

## Prevalence of the metabolic syndrome in patients with hypertension treated in general practice in Spain: an assessment of blood pressure and low-density lipoprotein cholesterol control and accuracy of diagnosis

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### Abstract

This study was designed to evaluate whether primary care physicians in Spain accurately diagnose the metabolic syndrome in hypertensive patients, to define the profile and management of these patients in clinical practice, and to ascertain the level of blood pressure and low-density lipoprotein cholesterol control. Data were analyzed from a cross-sectional survey involving 12,954 patients with hypertension (Prevención Cardiovascular en España en Atención Primaria: Intervención Sobre el Colesterol en Hipertensión [PRESCOT] study), wherein 52% of the cohort fulfilled the National Cholesterol Education Program-Adult Treatment Panel criteria for the metabolic syndrome. The majority of patients (54.6%) had 3 risk factors, 32.4% had 4, and 13% had 5 risk factors. Physician diagnosis of the metabolic syndrome was poor, with 43.7% of physicians missing the diagnosis and 12.9% wrongly diagnosing the metabolic syndrome. Blood pressure and low-density lipoprotein cholesterol control rates were very low, with only 4.7% of metabolic syndrome patients achieving control for both blood pressure and low-density lipoprotein cholesterol vs 13.5% for non-metabolic syndrome patients ( $P < .0001$ ). These findings demonstrate that the metabolic syndrome is common in patients with hypertension and that it is generally poorly diagnosed and treated by primary care physicians.

The metabolic syndrome (MetS) is characterized by an array of cardiovascular risk factors that may be predictive of longer-term disease sequelae in certain individuals. The syndrome is associated with insulin resistance and hyperglycemia and coincides with an increased risk of developing type 2 diabetes and cardiovascular disease.<sup>1-5</sup> Although Reaven<sup>6</sup> described the syndrome in the late 1980s, a precise definition and the clinical importance of MetS are still evolving. In the United States, the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III)<sup>7</sup> has provided a relatively simple definition of MetS. NCEP-ATP III criteria are widely used in clinical practice, and they facilitate an easy identification of the syndrome with uncomplicated criteria that can be applied in the most basic health care setting. Recently, the International Diabetes Federation (IDF) proposed a definition that emphasizes the importance of abdominal obesity and lowers the threshold for several parameters such as waist circumference, blood pressure (BP), and fasting plasma glucose.<sup>8</sup>

As diabetes and obesity in Western countries are increasing, almost to epidemic proportions, not surprisingly the prevalence of MetS is progressively growing.<sup>9</sup> Without intervention this will almost certainly result in an increase in cardiovascular morbidity and place a greater burden on Western society.<sup>10,11</sup>

Although MetS is associated with cardiovascular disease, the risk is not homogeneous and may vary according to age, sex, and severity.<sup>12,13</sup> Patients with hypertension and MetS represent a particularly high-risk group, not only because of the higher prevalence of target organ damage,<sup>14</sup> but also because of the increased incidence of cardiovascular complications observed in this population.<sup>12,15</sup> The presence of MetS in hypertensive patients acquires greater clinical relevance and, to improve prognosis, it is important to be able to accurately diagnose MetS, to better understand the long-term impact, and to reduce the number and severity of risk factors. BP and low-density lipoprotein cholesterol (LDL-C) are established risk factors that are strongly associated with cardiovascular morbidity and mortality, and longer-term control of these will likely significantly improve the survival of MetS patients.<sup>16</sup>

MetS has been associated with an increased risk for cardiovascular disease in a number of pivotal trials, including community-based populations, and in primary preventive settings.<sup>1</sup> Studies involving large numbers of patients with hypertension and MetS treated in Spanish general practice facilities are not so common. Furthermore, few data are available regarding the ability of primary care physicians to accurately diagnose MetS. The goals of this general practice study undertaken in Spain were to:

- Determine the prevalence of MetS according to the NCEP-ATP III definition;
- Determine accuracy in physician diagnosis of MetS;
- Determine the demographics of and medications used in patients with MetS compared with those without MetS; and
- Compare control rates of BP and lipids in patients with and without MetS.

## **Patients and Methods**

### *Study Population.*

The study population involved patients with hypertension included in the *Prevención Cardiovascular en España en Atención Primaria: Intervención Sobre el Colesterol en Hipertensión (PRESCOT)* cross-sectional epidemiologic survey. The aim was to determine the clinical profile and associated risk factors, including MetS, in a population of patients with hypertension attending general practice clinics across Spain. Approximately 2000 primary care physicians participated in the study, which was performed during the first quarter of 2004. Each investigator was asked to include the first 6 patients with hypertension who attended their outpatient clinic. Inclusion criteria were age 18 years and older, man or woman, hypertension (systolic BP >140 mm Hg and/or diastolic BP >90 mm Hg or receiving antihypertensive treatment), and an available blood test with a complete lipid profile within the past 6 months. To best reflect clinical practice in Spain, no specific exclusion criteria were defined.

### *Methodology and Data Collection.*

Seated BP was measured after 5 minutes of resting. Two measurements were taken and the mean was recorded. BP was considered to be well controlled using the guidelines of the European Society of Hypertension (<140/90 mm Hg for the general population and <130/80 mm Hg for diabetic patients).<sup>15</sup>

Patients were classified as dyslipidemic when they had a confirmed diagnosis of an impaired lipid profile (hypercholesterolemia, hypertriglyceridemia, or mixed hyperlipidemia) according to NCEP-ATP III or were receiving lipid-lowering therapy.

Coronary risk stratification was performed using the NCEP-ATP III classification.<sup>7</sup> High-risk patients were those with coronary disease or a risk equivalent (10-year coronary risk >20%), medium-risk patients were those with 2 or more risk factors (10-year coronary risk 10%–20%), and low-risk patients were those with 1 or no cardiovascular risk factors (10-year coronary risk <10%). Coronary risk equivalents included peripheral arterial disease, abdominal aortic aneurysm, carotid disease, and diabetes. Risk factors included smoking, high BP, decreased levels of high-density lipoprotein cholesterol (HDL-C) (<40 mg/dL), family history of premature coronary disease (first-degree relatives younger than 55 years in men and younger than 65 years in women), and age (45 or older in men and 55 and older in women).<sup>7</sup> LDL-C control was thus defined in relation to the above risk categories as established by NCEP-ATP III guidelines: LDL-C <100 mg/dL for the high-risk group, <130 mg/dL for the medium-risk group, and <160 mg/dL for the low-risk group.

MetS was diagnosed using NCEP-ATP III criteria requiring the presence of 3 or more of the following: abdominal obesity (waist circumference >102/88 cm or >40/35 inches for men/women); triglycerides  $\geq$ 150 mg/dL; HDL-C <40/50 mg/dL (men/women); fasting glucose  $\geq$ 110 mg/dL; or BP  $\geq$ 130/85 mm Hg.<sup>7</sup> Waist circumference was measured at the midway point between the iliac crest and the costal margin. NCEP-ATP III criteria were used to define MetS because of their ease in applying in primary care, which has caused this definition to be the most utilized by general practitioners in Spain. The physicians completed a specific individual case report form with all the collected clinical and analytic data. They were asked to identify the presence of MetS according ATP III criteria, and the diagnosis was specifically recorded in the case report form. To facilitate the physicians' task, a sheet with the ATP III diagnostic criteria was included in the study documentation. A post hoc analysis was performed using the IDF criteria.<sup>8</sup>

To evaluate whether primary care physicians correctly identified MetS, their diagnosis was compared with an independent control assessment using patient data stored on a central database.

## Statistical Analyses.

Various statistical tests were performed depending on the nature of variables being compared. The chi-square test was used to analyze the relationship between categorical variables; however, when >20% of the cells had an expected frequency lower than 5, the Fisher exact test was employed. Comparison of continuous variables between groups was performed using the Student *t* test. Database design was subjected to internal consistency rules and ranges to control inconsistencies/inaccuracies in the collection and tabulation of data (SPSS version 11.0.1; SPSS Inc, Cary, NC).

## Results

The PRESCOT survey enrolled a total of 15,707 patients, of which 12,954 (82.5%) were finally included in the analysis after excluding those who did not comply with the selection criteria and/or whose case report forms were incomplete and/or inconsistent. Of the 12,954 patients included in the survey, 5866 (52%) fulfilled NCEP-ATP III diagnostic criteria for MetS. Of these, 54.6% had the minimum of 3 MetS risk factors, 32.4% had 4 risk factors, and 13% had 5 risk factors. Interestingly, if the newer IDF classification<sup>8</sup> was applied, the prevalence of MetS in our hypertensive population would have risen from 52% to 75.5%.

Table I details the baseline characteristics of the overall study population subdivided into patients with MetS and patients without MetS. All risk factors for cardiovascular disease relating to BP control and hyperlipidemia were significantly worse in the MetS group (higher systolic and diastolic BP, total cholesterol, LDL-C and triglycerides, and lower HDL-C levels). Interestingly, there were more women than men in the MetS group (56.1% vs 43.9%, respectively;  $P<.0001$ ). Excluding hypertension, the most common components of MetS were abdominal obesity (as measured by waist circumference; 50.5% of cases) and increased triglyceride levels (49.8% of cases). There were some significant sex-related distribution differences in the patients with MetS (Table II), with more women than men presenting with abdominal obesity (59.6% vs 41.4%, respectively;  $P<.0001$ ) and low HDL-C levels (40.3% vs 18.7%, respectively;  $P<.0001$ ) and more men than women presenting with hypertriglyceridemia (56.7% vs 43.4%, respectively;  $P<.0001$ ).

**Table I.** Characteristics of Patients With Hypertension in the PRESCOT Trial by Presence or Absence of the Metabolic Syndrome (MetS)

Variables	Demographic Data		P
	Hypertensive Patients With MetS	Hypertensive Patients Without MetS	
Sex, male/female, %	43.9/56.1	55.5/44.5	<.0001*
Age, y	62.3±10.5	62.1±10.8	.5161†
BMI, kg/m <sup>2</sup>	29.6±4.3	27.3±3.7	<.0001†
Waist circumference, cm	104.9±15.4	93.4±14.3	<.0001†
SBP, mm Hg	145.8±14.3	142.2±13.8	<.0001†
DBP, mm Hg	86.0±9.1	83.9±8.9	<.0001†
Total cholesterol, mg/dL	237.3±40.9	227.3±42.2	<.0001†
Triglycerides, mg/dL	192.3±92.2	120.1±46.6	<.0001†
LDL cholesterol, mg/dL	154.2±93.5	144.8±76.0	<.0001†
HDL cholesterol, mg/dL	47.8±17.0	58.5±16.4	<.0001†
Fasting plasma glucose, mg/dL	124.4±37.7	96.8±16.7	<.0001†

PRESCOT indicates the Prevención Cardiovascular en España en Atención Primaria Intervención Sobre el Colesterol en Hipertensión study; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL, low-density lipoprotein; and HDL, high-density lipoprotein. \*Chi-square test. †Student *t* test.

**Table II.** Prevalence of the Different ATP III Components in Patients With the Metabolic Syndrome

Risk Factor	Total, %	Men, %	Women, %	<i>p</i> *
Hypertension (BP $\geq$ 130/85 mm Hg or Rx)	100	100	100	–
Waist circumference >102 cm for men or >88 cm for women	50.5	41.4	59.6	<.0001
Triglycerides $\geq$ 150 mg/dL	49.8	56.7	43.4	<.0001
Low HDL cholesterol <40 mg/dL for men or <50 mg/dL for women	29.5	18.7	40.3	<.0001
Fasting plasma glucose >110 mg/dL	35.6	35.7	35.5	.8079

ATP III indicates the third report of the Adult Treatment Panel; BP, blood pressure; Rx, receiving antihypertensive treatment; and HDL, high-density lipoprotein. \*Student *t* test for continuous variables; chi-square test for categoric variables.

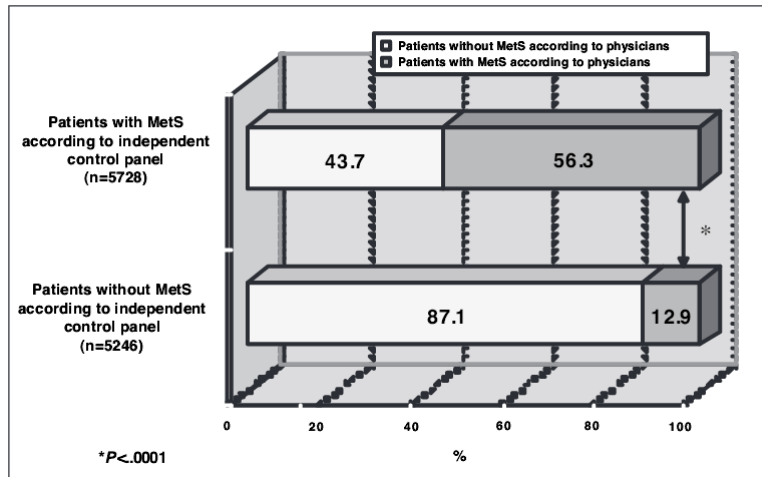
The 98.2% of patients with MetS were taking at least 1 antihypertensive drug; 17.7% were on monotherapy and 80.5% were treated with 2 or more drugs. MetS patients were taking significantly more antihypertensive medication than those without MetS (45.3% vs 36.6% were on combined therapy, respectively; *P*<.001). The use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers (74.8% vs 67.6%, respectively; *P*<.001) and statins (43.0% vs 39.1%, respectively; *P*<.001) was more frequent in MetS patients. Table III represents the percentage of antihypertensive and lipid-lowering drugs used in patients according to the presence of MetS.

**Table III.** Percentage of Antihypertensive and Lipid-Lowering Drugs Used in Patients According to the Presence of the Metabolic Syndrome (MetS)

Type Of Treatment	Hypertensive Patients With MetS, %	Hypertensive Patients Without MetS, %
Antihypertensive drugs		
ACEIs	43.5	39.6
Diuretics	38.3	32.8
ARBs	32.7	28.7
Calcium antagonists	20.3	17.7
$\beta$ -Blockers	12.7	13.0
ACEI and ARB	74.8	67.6
Other	4	3.5
Lipid-lowering drugs		
Statins	43.0	39.1
Other	5.8	2.6

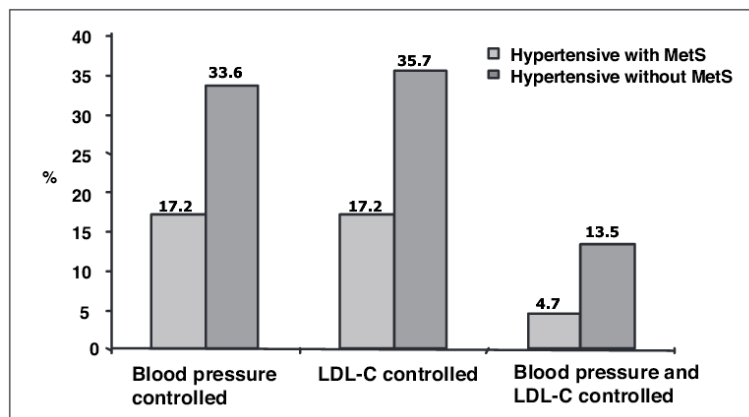
ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

The diagnosis concordance between physicians and a control assessment was 56.3% for the presence of MetS and 87.1% for the absence of MetS (Figure 1). Crucially, general practitioners did not diagnose 43.7% of cases of MetS and 12.9% of patients were wrongly diagnosed as having MetS despite not meeting NCEP-ATP III criteria.



**Figure 1.** Diagnosis of the metabolic syndrome (MetS) by primary care physicians compared with independent assessment.

Findings with regard to BP and LDL-C control are presented in [Figure 2](#). BP was controlled in fewer patients with MetS compared with those without MetS (17.2% vs 33.6%, respectively;  $P<.001$ ). Systolic BP was controlled in 20.7% of MetS patients and in 37.2% of non-MetS patients ( $P<.0001$ ), while diastolic BP was controlled in 39.0% vs 63.7% ( $P<.0001$ ), respectively. Similarly, LDL-C control was worse in MetS patients than in patients without MetS (17.2% vs 35.7%, respectively;  $P<.0001$ ). As expected, the degree of control of BP and LDL-C combined was also lower in patients with MetS (4.7% vs 13.5%;  $P<.0001$ ).



**Figure 2.** Degree of blood pressure and low-density lipoprotein cholesterol (LDL-C) control in hypertensive patients according to the presence of the metabolic syndrome (MetS).

Among the patients with MetS, the BP and LDL-C controls were worse in the subgroup of MetS patients with diabetes compared with nondiabetics (Table IV). BP was controlled in 23.0% of MetS patients without diabetes and in 9.5% of MetS patients with diabetes ( $P<.001$ ). Similar results were observed for LDL-C, control being achieved in 22.2% of MetS nondiabetic patients and 10.5% of MetS patients with diabetes ( $P<.0001$ ). The combined BP and LDL-C control was achieved in 6.3% of nondiabetic patients with MetS and in only 2.6% of diabetics with MetS ( $P<.001$ ).

**Table IV.** Percentage of Patients With Hypertension and Coexisting Metabolic Syndrome (MetS) (With or Without Diabetes) Achieving Control of BP and LDL-C

Variables	Hypertensive Patients With MetS and Diabetes, %	Hypertensive Patients With MetS Without Diabetes, %	<i>p</i> *
BP controlled	9.5	23.0	<.0001
LDL-C controlled	10.5	22.2	<.0001
Both BP and LDL-C controlled	2.6	6.3	<.0001

BP indicates blood pressure; LDL-C, low-density lipoprotein cholesterol.\*Student *t* test for continuous variables; chi-square test for categorical variables.

## Discussion

A number of pivotal studies have been reported in the past 5 years that have investigated the prevalence of MetS. One of the pioneering studies in this regard was the third report of the National Health and Nutrition Examination Survey (NHANES III) study,<sup>17</sup> which randomly selected 8800 Americans between the ages of 20 and 89 years. The overall prevalence of MetS in this survey was 21.8%, and studies such as Framingham,<sup>18</sup> West of Scotland Coronary Prevention Study (WOSCOPS),<sup>19</sup> the Women's Health Study,<sup>20</sup> and other studies carried out in Western countries<sup>3-5</sup> have reported similar prevalence rates.

Few studies have been carried out in Spain investigating MetS. Martínez-Larrad and colleagues<sup>21</sup> reported a prevalence of 17% in urban and rural areas using NCEP-ATP III criteria. A prevalence of 24.4% was observed in the Canary Islands, and the rate increased with age and decreased with educational level.<sup>22</sup> In a primary care study, Ascaso and colleagues<sup>23</sup> found that MetS prevalence was 48.4% in subjects with abdominal obesity compared with 18.8% in those without abdominal obesity. A large study that included more than 19,000 workers recorded a MetS prevalence of 12% (16% in men and 8% in women).<sup>24</sup> Clear geographic differences regarding the distribution of MetS have been detected, and these are probably a consequence of different environmental factors such as diet and physical exercise. More recently, de la Sierra and associates<sup>25</sup> reported a prevalence of 44.6% using NCEP-ATP III criteria and 61.7% using IDF criteria in a primary care study in Spain involving 19,039 patients with hypertension. The results of our large cross-sectional survey involving hypertensive patients attending primary health care centers in Spain demonstrated an even higher prevalence of MetS: 52% using NCEP-ATP III criteria and 75.5% using IDF criteria. In our series, the presence of MetS was more frequent in women (56.1% vs 43.9% for men;  $P < .0001$ ). It should be taken into account that this study was carried out in Spanish primary care; therefore, these results could somehow differ in other sites and may not be generalizable to other countries with different health care delivery.

It is notable that despite being American, the NCEP-ATP III criteria have been widely accepted in Spain. It is probably because NCEP-ATP III criteria are easy to apply, which results in the MetS being easily diagnosed in primary care. Although the NCEP-ATP III guidelines define MetS as the presence of 3 or more diagnostic criteria, the risk is not homogeneous and may vary according to age, sex, and severity of MetS.<sup>12,13</sup> In the current study, almost half of the MetS patients (45.5%) had 4 or 5 diagnostic criteria, which is indicative of high cardiovascular risk.<sup>12</sup> Furthermore, this study was performed in a hypertensive cohort, which, in itself, confers added risk. Therefore, it is not surprising that a higher prevalence of MetS was detected in this study compared with general population studies and is more in line with findings from trials involving patients with diabetes or heart disease. For example, a prevalence of 77% was noted in a study involving 318 type 2 diabetics<sup>26</sup> and a rate of 41.1% in patients with heart disease.<sup>27</sup>

Japanese researchers reported a positive correlation between MetS prevalence and BP in a study involving 506 untreated hypertensive patients.<sup>28</sup> Patients were divided into 3 groups according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) classification and the prevalence of MetS was 9.9% in normotensive subjects, 19.2% in prehypertensive patients, and 35.5% in the hypertensive subjects. A positive correlation between insulin resistance and BP was also documented, and the authors noted that the higher the BP, the greater the number of risk factors for MetS. A somewhat higher prevalence of 37.6% for MetS in prehypertensive patients was recently reported in the Trial for Preventing Hypertension (TROPHY)

substudy.<sup>29</sup> With regard to MetS prevalence, our study confirms the finding of Ford<sup>30</sup> who reported that the rate is significantly higher when IDF criteria are used.

Evaluation of the quality of diagnosis of MetS in the current trial showed that physician diagnosis of MetS was generally poor: in 43.7% of cases they missed the diagnosis and in 12.9% they wrongly diagnosed MetS when diagnostic criteria were not met. These data highlight the need for continuous medical education to improve the management of this syndrome in general practice. Previous studies had noted an underestimation of the cardiovascular risk in this setting.<sup>31,32</sup> Thus, in the Estratificación del Riesgo Cardiovascular en Hipertensión en Atención Primaria e Impacto Sobre el Tratamiento Antihipertensivo (DIORISC) study,<sup>31</sup> which included 9374 hypertensive patients managed in primary care, 61% of patients belonged to a high or very high-risk group, yet physicians only identified 39% of these patients as being at high or very high risk ( $P < .0001$ ).<sup>31</sup>

There is now a body of evidence demonstrating that MetS increases cardiovascular morbidity and mortality, reinforcing the importance of optimizing management of these patients and achieving adequate control of risk factors.<sup>16</sup> Furthermore, in hypertensive patients with MetS, cardiovascular morbidity and mortality are significantly higher and so the relative risk is compounded. Schillaci and colleagues<sup>12</sup> observed that hypertensive patients with MetS had double the number of cardiovascular events compared with patients without MetS. They also noted that the greater the number of MetS risk factors, the worse the prognosis.

The results of the current study provide an insight into the status of the treatment of patients with hypertension and coexisting MetS in general practice and highlight some important concerns regarding the management of cardiovascular risk. Indeed, the overall control of hypertension and dyslipidemia was relatively poor in this cohort. The proportion of patients achieving control of both BP and LDL-C was low for the total patient population, but it was worse in patients with MetS than in those without MetS (4.7% vs 13.5%, respectively;  $P < .0001$ ) and worse still in hypertensive patients with MetS and diabetes (2.6%). These results indicate that in patients with hypertension, management of BP and LDL-C and risk factors for cardiovascular disease is generally very poor in Spain. Management is worse in patients with coexisting MetS and, interestingly, this occurs despite the fact that patients with MetS were receiving more medications to reduce both BP and LDL-C than patients without MetS and were also receiving more antihypertensive drugs than was reported in previous studies.<sup>31,33</sup>

The cross-sectional design of the study was chosen to best represent real-world clinical practice. Consequently, a large population of hypertensive patients was included in the trial with very few patient exclusion criteria. This was achieved by consecutive sampling. This methodology has its limitations since it reduces the level of control that can be exercised to reduce variation and bias (eg, random sampling and “blind” controls). The large number of patients included in the study, however, and the nature of the end points being measured, with no comparators under review, minimizes this theoretical limitation. It is notable that, since this study was performed in primary care in Spain, the results may not be generalizable to other countries with different health care delivery.

Overall, the study was designed to represent clinical practice, presenting an accurate picture of the hypertensive population attending primary care.

## Conclusions

These data demonstrate the high prevalence of MetS in a hypertensive population attending primary care facilities in Spain. More than half of the patients fulfilled NCEP-ACT III criteria for MetS. Management of BP and LDL-C, key risk factors for cardiovascular morbidity and mortality, was worse in patients with MetS than in those without the syndrome.

Although interest in MetS has recently increased, it is not always accurately identified. The findings of this study show that it is clearly underdiagnosed and undertreated. This highlights the need for ongoing medical education to improve the management of this syndrome in general practice, with the goal of aggressively reducing cardiovascular risk.

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