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Metabolic Syndrome and Incident Cardiovascular Morbidity and Mortality in a Mediterranean Hypertensive Population

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Background: Although the metabolic syndrome (MetS) is associated with adverse cardiovascular disease (CVD) risk in the general population, it is not clear whether its existence is independently associated with CVD in hypertensives. We investigated the presence of MetS in subjects with hypertension and its impact on the incidence of CVD.

Methods: We prospectively investigated 1007 hypertensive individuals. The MetS was assessed using the National Cholesterol Education Program–Adult Treatment Panel III (NCEP-ATP III) criteria. The incidence of fatal and nonfatal cardiovascular events was ascertained during a median follow-up period of 2.1 years.

Results: The prevalence of MetS was 42.1% (39.0% in men and 44.7% in women). In addition to hypertension, four MetS components were present in 3.6% of the individuals, three in 13.7%, two in 24.8%, and only one in 33.7%. The incidence of cardiac, cerebrovascular, and total cardiovascular events/1000 person-years was higher among MetS subjects than among those without (31.0% *v* 21.3%, $P = .050$, 25.5% *v* 13.7%, $P = .045$, and 55.4% *v* 35.8% $P = .009$, respectively). After adjustment, MetS subjects had higher risk for cardiac, cerebrovascular, and total cardiovascular events (by 72%, 90%, and 75%, respectively). Hypertensive subjects with three or more components of MetS had threefold higher risk for cardiac events, 2.59 for cerebrovascular, and 2.26 for total cardiovascular events compared with those with no other component.

Conclusions: The MetS is a significant predictor of cardiovascular morbidity and mortality. The clustering of three or more components of the syndrome in addition to hypertension recognizes a population of even higher cardiovascular risk independently of other traditional risk factors. Am J Hypertens 2007;20:558–564 © 2007 American Journal of Hypertension, Ltd.

Key Words: Arterial hypertension, metabolic syndrome, cardiovascular morbidity and mortality.

Subjects with arterial hypertension have a two- to fourfold increased risk of future cardiovascular events. A tendency of hypertension to cluster with other major cardiovascular disease (CVD) risk factors has been reported.[1] Moreover, a stepwise increase in the CVD risk was associated not only with the degree of blood pressure (BP) elevation but also with the burden of other risk factors.[2] The frequent clustering of certain cardiovascular risk factors is well recognized and is formally defined as the metabolic syndrome (MetS).[3] Several studies demonstrated that MetS is associated with increased cardiovascular morbidity and mortality both in the general population and in subjects with type 2 diabetes.[4,5] Although there is no doubt that multiple risk factors markedly increase the risk of cardiovascular events, it has not yet been clarified whether identification of MetS confers clinical advantage over and above the identification of its single components. In particular, it is not clear whether the presence of MetS in individuals with arterial hypertension amounts to an important risk factor for cardiovascular events.

The aim of this study was to investigate the prevalence of MetS in a Mediterranean hypertensive population and to evaluate its predictive role in cardiovascular morbidity and mortality, independently of conventional cardiovascular risk factors.

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Methods

Study Population

The study population was recruited from hypertensive individuals who attended the Blood Pressure Clinic of our Department during the period of 1992 to 2005 and originated from the population living in the greater Athens area. Office measurements of systolic and diastolic BP were performed manually with a calibrated mercury sphygmomanometer. The diagnosis and classification of arterial hypertension was based on the average of three or more properly measured seated BP readings on three or more consecutive office visits, 1 week apart.[6] Hypertension was defined as systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg, or taking antihypertensive medication. Criteria for exclusion were secondary hypertension, pregnancy, any coexisting disease that might seriously reduce life expectancy (eg, advanced cancer), presence of CVD, and refusal to attend follow-up visits. All subjects gave written informed consent that they were willing to participate in the study, which has been approved by the scientific committee of the Evangelismos State General Hospital. At baseline all hypertensives were interviewed and examined by trained investigators. Participants were asked to fast and to refrain from smoking for 12 h and to avoid alcohol intake for 3 days before blood sampling. Body mass index was calculated as weight in kilograms divided by the square of height in meters. Smoking habit was self-reported and classified into one of three categories: never been a smoker, ex-smoker if the subject stopped smoking at least 1 month before the visit, and smoker. Plasma concentrations of total and HDL cholesterol and triglycerides were measured enzymatically using the Modular Roche biochemical analyzer (Roche Diagnostics GmbHD-68298, Manheim, Germany). Low-density lipoprotein cholesterol was calculated by the Friedwald formula.[7] In participants with triglycerides >400 mg/dL the lipoprotein fractions were separated using preparative ultracentrifugation of plasma by β quantification.[8] Blood glucose was measured using a glucose dehydrogenase method after precipitation of proteins by trichloroacetic acid. A total of 1007 individuals fulfilling these criteria were included in the study after their first visit at the outpatient Blood Pressure Clinic of our Department and were evaluated prospectively.

Definition of the Metabolic Syndrome

Individuals were considered as having MetS if three or more of the following criteria were present at baseline: waist circumference >102 cm in men and >88 cm in women, serum triglyceride levels ≥150 mg/dL, HDL cholesterol <40 mg/dL in men and <50 mg/dL in women or under hypolipidemic treatment, fasting blood glucose ≥110 mg/dL or under antidiabetic treatment, and BP ≥130/85 mm Hg or taking antihypertensive medication.[3] All study participants fulfilled the last criterion as they were hypertensives.

Ascertainment of Cardiovascular Disease Morbidity and Mortality

During the follow-up period, 1992 to 2005, subjects were regularly examined at the Blood Pressure Clinic three to four times per year. The relevant time scale for the analysis was the period between the study entry to death or to December 31, 2005. Information regarding subjects who had died was obtained from hospital discharge, and death certificates were provided by their relatives. The main outcomes were death from cardiovascular causes occurring within 24 h after the onset of symptoms without clinical or postmortem evidence of another cause; deaths from myocardial infarction or stroke; that occurred within 7 days after the onset of myocardial infarction or stroke; and deaths from congestive heart failure or ruptured abdominal aortic aneurysm. Cardiovascular disease was defined as myocardial infarction, unstable angina (defined as worsening angina or angina at rest requiring hospitalization), hospitalization for heart failure with clinical and radiologic signs of congestion, arrhythmias (atrial fibrillation, ventricular tachycardia, ventricular extrasystoles, and supraventricular tachycardia with bundle brunch block), revascularization or limb amputation, and the development of heart failure or new or worsening angina regardless of the need for hospitalization. Myocardial infarction was diagnosed when two of the following three criteria were met: typical symptoms, increased cardiac enzyme levels (at least twice the normal upper limit), and diagnostic electrocardiographic changes. Cerebrovascular disease was defined as stroke or transient ischemic attack (TIA). Stroke was diagnosed as a neurologic deficit lasting more than 24 h in contrast to TIA. A computed tomographic or magnetic resonance imaging examination was performed to define the type of stroke.

Statistical Analysis

Because data on waist circumference were not available for all subjects at baseline, waist circumference >102 cm for men and >88 cm for women was estimated by body mass index (BMI) using receiver operating characteristic (ROC) curves. Sensitivity and specificity were calculated for optimal cutoffs. The area under the curve (AUC) was also calculated (Figs. 1 and 2). For this estimation a population of 659 individuals that had both waist circumference and BMI were analyzed. This cohort was derived from an ongoing clinical trial in our Department, the CARMOS (Cardiovascular Risk Modification Study),[9] in which the participants had similar age and ethnic background as the studied hypertensive population. Demographics were reported as mean ± standard deviation. Number of events and incidence rates were presented as the number of events/1000 person-years and provided by the presence of MetS. Cardiac and cerebrovascular events were analyzed. Because of the small number of deaths, a separate analysis for mortality was not conducted. A variable "total CVD" was used to represent the cases in which

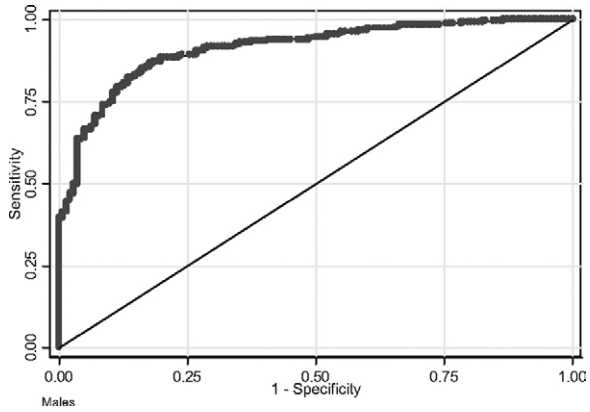

FIG. 1. The receiver operating characteristic curve for the prediction of waist >102 cm from body mass index in men.

cardiac or cerebrovascular events or death had occurred and was also analyzed. Event rates were calculated dividing the number of events occurring during the study period by the number of person-years of observation. Cox proportional hazards models adjusted for sex, age, smoking, and LDL cholesterol were used to calculate hazards ratios (HRs) for end point events in relation to MetS and its individual components. The assumption of proportional HRs was evaluated by testing for interaction with a continuous time variable. The *P* values for trend in HRs for severity of disease were also estimated. Kaplan-Meier survival estimates for cardiac and cerebrovascular events were graphed during the follow-up period for participants with and without MetS. All reported *P* values are two-tailed. The predictive value for cardiac, total CVD, and cerebrovascular events of the Framingham risk score (FRS) in comparison to that of MetS was also evaluated through ROC curves and their respective AUCs. Statistical significance was set at $P < .05$, and analyses were conducted using STATA statistical software (version 6.0, Stata Corporation, College Station, TX).

Results

Data from 410 men were analyzed, using the ROC curve, and a BMI value of 28.4 kg/m^2 was found to represent the optimal cutoff for waist circumference >102 cm for men (sensitivity 88.8% and specificity 76.8%) (Fig. 1). Similarly, data from 249 women were analyzed and BMI value of 27 kg/m^2 represented the optimal cutoff for waist circumference >88 cm for women (sensitivity 81.2% and specificity 81.9%) (Fig. 2). The AUC was 0.91 for men and 0.89 for women, which significantly differs from 0.5 ($P < .001$).

A total of 1007 hypertensive subjects (mean age 59.3 ± 12.4 years), 459 men and 548 women (mean age 60.7 ± 11.5 and 57.7 ± 13.3 years, respectively), were included in the study. The demographic and CVD risk factor characteristics are shown in Table 1. The prevalence of MetS was 42.1% (39.0% and 44.7% among men and women, respectively). Hypertensive individuals with MetS had greater risk for cardiac (HR = 1.72, 95% CI: 1.00–2.94, $P \leq .05$), cerebrovascular (HR = 1.93, 95% CI: 1.00–3.72, $P \leq .05$), or total CVD events (HR = 1.69, 95% CI: 1.10–2.57, $P \leq .05$) after adjustment for systolic BP in the multivariate model. In addition to hypertension, four components of MetS were present in 3.6% of the subjects, three in 13.7%, two in 24.8%, and only one in 33.7% (Table 2). The prevalence of each component of MetS was as follows: central obesity 49.1%, high serum triglyceride levels 29.6%, low HDL-cholesterol levels 36.9%, and high blood glucose levels 23.1%. During the follow-up period (median 2.1 years, range 0.1 to 13.8 years), 56 subjects had experienced a cardiac event (23 had new onset angina; 7 acute myocardial infarction; 13 arrhythmias, of which 10 were atrial fibrillation; 1 ventricular tachycardia; 1 ventricular extrasystole and 1 supraventricular tachycardia with bundle brunch block; and 13 new onset congestive heart failure). Furthermore, 41 individuals had experienced a cerebrovascular event (15 stroke and 26 TIA). During this period, five deaths occurred (one from cardiac and four from cerebrovascular events). Unadjusted Kaplan-Meier survival estimates during the follow-up period for total CVD in hypertensive individuals without and with MetS, as well as according to the number of the components of MetS, are illustrated in Figs. 3 and 4. The number of event rates/1000 patient-years according to MetS are shown in Table 3. Adjusted HRs for cardiac and cerebrovascular events or total CVD indicate that the presence of MetS is significantly associated with the risk of cardiac or cerebrovascular events. Individuals with MetS have a 72% greater HR for cardiac event, 90% greater HR for cerebrovascular events, and 75% greater HR for total CVD, after adjustment for sex, age, smoking, and LDL-cholesterol levels.

The prevalence of obesity (BMI ≥30 kg/m^2) was 29.2%. After the exclusion of obese subjects, the relationship of MetS with cardiac morbidity remained significant (HR = 2.08, 95% CI: 1.12–3.86, $P \leq .05$), and the risk for cerebrovascular events was still higher for those with

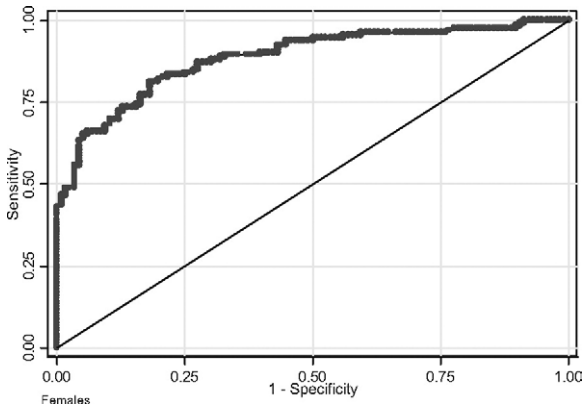

FIG. 2. The receiver operating characteristic curve for the prediction of waist >88 cm from body mass index in women.

Table 1. Characteristics of the hypertensive subjects with and without metabolic syndrome

	Metabolic syndrome		
	Absent ***N*** **= 583 (57.9%)**	**Present** ***N*** **= 424 (42.1%)**	***P***
Age (y)			
<50	152 (26.1)	74 (17.4)	
50–59	159 (27.3)	139 (32.8)	.080*
60–69	155 (26.6)	120 (28.3)	
>70	117 (20.0)	91 (21.5)	
Men	280 (48)	179 (42.2)	.068*
Women	303 (51.9)	245 (57.8)	
BMI (kg/m^2)	26.6 ± 3.8†	30.6 ± 4.8†	<.001‡
Systolic BP (mm Hg)	150.5 ± 21.6†	153.5 ± 23.7†	.038‡
Diastolic BP (mm Hg)	93.6 ± 12.4†	93.6 ± 13.4†	.982‡
HDL-C (mg/dL)	57.2 ± 38.3†	43.24 ± 11.4†	<.001‡
Triglycerides (mg/dL)	102.5 ± 41.8†	178.9 ± 123.2†	<.001‡
Plasma glucose (mg/dL)	94.7 ± 14.6†	116.0 ± 41.5†	<.001‡
Smoking			
Never smoker	334 (57.3)	256 (60.4)	
Ex-smoker	90 (15.5)	62 (14.5)	.654*
Smoker	159 (27.2)	106 (25.1)	

BMI = body mass index; HDL-C = HDL cholesterol.
* χ^2 test; † Data are mean ± 1 SD; ‡ Student's *t*-test.

MetS in comparison to those without (HR = 1.84, 95% CI: 1.00–3.36, $P \leq .05$). Also, in the hypertensive nonobese individuals with MetS, the risk for total CVD events was significantly higher (HR = 1.71, 95% CI: 1.04–2.82, $P \leq .01$). Furthermore, in the studied hypertensive population, the prevalence of diabetes was 13.2%. After the exclusion of subjects with frank diabetes, the relationship of MetS with cardiac morbidity as well as with the risk for cerebrovascular events was still high (HR = 1.69, 95% CI: 1.00–2.84, $P \leq .05$; HR = 2.06, 95% CI: 1.03–4.09, $P \leq .05$, respectively). Moreover, in hypertensives with MetS but without diabetes the risk for total CVD events was significantly higher (HR = 1.67, 95% CI: 1.01–2.74, $P \leq .01$).

Subjects with three or more components of MetS in addition to hypertension have almost three times greater risk for cardiac events compared with those without MetS. Furthermore, hypertensives with three or more components of MetS have 2.59 and 2.26 times greater risk for

Table 2. Distribution of the different components of the metabolic syndrome among the hypertensive subjects

Components of MetS	***N*** **= 1007 (%)**
Four	36 (3.6)
Central obesity + (↑) triglycerides + (↓) HDL + (↑) glucose	36 (3.6)
Three	138 (13.7)
Central obesity + (↑) triglycerides + (↓) HDL	55 (5.5)
Central obesity + (↑) triglycerides + (↑) glucose	23 (2.3)
Central obesity + (↓) HDL + (↑) glucose	41 (4.1)
(↑) Triglycerides + (↓) HDL + (↑) glucose	19 (1.8)
Two	250 (24.8)
Central obesity + (↑) triglycerides	50 (5.0)
Central obesity + (↓) HDL	74 (7.3)
(↑) Triglycerides + (↓) HDL	50 (5.0)
(↑) Triglycerides + (↑) glucose	17 (1.6)
(↓) HDL + (↑) glucose	17 (1.7)
Central obesity + (↑) glucose	42 (4.2)
One	339 (33.7)
Central obesity	173 (17.2)
(↑) Triglycerides	48 (4.8)
(↑) Glucose	38 (3.8)
(↓) HDL	80 (8.0)
Hypertension only	244 (24.2)

(↑) and (↓) are as set by the NCEP-ATP III criteria.

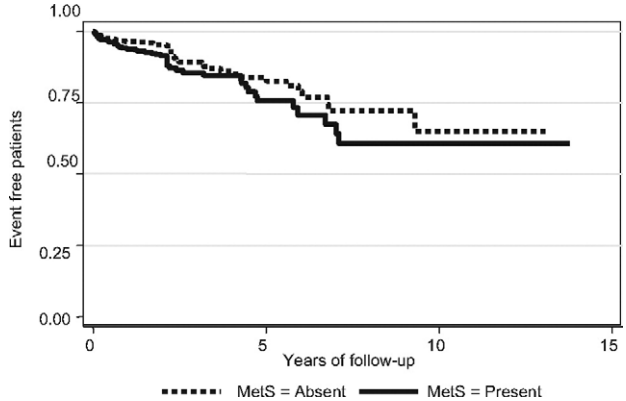

FIG. 3. Kaplan-Meier estimates for total cardiovascular morbidity and mortality of individuals with and without metabolic syndrome (MetS).

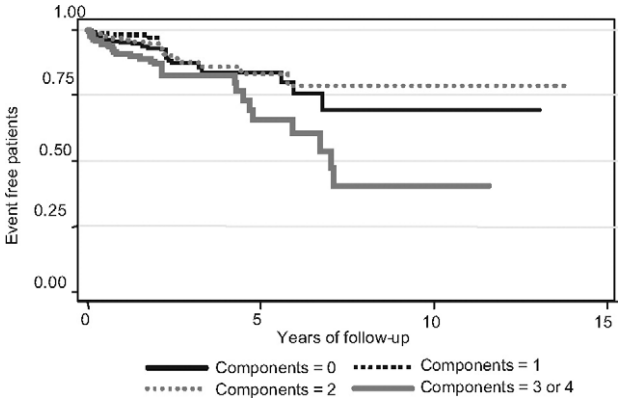

FIG. 4. Kaplan-Meier estimates for total cardiovascular morbidity and mortality of individuals according to the number of the components of metabolic syndrome (MetS).

cerebrovascular events or total CVD, respectively, compared with those without any other component, after adjustment for sex, age, smoking, and LDL cholesterol. Moreover, hypertensive subjects with three or more components of MetS have a higher cardiac, cerebrovascular, and total CVD risk compared with those with less than three components (*P* for trend .041, .028, and .014, respectively) (Table 3). The FRS had the same accuracy (AUC = 0.58, 95% CI: 0.48–0.68) for the prediction of cerebrovascular events with MetS (AUC = 0.58, 95% CI: 0.47–0.69, *P* = .993). The FRS was a better predictor for cardiac events (AUC = 0.69, 95% CI: 0.61–0.76) than MetS (AUC = 0.58, 95% CI: 0.51–0.67, *P* = .027), as well as for total CVD (AUC = 0.64, 95% CI: 0.59–0.69 *v* AUC = 0.57, 95% CI: 0.49–0.64, *P* = .046).

Discussion

This prospective population-based cohort study indicates the impact of MetS on cardiovascular morbidity and mortality in hypertensive subjects independently of the other major CVD risk factors. According to the National Cholesterol Education Program–Adult Treatment Panel III (NCEP-ATP III) criteria, which can easily be applied in daily clinical practice, approximately one-half (42.1%) of

Table 3. Incidence and hazards ratios of cardiac, cerebrovascular, and total cardiovascular (CVD) events in hypertensive individuals

End point events	n (%)	Event rates/ 1000 patient-years (95% CI)	HR (95% CI)	*P*
Cardiac events				
Metabolic syndrome				
Absent	28/583 (4.8)	21.3 (14.7–30.9)	1.00	
Present	28/424 (6.6)	31.0 (21.4–44.9)	1.73 (1.00–3.00)	.050
No. of MetS components				
0	11/244 (4.5)	20.1 (11.1–36.3)	1.00	
1	17/339 (5.0)	22.2 (13.8–35.7)	1.40 (0.61–3.19)	.424
2	12/250 (4.8)	22.0 (12.5–38.8)	1.54 (0.64–3.68)	.337
3 or 4	16/174 (9.2)	44.7 (27.4–72.9)	2.96 (1.29–6.82)	.011
		P value for trend = .041		
Cerebrovascular events				
Metabolic syndrome				
Absent	18/583 (3.1)	13.7 (8.6–21.8)	1.00	
Present	23/424 (5.4)	25.5 (16.9–38.3)	1.91 (1.01–3.58)	.045
No. of MetS components				
0	10/244 (4.1)	18.3 (9.8–34.0)	1.00	
1	8/339 (2.4)	10.4 (5.2–20.9)	0.70 (0.28–1.78)	.454
2	9/250 (3.6)	16.5 (8.6–31.7)	1.01 (0.41–2.52)	.982
3 or 4	14/174 (8.1)	39.1 (23.2–66.0)	2.59 (1.12–5.98)	.026
		P value for trend = .028		
Total CVD				
Metabolic syndrome				
Absent	47/583 (8.1)	35.8 (26.9–47.6)	1.00	
Present	50/424 (11.8)	55.4 (42.0–73.0)	1.75 (1.15–2.66)	.009
No. of MetS components				
0	25/244 (10.3)	45.7 (30.9–67.6)	1.00	
1	22/339 (6.5)	28.7 (18.9–43.6)	0.78 (0.42–1.44)	.434
2	20/250 (8.0)	36.7 (23.7–56.9)	1.03 (0.55–1.93)	.931
3 or 4	30/174 (17.2)	83.8 (58.6–119.8)	2.26 (1.27–4.02)	.006
		P value for trend = .014		

HR = hazards ratios (95% confidence interval), adjusted for sex, age, smoking, and LDL cholesterol; Total CVD = cases in which cardiac and cerebrovascular events or death had occurred.

this Mediterranean hypertensive population has MetS, whereas the unadjusted prevalence of MetS among US adults in the general population is only 21.7%.[10] Higher prevalence of MetS has been observed in older individuals (28.1%),[11] in middle-aged adults from the San Antonio Heart Study in non-Hispanic whites (23%) and in Hispanic whites (30%), and in the Framingham Offspring Study (24%).[12] In subjects with type 2 diabetes mellitus the prevalence of MetS is even higher (75.6%).[13] In a review of prospective studies, Ford,[14] using definitions of MetS developed by NCEP-ATP III and World Health Organization (WHO), suggests that the risk for cardiovascular disease may be higher among women than men, although in other studies no such sex-specific difference has been observed. In a recent metaanalysis from 21 studies, a greater impact of MetS on the cardiovascular risk in women than in men has been reported but only in studies that used the WHO and not the NCEP-ATP III definition.[15]

In our hypertensive population, MetS proved to be an independent predictor of cardiovascular morbidity and has a greater independent effect than its components. It has also been shown that in nonobese individuals, a 1.7- to 2-fold increase in risk for cardiac, cerebrovascular, and total CVD is observed in subjects with MetS in comparison to those without MetS. Furthermore, in our nondiabetic hypertensives, MetS confers a 1.7-fold increase in relative risk for cardiac and a twofold increase in cerebrovascular disease as compared with individuals without the syndrome. Several studies have evaluated the ability of MetS to predict CVD independently of individuals' conventional risk factors, providing conflicting outcomes.[12,13,16] In a recent review the imprecision of MetS definition led the investigators to doubt the value of using the syndrome as a marker for CVD risk and to emphasize the treatment of all CVD risk factors independently.[17] In middle-aged individuals from the San Antonio Heart Study, the NCEP-ATP III and the WHO definitions of MetS were predictive of cardiovascular mortality, and the NCEP-ATP III definition was a stronger predictor in low-risk subjects, according to the estimated Framingham score.[12] In the studied population MetS proved to have the same accuracy with the FRS to predict cerebrovascular events, whereas the latter seems to be superior for the prediction of cardiac and total CVD. Estimating 10-year risk entails key risk factors beyond those of MetS (ie, age, sex, smoking, and total cholesterol). Moreover, risk factors of MetS are not graded for severity, as are the risk factors contained in FRS. Framingham investigators found little or no increase in predictive power for cardiac disease by adding obesity, triglycerides, or fasting glucose to their 10-year risk algorithm. These factors come into play in the longer term. Thus, for subjects who manifest MetS, the long-term risk may be elevated regardless of the Framingham score.

A notable exception to the large body of evidence documenting the adverse impact of MetS is a study conducted in elderly diabetic subjects, which showed that the HRs for all cause and CVD mortality did not differ among those with and without the syndrome.[13]

According to our findings, hypertensive subjects with three or four components of the syndrome have a threefold higher risk of cardiac events and more than twofold higher risk of cerebrovascular events or total CVD than hypertensives with no other risk factors. Even after adjustment for sex, age, smoking, and serum LDL-cholesterol levels, the presence of MetS was associated with a 72% increase in the risk for cardiac events, 90% for cerebrovascular events, and 75% for total CVD. This additional risk might be explained by the individual component of the syndrome in association with other not routinely measured aspects of MetS, such as oxidative stress, increased small dense LDL, and hyperinsulinemia. Schillaci et al[18] described for the first time the adverse prognostic impact of MetS in hypertensive subjects, suggesting that MetS represents an independent risk factor for future cardiovascular events in hypertensives. In this study the event rate increased progressively with an increasing number of components of MetS. In our hypertensive population the prognostic significance of MetS proved to be strong only when three or four components of MetS coexisted.

Several mechanisms have been proposed to explain the relation between MetS and CVD. One hypothesis is that MetS may exert its deleterious effects by adversely affecting the structural and functional properties of the vasculature, such as arterial wall thickness and stiffness.[19] In our study the higher systolic BP in MetS subjects supports the view that MetS might selectively contribute to increase aortic stiffness, recognized as the predominant cause of increased pulse pressure, which constitutes a more sensitive measure of risk than other indices of BP in middle-aged and older persons.[20] Furthermore, Bonora et al[21] observed that MetS conferred a significantly increased risk for developing new carotid plaques, new carotid stenosis, and new coronary events. In addition, insulin resistance, which is related to MetS, is associated with central obesity and activation of a proinflammatory and prothrombotic state, characterized by elevation of C-reactive protein, plasminogen activator inhibitor-1, and fibrinogen. Thus, important differences may exist between hypertensive subjects who are insulin sensitive and those with hypertension combined with insulin resistance, as the latter are more likely to develop cardiovascular disease.[22]

In conclusion, this study demonstrates that MetS is highly prevalent in hypertensive subjects. The existence of MetS in hypertensive subjects is a strong predictor of cardiac and cerebrovascular events, as well as a predictor of total cardiovascular morbidity and mortality. The clustering of more than three components of the syndrome, besides hypertension, identifies a population at an even higher cardiovascular risk.

Perspectives

In this Mediterranean hypertensive population, MetS, as defined by NCEP-ATP III criteria, could predict cardiovascular disease independently of other established cardiovascular risk factors. More research is needed to elucidate the reasons for this. If confirmed, these results suggest that in hypertensive subjects with MetS, specifically, those found to be at a high or even intermediate 10-year risk for cardiovascular disease, aggressive management of both major and metabolic risk factors can contribute to risk reduction.

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