (≥94 cm). In this regard, it is possible that the NCEP-ATP III waist girth cutoff value (>102 cm) may be too high and may therefore lead to a misclassification of many men. However, the optimal waist circumference threshold to

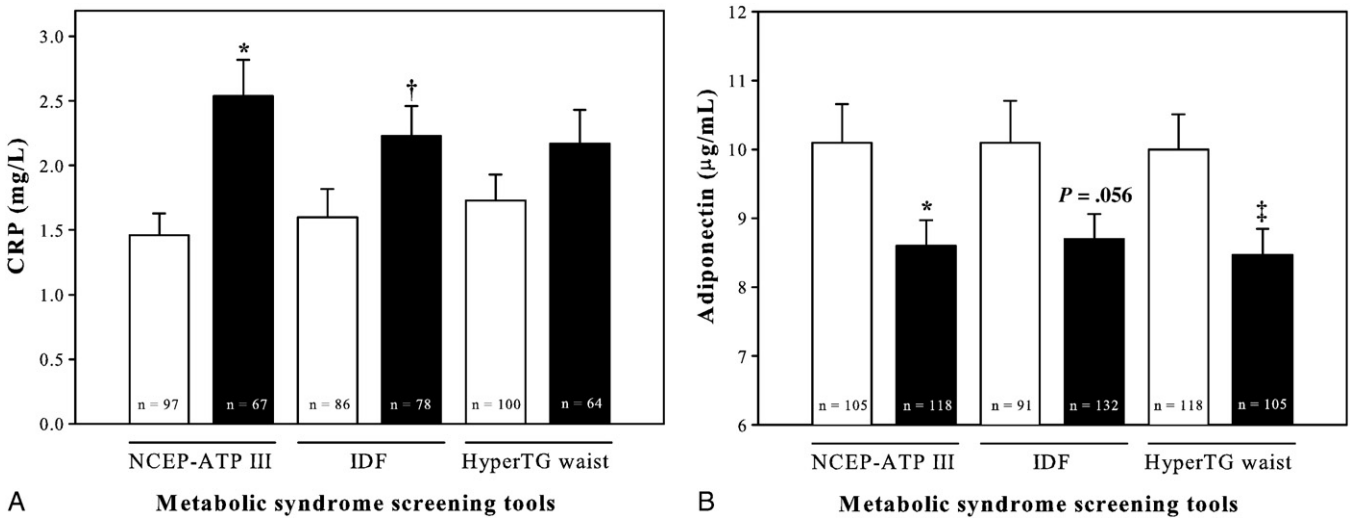

Fig. 2. C-reactive protein (A) and adiponectin levels (B) among men without (□) and with (■) the NCEP-ATP III, the IDF, or the hypertriglyceridemic waist phenotype. Numbers below each bar represent the frequency of men in each subgroup. *$P < .03$, different from men without the NCEP-ATP III criteria; †$P < .05$, different from men without the IDF criteria; and ‡$P < .02$, different from men without the hypertriglyceridemic waist phenotype. HyperTG indicates hypertriglyceridemic.

identify high-risk subjects remains to be determined, particularly in various ethnic groups.

Our results indicate that men characterized by the metabolic syndrome clinical criteria presented higher visceral adipose tissue accumulation compared with men without this condition. Small LDL particles, hyperinsulinemia, and elevated apolipoprotein B levels are abnormalities also found in these subjects. In this regard, evidence supports the fact that the presence of these cardiometabolic risk markers may substantially increase the risk of CVD [46-48].

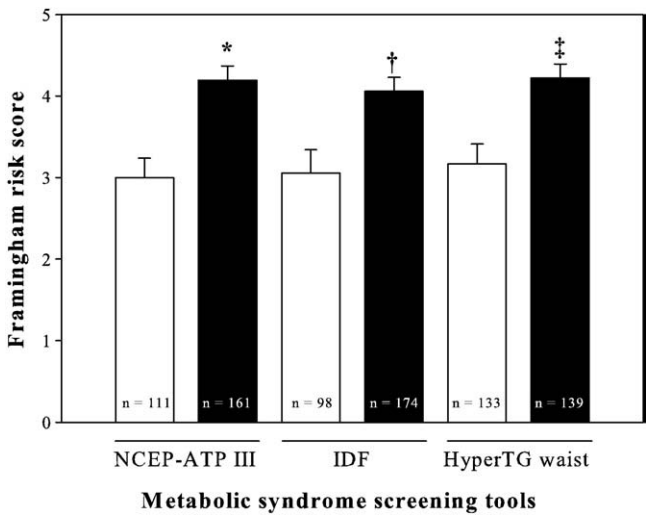

Fig. 3. Framingham risk score among men without (□) and with (■) the NCEP-ATP III, the IDF, or the hypertriglyceridemic waist phenotype. Numbers below each bar represent the number of men in each subgroup. *$P < .0001$, different from men without the NCEP-ATP III criteria; †$P = .002$, different from men without the IDF criteria; and ‡$P = .0004$, different from men without the hypertriglyceridemic waist phenotype. HyperTG indicates hypertriglyceridemic.

It is also well recognized that adipose tissue expresses numerous active molecules such as adiponectin [49]. In this regard, it has been proposed that hypoadiponectinemia associated with an excess of visceral adipose tissue might be a major factor involved in the vascular damages and cardiometabolic disorders observed in visceral obesity [50]. In the present study, subjects characterized by hypertriglyceridemic waist, NCEP-ATP III, or IDF criteria were all characterized by hypoadiponectinemia. However, we found no significant differences in LDL cholesterol concentrations between subjects with and without hypertriglyceridemic waist, NCEP-ATP III, or IDF criteria. It has been reported that plasma LDL cholesterol concentrations are not increased in viscerally obese patients characterized by features of the metabolic syndrome [25]. Rather, these individuals are characterized by an increased proportion of small LDL particles [25]. In this regard, clinicians should not rely on LDL cholesterol levels to identify patients with the metabolic syndrome. We also found that the Framingham risk score, commonly used to predict 10-year risk of CVD, was higher in men meeting our 3 screening criteria compared with men without them. However, we have to keep in mind that the Framingham risk score was not markedly elevated (about 4, which corresponds to a 7% probability to develop CVD over a period of 10 years) probably because our subjects did not have diabetes, did not smoke, and were fairly young. Thus, Framingham may not be optimal to estimate lifetime CVD risk in our specific population of men.

Prevention, identification, and treatment of the metabolic syndrome represent important challenges as we actually face an epidemic of abdominal obesity [51]. Consequently, as the prevalence of the metabolic syndrome increases, health care professionals are confronted with the challenge of properly evaluating the health burden associated with this condition.

The relative advantage of the hypertriglyceridemic waist phenotype compared with the NCEP-ATP III and IDF criteria is its use in the context of primary care medicine. Unfortunately, this study was restricted to men of only 1 racial group; and the sample cannot be considered as representative of any population. Nevertheless, results of the present study provide further support to the notion that hypertriglyceridemic waist represents a useful, simple, and discriminant screening phenotype to identify individuals likely to be characterized by an altered cardiometabolic risk profile.

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References

[1] Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486-97.

[2] Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA 2002;288:2709-16.

[3] Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001; 24:683-9.

[4] Scuteri A, Najjar SS, Morrell CH, et al. The metabolic syndrome in older individuals: prevalence and prediction of cardiovascular events: the Cardiovascular Health Study. Diabetes Care 2005;28:882-7.

[5] Després JP, Lemieux I. Abdominal obesity and metabolic syndrome. Nature 2006;444:881-7.

[6] Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143-421.

[7] De Backer G, Ambrosioni E, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. Eur Heart J 2003;24:1601-10.

[8] Alberti KG, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. Lancet 2005;366:1059-62.

[9] Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1998;15:539-53.

[10] Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). Diabet Med 1999;16:442-3.

[11] Grundy SM, Brewer HB, Cleeman JI, et al. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/ American Heart Association conference on scientific issues related to definition. Circulation 2004;109:433-8.

[12] Lemieux I, Pascot A, Couillard C, et al. Hypertriglyceridemic waist: a marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapolipoprotein B; small, dense LDL) in men? Circulation 2000;102: 179-84.

[13] Després JP, Lemieux I, Bergeron J, et al. Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk. Arterioscler Thromb Vasc Biol 2008;28:1039-49.

[14] Katzmarzyk PT, Janssen I, Ross R, et al. The importance of waist circumference in the definition of metabolic syndrome: prospective analyses of mortality in men. Diabetes Care 2006;29:404-9.

[15] Lemieux I, Alméras N, Mauriège P, et al. Prevalence of "hypertriglyceridemic waist" in men who participated in the Quebec Health Survey: association with atherogenic and diabetogenic metabolic risk factors. Can J Cardiol 2002;18:725-32.

[16] Tankó LB, Bagger YZ, Qin G, et al. Enlarged waist combined with elevated triglycerides is a strong predictor of accelerated atherogenesis and related cardiovascular mortality in postmenopausal women. Circulation 2005;111:1883-90.

[17] Lohman TG, Roche AF, Martorell R, eds. Anthropometric standardization reference manual. Champaign (Ill): Human Kinetics; 1988.

[18] van der Kooy K, Seidell JC. Techniques for the measurement of visceral fat: a practical guide. Int J Obes Relat Metab Disord 1993;17: 187-96.

[19] Ferland M, Després JP, Tremblay A, et al. Assessment of adipose tissue distribution by computed axial tomography in obese women: association with body density and anthropometric measurements. Br J Nutr 1989;61:139-48.

[20] Fossati P, Prencipe L. Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. Clin Chem 1982;28: 2077-80.

[21] Allain CC, Poon LS, Chan CSG, et al. Enzymatic determination of total serum cholesterol. Clin Chem 1974;20:470-5.

[22] Burstein M, Samaille J. Sur un dosage rapide du cholestérol lié aux beta-lipoprotéines du sérum. Clin Chim Acta 1960;5:609-10.

[23] Laurell CB. Quantitative estimation of proteins by electrophoresis in agarose gel containing antibodies. Anal Biochem 1966;15:45-52.

[24] Moorjani S, Dupont A, Labrie F, et al. Increase in plasma high density lipoprotein concentration following complete androgen blockage in men with prostatic carcinoma. Metabolism 1987;36:244-50.

[25] Tchernof A, Lamarche B, Prud'homme D, et al. The dense LDL phenotype. Association with plasma lipoprotein levels, visceral obesity, and hyperinsulinemia in men. Diabetes Care 1996;19:629-37.

[26] Richterich R, Dauwalder H. Determination of plasma glucose by hexokinase-glucose-6-phosphate dehydrogenase method. Schweiz Med Wochenschr 1971;101:615-8.

[27] Desbuquois B, Aurbach GD. Use of polyethylene glycol to separate free and antibody-bound peptide hormones in radioimmunoassays. J Clin Endocrinol Metab 1971;37:732-8.

[28] Ledue TB, Weiner DL, Sipe JD, et al. Analytical evaluation of particle-enhanced immunonephelometric assays for C-reactive protein, serum amyloid A and mannose-binding protein in human serum. Ann Clin Biochem 1998;35:745-53.

[29] Wilson PW, D'Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. Circulation 1998;97:1837-47.

[30] Malik S, Wong ND, Franklin SS, et al. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. Circulation 2004;110: 1245-50.

[31] Dekker JM, Girman C, Rhodes T, et al. Metabolic syndrome and 10-year cardiovascular disease risk in the Hoorn Study. Circulation 2005; 112:666-73.

[32] Hanley AJ, Karter AJ, Williams K, et al. Prediction of type 2 diabetes mellitus with alternative definitions of the metabolic syndrome: the

Insulin Resistance Atherosclerosis Study. Circulation 2005;112: 3713-21.
[33] Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among US adults. Diabetes Care 2004;27:2444-9.
[34] Kahn HS, Valdez R. Metabolic risks identified by the combination of enlarged waist and elevated triacylglycerol concentration. Am J Clin Nutr 2003;78:928-34.
[35] Solati M, Ghanbarian A, Rahmani M, et al. Cardiovascular risk factors in males with hypertriglycemic waist (Tehran Lipid and Glucose Study). Int J Obes Relat Metab Disord 2004;28:706-9.
[36] LaMonte MJ, Ainsworth BE, DuBose KD, et al. The hypertriglyceridemic waist phenotype among women. Atherosclerosis 2003;171: 123-30.
[37] Hiura Y, Acklin F, Newman J, et al. Hypertriglyceridemic waist as a screening tool for CVD risk in indigenous Australian women. Ethn Dis 2003;13:80-4.
[38] Blackburn P, Lamarche B, Couillard C, et al. Postprandial hyperlipidemia: another correlate of the "hypertriglyceridemic waist" phenotype in men. Atherosclerosis 2003;171:327-36.
[39] Esmaillzadeh A, Mirmiran P, Azizi F. Clustering of metabolic abnormalities in adolescents with the hypertriglyceridemic waist phenotype. Am J Clin Nutr 2006;83:36-46 [quiz 183-4].
[40] Senechal M, Lemieux I, Beucler I, et al. Features of the metabolic syndrome of "hypertriglyceridemic waist" and transplant coronary artery disease. J Heart Lung Transplant 2005;24:819-26.
[41] Bos G, Dekker JM, Heine RJ. Non-HDL cholesterol contributes to the "hypertriglyceridemic waist" as a cardiovascular risk factor: the Hoorn study. Diabetes Care 2004;27:283-4.
[42] Correll CU, Frederickson AM, Kane JM, et al. Metabolic syndrome and the risk of coronary heart disease in 367 patients treated with second-generation antipsychotic drugs. J Clin Psychiatry 2006;67: 575-83.
[43] Czernichow S, Bruckert E, Bertrais S, et al. Hypertriglyceridemic waist and 7.5-year prospective risk of cardiovascular disease in asymptomatic middle-aged men. Int J Obes (Lond) 2007;31:791-6.
[44] Pollex RL, Hanley AJ, Zinman B, et al. Clinical and genetic associations with hypertriglyceridemic waist in a Canadian aboriginal population. Int J Obes (Lond) 2006;30:484-91.
[45] Gazi IF, Filippatos TD, Tsimihodimos V, et al. The hypertriglyceridemic waist phenotype is a predictor of elevated levels of small, dense LDL cholesterol. Lipids 2006;41:647-54.
[46] Després JP, Lamarche B, Mauriège P, et al. Hyperinsulinemia as an independent risk factor for ischemic heart disease. N Engl J Med 1996; 334:952-7.
[47] Lamarche B, Tchernof A, Mauriège P, et al. Fasting insulin and apolipoprotein B levels and low-density lipoprotein particle size as risk factors for ischemic heart disease. JAMA 1998;279:1955-61.
[48] Lamarche B, Moorjani S, Lupien PJ, et al. Apolipoprotein A-I and B levels and the risk of ischemic heart disease during a five-year follow-up of men in the Quebec cardiovascular study. Circulation 1996;94:273-8.
[49] Motoshima H, Wu X, Sinha MK, et al. Differential regulation of adiponectin secretion from cultured human omental and subcutaneous adipocytes: effects of insulin and rosiglitazone. J Clin Endocrinol Metab 2002;87:5662-7.
[50] Matsuzawa Y, Funahashi T, Kihara S, et al. Adiponectin and metabolic syndrome. Arterioscler Thromb Vasc Biol 2004;24: 29-33.
[51] Ford ES, Mokdad AH, Giles WH. Trends in waist circumference among US adults. Obes Res 2003;11:1223-31.