### Original article

### Prevalence of Metabolic Syndrome and its Components in Patients With Acute Coronary Syndrome

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#### ABSTRACT

*Introduction and objectives*: A large proportion of patients with coronary disease have metabolic syndrome, although the frequency and association of its different components are not well understood. The aim of this study was to determine the prevalence of metabolic syndrome and the combination of its components in a Spanish cohort of patients with acute coronary syndrome.

*Methods:* Clinical histories of 574 inpatients with acute coronary syndrome in 6 tertiary hospitals were reviewed and the presence of metabolic syndrome and its components determined by applying Adult Treatment Panel III criteria. In a second step, the components of the metabolic syndrome were analyzed, excluding those patients with diabetes mellitus.

**Results:** The metabolic syndrome was present in 50.9% of patients and was more frequent in women than in men (66.3% vs. 47.3%; P < .001). The most prevalent component was carbohydrate metabolism disorder (85.3%), followed by low high-density lipoprotein cholesterol (HDLc) levels (80.5%). In nondiabetic patients, 34.6% had metabolic syndrome and the most prevalent component was low HDLc levels (86%), followed by high blood pressure and hypertriglyceridemia and, in fourth place, impaired fasting serum glucose levels.

*Conclusions:* The metabolic syndrome has a high prevalence in patients with an acute coronary syndrome, especially in women. The most frequent components are hyperglycemia and low HDLc levels. After excluding diabetic patients, the most prevalent diagnostic criterion of metabolic syndrome was low HDLc levels.

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# Prevalencia del síndrome metabólico y de sus componentes en pacientes con síndrome coronario agudo

#### RESUMEN

*Introducción y objetivos:* El síndrome metabólico está presente en una gran proporción de pacientes con enfermedad coronaria, aunque no se conoce bien la frecuencia y la asociación de sus distintos componentes. El objetivo de este estudio es determinar la prevalencia de síndrome metabólico, así como la combinación de sus distintos componentes en una cohorte española de pacientes con síndrome coronario agudo.

*Métodos:* Se revisaron 574 historias clínicas de pacientes ingresados en 6 hospitales de tercer nivel por un síndrome coronario agudo, determinando la presencia de síndrome metabólico según los criterios del *Adult Treatment Panel III*, así como de sus distintos componentes. En un segundo paso, se analizaron los distintos componentes del síndrome metabólico excluyendo a los pacientes diabéticos.

**Resultados:** El 50,9% de pacientes tenían síndrome metabólico, que fue más frecuente en mujeres que en varones (el 66,3 frente al 47,3%; p < 0,001). La alteración del metabolismo de los hidratos de carbono (85,3%) fue el factor más prevalente, seguido del colesterol unido a lipoproteínas de alta densidad (cHDL) bajo (80,5%). Entre los pacientes no diabéticos, el 34,6% presentaba síndrome metabólico, y su componente más frecuente fue el cHDL bajo (86%), seguido de hipertensión arterial e hipertriglice-ridemia, mientras que la glucemia basal alterada fue menos frecuente.

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*Conclusiones:* El síndrome metabólico tiene una elevada prevalencia en los pacientes con síndrome coronario agudo, especialmente en las mujeres. Los componentes más frecuentes son la hiperglucemia y el cHDL bajo. Al excluir a los pacientes diabéticos, el criterio diagnóstico más prevalente fue el cHDL bajo. © 2011 Sociedad Española de Cardiología. Publicado por Elsevier España, S.L. Todos los derechos reservados.

#### Abbreviations

ACS: acute coronary syndrome ATPIII: National Cholesterol Education Program-Adult Treatment Panel III BMI: body mass index DM2: type 2 diabetes mellitus HDLc: high-density lipoproteins cholesterol MS: metabolic syndrome

#### **INTRODUCTION**

The metabolic syndrome (MS) is a combination of interrelated metabolic abnormalities that significantly increase the risk of cardiovascular disease, and type 2 diabetes mellitus (DM2).<sup>1–6</sup> Its prevalence is increasing worldwide and is a serious public health problem. Each component of MS is individually associated with an increased risk of cardiovascular disease; however, whether MS leads to greater cardiovascular risk than the sum of its components remains a matter of debate.<sup>7</sup> It has been suggested that the number of MS components may be more useful in predicting cardiovascular disease than MS itself,<sup>8</sup> since cardiovascular risk increases as the number of components increases.<sup>9–11</sup> Similarly, given the heterogeneity of MS, the impact of the possible combinations of its components on predicting cardiovascular risk has been investigated. In this sense, DM2 is the predominant risk factor associated with the development of ischemic heart disease.<sup>7,12</sup>

Some studies have analyzed the prevalence of MS in patients with acute coronary disease, reporting an estimated prevalence of 41%-50% in Europe and the United States.<sup>8,13</sup> In Spain, our group conducted a study 7 years ago that applied the European Group for the study of Insulin Resistance (EGIR) criteria and found a prevalence of 41% in patients with stable chronic ischemic heart disease.<sup>14</sup>

The definition of MS provided by the National Cholesterol Education Program-Adult Treatment Panel III (ATPIII) includes individuals with DM2. It is known that DM2 strongly increases the risk of cardiovascular disease, and in fact is considered equivalent to having suffered a coronary event in terms of cardiovascular risk.<sup>15,16</sup> Hence, some definitions of MS exclude DM2, such as that established by the EGIR or the American College of Endocrinology.<sup>17,18</sup> However, few studies have analyzed the frequency of the different components of MS and their associations in nondiabetic populations with coronary disease.<sup>11</sup>

The aim of the present study was to determine the prevalence of MS and the frequency and combination of its definitive components in patients with acute coronary syndrome (ACS) in Spain. We also analyzed all the previously mentioned variables in nondiabetic patients, in light of possible differences in the prevalence and association of the remaining components of MS.

#### **METHODS**

#### **Study Population**

Clinical histories from inpatients with ACS admitted to coronary or intensive care units in 6 tertiary hospitals between January 2004 and September 2007 were selected based on the following inclusion criteria: *a*) availability of plasma high-density lipoprotein cholesterol (HDLc) measurements, and *b*) body mass index (BMI) determined during admission. ACS was defined according to the international guidelines for clinical practice.<sup>19–21</sup> In total, 574 patients were included in the analysis.

In a second step, 309 patients underwent a second blood test for glycemia; the remaining 265 patients had a previous diagnosis of DM2 or fasting plasma glucose levels  $\geq$  126 mg/dL (7 mmol/L) at admission, subsequently tested and confirmed.

#### **Definition of Variables**

Demographic and clinical data were obtained from the clinical histories: age, sex, weight, height, previous atherosclerotic vascular disease (defined as previous coronary disease, stroke, or peripheral arterial disease), hypertension, DM2, a sedentary lifestyle (defined as performing less than 30 min of moderate exercise 3 days per week), smoking, alcohol consumption, and previous lipid-lowering treatment. Individuals were classified as being nonsmokers, current smokers, and former smokers (patients who had guit smoking at least 3 months before admission). Fasting plasma glucose levels and lipid profile (total cholesterol, low density lipoprotein cholesterol [LDLc], cholesterol other than HDLc [non-HDLc], HDLc, and triglycerides) were measured. Total cholesterol and triglycerides were measured using an automated enzyme analyzer, and HDLc was measured after separation by precipitation. LDLc concentrations were calculated using the Friedewald formula whenever plasma triglyceride concentrations were < 400 mg/dL. Non-HDLc was calculated as total cholesterol minus HDLc. The diagnosis of MS was established using modified ATPIII criteria<sup>2</sup> based on the presence of 3 or more of the following 5 factors: *a*) BMI >29 kg/m<sup>2</sup> for men and >29.9 kg/m<sup>2</sup> for women (replacing the ATPIII criterion of a waist circumference of  $\geq$ 102 cm for men and 288 cm for women as an indirect estimation  $(method)^{22,23}$ ; b) hypertension, defined as clinical history of documented elevated blood pressure or persistent systolic blood pressure >130 mmHg and diastolic blood pressure >85 mmHg; *c*) hypertriglyceridemia, defined as fasting plasma triglyceride levels >150 mg/dL previous to or within 24 h of admission; d) low plasma HDLc values, defined as < 40 mg/dL (1.04 mmol/L) for men and < 50 mg/dL (1.3 mmol/L) for women, measured either before or within the first 24 h of admission, and e) carbohydrate metabolism disorder, defined as previously documented impaired fasting plasma glucose levels or a history of DM2 or fasting plasma glucose levels >100 mg/dL (5.6 mmol/L) at least 48 h after admission.

#### **Statistical Analysis**

Quantitative variables are expressed as mean  $\pm$  standard deviation, and qualitative variables as absolute and relative frequencies. Normally distributed data were analyzed using the Student *t*-test to compare means; otherwise the Mann-Whitney U test was used. The  $\chi^2$  test was used to analyze differences between qualitative variables. A *P* value of < .05 was used as a cutoff for statistical significance. All the statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows software, v. 15.0; Chicago, Illinois, United States.

#### Table 1

Clinical Characteristics of the 574 Spanish Patients With Acute Coronary Syndrome and Differences by Sex

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	All patients (n=574)	Men (n=467)	Women (n=107)	Р
Age (years)	$62.4 \pm 11.9$	$61.7 \pm 11.6$	$65.3 \pm 12.8$	.004
Previous ischemic heart disease, % (n)	43.8 (245)	44.7 (204)	39.8 (41)	.362
Current smoker, % (n) Former smoker, % (n)	41.6 (234) 33.9 (191)	45 (206) 37.8 (173)	26.7 (28) 17.1 (18)	<.001
Sedentary lifestyle, % (n)	67.3 (302)	67.8 (246)	65.1 (56)	.637
Alcohol consumer, % (n) 15-30 g/d >30 g/d	12.7 (53) 9.6 (40)	15.1 (50) 11.8 (39)	3.5 (3) 1.2 (1)	<.001
BMI (kg/m <sup>2</sup> ) BMI <25, % (n) BMI 25-30, % (n) BMI >30, % (n)	$28.4 \pm 4.2$ 19.9 (114) 49 (281) 31.2 (179)	28.4±3.8 16.9 (79) 54.2 (253) 28.9 (135)	$28.7 \pm 4.2 \\32.7 (35) \\27.1 (29) \\40.2 (43)$	.395 < <b>.001</b>
DM2, % (n)	34.4 (191)	32.4 (146)	42.9 (45)	.042
Fasting plasma glucose (mg/dL)	$130.7\pm61.6$	$128.5\pm57.6$	$140\pm75.6$	.081
Total cholesterol (mg/dL)	$187.1\pm46.2$	$187.1\pm45.8$	$187.5\pm48.9$	.922
LDLc (mg/dL)	$120.5\pm42$	$121.7\pm42.4$	$115.9\pm40$	.203
HDLc (mg/dL)	$40.4\pm11.6$	$40 \pm 11.2$	$43.1\pm13.5$	.007
Non-HDLc (mg/dL)	$146.7\pm45.4$	$147.1\pm45.4$	$144.4\pm47$	.55
Triglycerides (mg/dL)	$152.2\pm86.7$	$151.3\pm76.1$	$159.3 \pm 123.9$	.363
Low HDLc + hypertriglyceridemia, % (n)	31.4 (180)	30.4 (142)	35.5 (38)	.304
Previous lipid-lowering therapy, $\%(n)$	35.7 (205)	36 (168)	34.6 (37)	.786
Statins	34 (195)	34 (159)	33.6 (36)	.937
Fibrates	2.3 (13)	2.6 (12)	0.9 (1)	.479
Metabolic syndrome, % (n)	50.9 (292)	47.3 (221)	66.4 (71)	<.001
Carbohydrate metabolism disorder, % (n)	66.2 (380)	66.8 (312)	63.6 (68)	.52
Low HDLc, % (n)	60.1 (345)	57 (266)	73.8 (79)	.001
Hypertension, % (n)	59.2 (340)	57.2 (267)	68.2 (73)	.036
Hypertriglyceridemia, % (n)	41.5 (238)	41.3 (193)	42.1 (45)	.89
High BMI, % (n)	31.7 (182)	29.3 (137)	42.1 (45)	.011

BMI, Body Mass Index; DM2, type 2 diabetes mellitus; HDLc, high-density lipoprotein cholesterol; LDLc, low-density lipoprotein cholesterol; non-HDL, cholesterol other than HDLc.

Values are expressed as mean  $\pm$  standard deviation, unless otherwise indicated.

Bold is used to underline data with standard deviation; the Student *t*-test was used for differences between means; the  $\chi^2$  test was used for differences between proportions; high BMI, BMI >29 for men and >29.9 for women.

#### RESULTS

The clinical characteristics of the study population are shown in Table 1. The total prevalence of MS using ATPIII criteria was 50.9% (292 patients). We found no MS components in 29 patients (5.1%), 1 in 96 (16.7%), 2 in 157 (27.4%), 3 in 135 (23.5%), 4 in 115 (20%), and all 5 in 42 (7.3%) patients. The most frequent component of MS was carbohydrate metabolism disorder, followed by reduced HDLc levels, hypertension, hypertriglyceridemia and, in last place, obesity.

#### Sex Differences

Women with ACS were older and had a higher prevalence of DM2; however, when the ATPIII criterion for carbohydrate metabolism disorder was applied, there were no significant differences between men and women (Table 1 and Fig. 1). Although the mean BMI for both sexes was similar, a greater percentage of women had a BMI <25 kg/m<sup>2</sup> or >30 kg/m<sup>2</sup>, whereas men were more frequently overweight. Mean HDLc levels were greater in women than in men, although a higher percentage of women had low HDLc levels when ATPIII criteria were applied. Men with ACS presented a greater frequency of current or previous alcohol consumption and smoking.

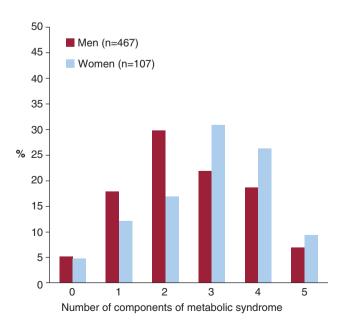


Figure 1. Frequency of the number of metabolic syndrome components by sex.

Women with ACS had a higher prevalence of MS (66.3% vs 47.3%; P<.001), and a greater number of MS components (median of 2 components for men and 3 for women; P = .004).

#### Analysis of the Patients Without Metabolic Syndrome

In total, 282 (49.1%) patients did not fulfill criteria for MS. The most frequent component present in the 96 patients with 1 MS component was carbohydrate metabolism disorder (39.6%, 38 patients), followed by low HDLc levels (27%, 26 patients) and hypertension (22.9%, 22 patients). Hypertriglyceridemia, as an isolated component of MS, was only found in 5 patients (5.2%); this was also the case for obesity.

Among those presenting 2 components (135 patients), the most frequent association was hypertension and carbohydrate metabolism disorder (28%, 44 patients), followed by low HDLc levels and carbohydrate metabolism disorder (17.8%, 28 patients).

#### Analysis of the Patients With Metabolic Syndrome

In total, 85.3% had carbohydrate metabolism disorder and the same percentage had low HDLc levels; 80.5% had hypertension, 65.4% had hypertriglyceridemia, and 51.7% had a BMI above the established cutoff point (Table 2).

## Comparative Analysis of Patients With and Without Metabolic Syndrome

The patients with ACS and MS had a greater prevalence of a sedentary lifestyle and increased non-HDLc levels than the patients without MS, as well as a greater prevalence of diagnostic components of MS. No differences were observed between the 2 groups by age, smoking, or alcohol consumption (Table 2). There was a trend toward a greater prevalence of MS among patients who had previous atherosclerotic vascular disease (P = .062).

#### Analysis of the Patients Without Diabetes Mellitus

Of the initial cohort, 309 patients did not have diabetes and, of these patients, 107 (34.6%) presented MS (Table 3). The most prevalent component of MS was low HDLc levels, followed by hypertension, hypertriglyceridemia, fasting plasma glucose  $\geq$ 100 mg/dL and, finally, a BMI above the cutoff point.

## Analysis of the Most Frequent Combinations of the Metabolic Syndrome Components

When we assessed the most prevalent ATPIII factors in the patients with MS, 160 patients (54.8%) fulfilled the triad of low

#### Table 2

Characteristics of the Patients With Acute Coronary Syndrome According to the Presence or Absence of Metabolic Syndrome (n = 574)

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	Without MS (n=282)	With MS (n=292)	Р
Women, % (n)	12.8 (36)	24.3 (71)	<.001
Age (years)	$62.3 \pm 12.7$	$62.4 \pm 11.1$	.891
Previous atherosclerotic vascular disease, % (n)	39.9 (110)	47.7 (135)	.062
Current smokers, % (n)	42.1 (115)	41 (119)	.928
Former smokers, % (n)	34.1 (93)	33.8 (98)	
Sedentary lifestyle, % (n)	61.7 (127)	72 (175)	.021
Alcohol consumers, % (n)			
15-30 g/day	13 (25)	12.5 (28)	.089
>30 g/day	8.8 (17)	10.3 (23)	
BMI (kg/m <sup>2</sup> )	$26.8\pm3.5$	$30\pm4.2$	<.001
BMI <25, % (n)	27.3 (77)	12.7 (37)	<.001
BMI 25-30, % (n)	61.7 (174)	36.6 (107)	
BMI >30, % (n)	11 (31)	50.7 (148)	
DM2, % (n)	18.4 (51)	50.2 (140)	<.001
Fasting plasma glucose (mg/dL)	$115.9\pm51.5$	$144.7\pm 66.8$	<.001
Total cholesterol (mg/dL)	$185.2\pm44.7$	$189\pm47.7$	.292
LDLc (mg/dL)	$117\pm40.8$	$124\pm42.4$	.054
HDLc (mg/dL)	45 ± 12.7	$36.2\pm8.9$	<.001
Non-HDLc (mg/dL)	$140.1\pm43.9$	$153.2\pm46.2$	.001
Triglycerides (mg/dL)	$119.5\pm62.8$	$184.1\pm94.7$	<.001
Low HDLc + hypertriglyceridemia, % (n)	6.4 (18)	55.5 (162)	<.001
Components of MS			
Carbohydrate metabolism disorder, % (n)	46.5 (131)	85.3 (249)	<.001
Low HDLc, % (n)	34 (96)	85.3 (249)	
Hypertension, % (n)	38.2 (105)	80.5 (235)	
Hypertriglyceridemia, % (n)	16.7 (47)	65.4 (191)	
High BMI, % (n)	11 (31)	51.7 (151)	

BMI, Body Mass Index; DM2, type 2 diabetes mellitus; HDLc, high-density lipoprotein cholesterol; LDLc, low-density lipoprotein cholesterol; MS, metabolic syndrome; non-HDLc, cholesterol other than HDLc.

Values are expressed as mean  $\pm$  standard deviation, unless otherwise indicated.

Bold is used to underline data with standard deviation; the Student *t*-test was used for differences between means; the  $\chi^2$  test was used for differences between proportions; high BMI, S29 for men and >29.9 for women; low HDLc levels, HDLc levels <40 mg/dL for men and <50 mg/dL for women.

#### Table 3

Characteristics of the Patients With Acute Coronary Syndrome According to the Presence or Absence of Metabolic Syndrome, Excluding Patients with Type 2 Diabetes Mellitus (n = 309)

	Without MS (n=202)	With MS (n = 107)	Р
Women, % (n)	14.4 (29)	18.7 (20)	.33
Age (years)	$60.4 \pm 13$	$59.5 \pm 11.01$	.545
Previous atherosclerotic vascular disease, % (n)	33.8 (67)	37.1 (39)	.613
Current smokers, % (n) Former smokers, % (n)	47.4 (93) 30.6 (60)	48.6 (52) 27.1 (29)	.787
Sedentary lifestyle, % (n)	55.2 (79)	67.4 (62)	.076
Alcohol consumers, % (n) 15-30 g/day >30 g/day	10.7 (15) 10 (14)	8.2 (7) 14.1 (12)	.394
BMI (kg/m <sup>2</sup> ) BMI <25, % (n) BMI 25-30, % (n) BMI >30, % (n)	$26.7 \pm 3.5 \\29.7 (60) \\58.9 (119) \\11.4 (23)$	$30.5 \pm 3.9$ 5.6 (6) 40.2 (43) 54.2 (58)	<.001 <.001
DM2, % (n)	NA	NA	NA
Fasting plasma glucose (mg/dL)	95 ± 12.4	$101 \pm 14.9$	<.001
Total cholesterol (mg/dL)	$187.5\pm43.1$	$195.2\pm42.7$	.126
LDLc (mg/dL)	$118.6\pm40$	$129.7\pm40$	.032
HDLc (mg/dL)	$\textbf{43.9} \pm \textbf{11.6}$	$36.6\pm8.1$	<.001
Non-HDLc (mg/dL)	$143.2\pm28.9$	$159\pm42$	.002
Triglycerides (mg/dL)	$123.9\pm 66.4$	$180.5\pm64.6$	<.001
Low HDLc + hypertriglyceridemia, $%(n)$	8.9 (18)	58.9 (63)	<.001
Components of MS Carbohydrate metabolism disorder, % (n) Low HDLc, % (n) Hypertension, % (n) Hypertriglyceridemia, % (n) High BMI, % (n)	25.1 (50) 39.6 (80) 38.1 (75) 21.8 (44) 11.4 (23)	60.4 (64) 86 (92) 81.1 (86) 66.4 (71) 55.1 (59)	< <b>.00</b> 1

BMI, Body Mass Index; DM2, type 2 diabetes mellitus; HDLc, high-density lipoprotein cholesterol; LDLc, low-density lipoprotein cholesterol; MS, metabolic syndrome; non-HDLc, cholesterol other than HDLc.

Values are expressed as mean  $\pm$  standard deviation, unless otherwise indicated.

Bold is used to underline data with standard deviation; the Student *t*-test was used for differences between means; the  $\chi^2$  test was used for differences between proportions; high BMI, BMI >29 for men and >29.9 for women; low HDLc levels, HDLc levels <40 mg/dL for men and <50 mg/dL for women.

HDLc levels, hypertension, and carbohydrate metabolism disorder; the most prevalent tetrad (89 patients) was low HDLc levels, hypertension, hypertriglyceridemia, and carbohydrate metabolism disorder (Table 4).

In the patients without diabetes, the most prevalent triad of ATPIII factors was low HDLc levels, hypertension, and hypertriglyceridemia; the most prevalent tetrad was low HDLc levels, hypertension, hypertriglyceridemia, and impaired fasting plasma glucose levels.

#### DISCUSSION

#### Prevalence of Metabolic Syndrome

The present study found that patients with ACS had a high prevalence of MS (50.9%). This percentage is similar to that described in other populations with atherosclerotic vascular disease. In a previous Spanish study conducted with patients in secondary prevention, the prevalence of MS was 41% when EGIR criteria were applied.<sup>14</sup>

In general population studies conducted in the United States, the prevalence of MS was 24%<sup>24</sup> whereas in a Spanish working

population the prevalence was 10.2%-13.4% and was much higher in men than in women.  $^{25,26}$ 

The fact that the prevalence of MS is higher in populations with ACS than in the general population demonstrates the association between MS and ischemic heart disease. It has recently been confirmed that MS is an independent predictor of ACS in patients in secondary prevention.<sup>27</sup> In this sense, the present study shows that MS tends to be more prevalent in patients with previous atherosclerotic vascular disease.

Although the prevalence of MS is greater in men than in women in the general population,<sup>26</sup> our study suggests that MS is more prevalent in women than in men (66.3% vs 47.3%), which is similar to the results obtained in other populations with ischemic heart disease.<sup>28–31</sup> This can be attributed, at least in part, to the fact that in the present study the women with ACS were older and presented a higher prevalence of obesity and DM2; these results are consistent with those of other similar studies.<sup>32,33</sup> On the other hand, the men presented a greater frequency of smoking, an important cardiovascular risk factor that is not taken into account in the diagnosis of MS. Furthermore, although the HDLc concentrations were slightly higher in women, there was a greater frequency of low HDLc levels when ATPIII criteria were applied. Taking this into account, we can assume that MS is an important marker of cardiovascular risk among women.

#### Table 4

Most Frequent Combinations of the Metabolic Syndrome Components

	All patients with MS	Patients with MS without DM2
Triads	(n=292)	(n=107)
BMI + HTG + AHT	23.3 (68)	24.3 (26)
BMI + HTG + I-HDLc	25 (73)	25.2 (27)
BMI + HTG + IGT	25.3 (74)	16.8 (18)
BMI + I-HDLc + AHT	31.5 (92)	31.8 (34)
BMI + 1-HDLc + IGT	32.2 (94)	17.8 (19)
BMI + AHT + IGT	32.9 (96)	20.6 (22)
HTG + 1-HDLc + AHT	38.7 (113)	42.1 (45)
HTG + AHT + IGT	39 (114)	24.3 (26)
HTG + I-HDLc + IGT	44.9 (131)	29.9 (32)
I-HDLc + AHT + IGT	54.8 (160)	35.5 (38)
Tetrads	(n=157)	(n=42)
BMI + HTG + I-HDLc + AHT	33.1 (52)	45.2 (19)
BMI + HTG + AHT + IGT	35 (55)	31 (13)
BMI + HTG + I-HDLc + IGT	36.9 (58)	28.6 (12)
BMI + 1-HDLc + AHT + IGT	45.2 (71)	31 (13)
HTG + I-HDLc + AHT + IGT	56.7 (89)	50 (21)
With all the components	(n=42)	(n=9)

AHT, hypertension; BMI, body mass index; DM2, type 2 diabetes mellitus; HTG, hypertriglyceridemia; IGT, carbohydrate metabolism disorder; I-HDLc, high-density lipoprotein cholesterol levels; MS, metabolic syndrome.

Values are expressed as % (n); BMI>29 for men and >29.9 for women; I-HDLc <40 mg/dL for men and <50 mg/dL for women.

#### **Components of Metabolic Syndrome**

MS increases cardiovascular risk and each of its components is associated with an increased risk of cardiovascular disease. Recent studies have shown that MS does not increase cardiovascular risk more than the sum of its components.<sup>7,34</sup> Some works have suggested that the number of markers of MS can be more useful then MS itself in predicting cardiovascular disease<sup>8</sup>, and that the risk of cardiovascular disease increases as the number of MS components increases.<sup>9–11</sup>

Recently, there has been growing interest in the components of MS, not only in relation to the number present but also their different combinations, in the prediction of cardiovascular risk. In our cohort, hyperglycemia and low HDLc levels were the most prevalent components of MS, followed by hypertension. In a recent study,<sup>35</sup> this was also the most frequent combination observed in patients with ischemic heart disease. Other studies have shown that the combination of DM and hypertension sharply increases cardiovascular risk.<sup>12</sup>

The principal guidelines recommend lowering LDLc levels as the main strategy for the primary and secondary prevention of cardiovascular risk, both in diabetic and nondiabetic patients.<sup>36</sup> However, despite achieving strong reductions in LDLc concentrations, even to "optimal" levels, the number of people who continue to present clinical complications of atherosclerosis remains very high. This is known as "residual risk", and is found in 65% to 75% of patients at 5 years compared to controls.<sup>37–39</sup> Residual risk depends to a great extent on low HDLc levels.

Multiple observational and prospective epidemiological studies have demonstrated that HDLc concentrations are inversely and independently associated with the development of ischemic heart disease.<sup>40</sup> However, the prevalence of low HDLc levels remains high in around 40% of European dyslipidemic patients, despite statin therapy,<sup>41</sup> and in up to 45% of patients with DM2.<sup>42</sup> The ATPIII concluded that low HDLc concentrations and high triglyceride levels are cardiovascular risk factors, regardless of LDLc levels.<sup>2</sup> The association in the same patient of increased triglyceride levels and low HDLc concentrations is usually associated with an increase in small, dense, LDLc particles, and these are considered to be highly atherogenic.<sup>43</sup> This profile, known as atherogenic dyslipidemia, is very common in patients with MS and DM2.<sup>44,45</sup>

Statin therapy effectively lowers LDLc levels, but has little effect on triglyceride and HDLc concentrations.

Our study demonstrates the high prevalence of low HDLc levels in patients with ACS in Spain, both in diabetic and nondiabetic patients. There is increasing evidence that treatment of patients with MS and/or DM2 should not be exclusively aimed at lowering LDLc levels, but should also aim to increase HDLc levels.<sup>39,46</sup>

#### Limitations

Our study presents several limitations, given its retrospective design. As the figures for waist circumference were unavailable, we used BMI as an indirect estimation; this method is widely accepted in previous studies,<sup>10,24,47</sup> as there is a direct correlation between BMI and waist circumference.<sup>22,48</sup> In addition, a standardized estimation method is available for measuring waist circumference in relation to the BMI percentiles for the Spanish population,<sup>23</sup> and thus can be adapted to the cutoff points established for the diagnosis of MS. Even so, the prevalence of abdominal obesity may have been underestimated. Despite this, the prevalence of MS in our population is similar to that reported by other studies.<sup>8,13,14</sup>

When assessing lipid profile, falsely low HDLc concentrations may be observed in the presence of acute-phase reactants, as may occur after an ACS. In order to mitigate this effect, blood samples were extracted within the first 24 h after the cardiovascular episode if no blood test had been performed previously, since decreased HDLc and triglyceride levels are of little relevance during this period.<sup>49,50</sup> Although 34% of the patients were undergoing treatment with statins, their effect on HDLc concentrations is marginal. Nevertheless, the prevalence of low HDLc levels in this population is very high.

#### **CONCLUSIONS**

The present study shows a high prevalence of MS in patients with ACS.

Women with ACS show a higher prevalence and a greater number of components of MS than men.

The most prevalent components of the MS were hyperglycemia and low HDLc concentrations, followed by hypertension. When diabetic patients were excluded from the analysis, the most prevalent components of MS in this population were low HDLc levels, followed by hypertension.

#### **CONFLICTS OF INTEREST**

None declared.

#### REFERENCES

- Laaksonen DE, Lakka HM, Niskanen LK, Kaplan GA, Salonen JT, Lakka TA. Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study. Am J Epidemiol. 2002;156:1070–7.
- Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112:2735–52.
- Hanley AJ, Festa A, D'Agostino Jr RB, Wagenknecht LE, Savage PJ, Tracy RP, et al. Metabolic and inflammation variable clusters and prediction of type 2 diabetes: factor analysis using directly measured insulin sensitivity. Diabetes. 2004; 53:1773–81.
- Lindsay RS, Howard BV. Cardiovascular risk associated with the metabolic syndrome. Curr Diab Rep. 2004;4:63–8.
- Stern MP, Williams K, González-Villalpando C, Hunt KJ, Haffner SM. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? Diabetes Care. 2004;27:2676–81.
- Alberti KG, Zimmet P, Shaw J. The metabolic syndrome: a new worldwide definition. Lancet. 2005;366:1059–62.
- Mente A, Yusuf S, Islam S, McQueen MJ, Tanomsup S, Onen CL, et al. Metabolic syndrome and risk of acute myocardial infarction. A case-control study of 26,903 subjects from 52 countries. J Am Coll Cardiol. 2010;55:2390–8.
- Solymoss BC, Bourassa MG, Campeau L, Sniderman A, Marcil M, Lespérance J, et al. Effect of increasing metabolic syndrome score on atherosclerotic risk profile and coronary artery disease angiographic severity. Am J Cardiol. 2004;93:159–64.
- Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA. 2002;288:2709–16.
- Sattar N, Gaw A, Scherbakova O, Ford I, O'Reilly D, Haffner SM, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. Circulation. 2003;108:414–9.
- Malik S, Wong ND, Franklin SS, Kamath TV, L'Italien GJ, Pio JR, 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.
- Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the multiple risk factor intervention trial. Diabetes Care. 1993;16:434–44.
- Chung EH, Curran PJ, Sivasankaran S, Chauhan MS, Gossman DE, Pyne CT, et al. Prevalence of metabolic syndrome in patients ≥ 45 years of age with acute myocardial infarction having percutaneous coronary intervention. Am J Cardiol. 2007;100:1052–5.
- Hernández Mijares A, Riera Fortuny C, Solá Izquierdo E, Oliver Oliver MJ, Martínez Triguero ML, Morillas Ariño C, et al. Prevalencia del síndrome metabólico entre pacientes con cardiopatía isquémica. Med Clin (Barc). 2003; 121:204–8.
- Haffner SM, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med. 1998;339:229–34.
- 16. Saydah SH, Eberhardt MS, Loria CM, Brancati FL. Age and the burden of death attributable to diabetes in the United States. Am J Epidemiol. 2002;156:714–9.
- 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.
- Einhorn D, Reaven GM, Cobin RH, Ford E, Ganda OP, Handelsman Y, et al. American College of Endocrinology position statement on the insulin resistance syndrome. Endocr Pract. 2003;9:237–52.
- 19. The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined —a consensus document of The

Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction. Eur Heart J. 2000;21:1502–13.

- Thygesen K, Alperts JS, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. Eur Heart J. 2007;28:2525–38.
- 21. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al.; American College of Cardiology; American Heart Association. Committee on the Management of Patients With Unstable Angina. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). J Am Coll Cardiol. 2002;40:1366–74.
- Ryan MC, Fenster Farin HM, Abbasi F, Reaven GM. Comparison of waist circumference versus body mass index in diagnosing metabolic syndrome and identifying apparently healthy subjects at increased risk of cardiovascular disease. Am J Cardiol. 2008;102:40–6.
- 23. López de la Torre M, Bellido D, Soto A, Carreira J, Hernández Mijares A. Stansardisation of the waist circumference for each range of body mass index in adult outpatients attended to in Endocrinology and Nutrition Departments. Nutr Hosp. 2010;25:262–9.
- 24. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA. 2002;287:356–9.
- Alegría E, Cordero A, Laclaustra M, Grima A, León M, Casasnovas JA, et al. Prevalencia del síndrome metabólico en población laboral española: registro MESYAS. Rev Esp Cardiol. 2005;52:797–806.
- León Latre M, Andrés EM, Cordero A, Pascual I, Vispe C, Laclaustra M, et al. Relación entre el síndrome metabólico y la mortalidad por cardiopatía isquémica en España. Rev Esp Cardiol. 2009;62:1469–72.
- Nakatani D, Sakata Y, Sato H, Mizuno H, Shimizu M, Suna S, et al.; Osaka Acute Coronary Insufficiency Study (OACIS) Group. Clinical impact of metabolic syndrome and its additive effect with smoking on subsequent cardiac events after acute myocardial infarction. Am J Cardiol. 2007;99:885–9.
- Zaliunas R, Slapikas R, Babarskiene R, Slapikiene B, Luksiene D, Milvidaite I, et al. The prevalence of the metabolic syndrome components and their combinations in men and women with acute ischemic syndromes. Medicina (Kaunas). 2008;44:521-8.
- Anand SS, Islam S, Rosengren A, Franzosi MG, Steyn K, Yusufali AH, et al.; INTERHEART Investigators. Risk factors for myocardial infarction in women and men: insights from the INTERHEART study. Eur Heart J. 2008;29:932–40.
- Zeller M, Steg PG, Ravisy J, Laurent Y, Janin-Manificat L, L'Huillier I, et al. Prevalence and impact of metabolic syndrome on hospital outcomes in acute myocardial infarction. Arch Intern Med. 2005;165:1192–8.
- 31. Birhan Yilmaz M, Guray U, Guray Y, Altay H, Demirkan B, Caldir V, et al. Metabolic syndrome is associated with extension of coronary artery disease in patients with non-ST segment elevation acute coronary syndromes. Coron Artery Dis. 2005;16:287–92.
- 32. Blomkalns AL, Chen AY, Hochman JS, Peterson ED, Trynosky K, Diercks DB, et al.; CRUSADE Investigators. Gender disparities in the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: large-scale observations from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) National Quality Improvement Initiative. J Am Coll Cardiol. 2005;45:832–7.
- El-Menyar A, Zuabid M, Rashed W, Almahmeed W, Al-Lawati J, Sulaiman K, et al. Comparison of men and women with acute coronary syndrome in six Middle Eastern countries. Am J Cardiol. 2009;104:1018–22.
- 34. McNeill AM, Rosamond WD, Girman CJ, Golden SM, Schmidt M, East HE, et al. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the Atherosclerosis Risk in Communities study. Diabetes Care. 2005;28: 385–90.
- 35. Kim JY, Mun HS, Lee BK, Yoon SB, Choi EY, Min PK, et al. Impact of metabolic syndrome and its individual components on the presence and severity of angiographic coronary artery disease. Yonsei Med J. 2010;51:676–82.
- Moutzouri E, Kei A, Elisaf MS, Milionis HJ. Management of dyslipidemias with fibrates, alone and in combination with statins: role of delayed-release fenofibric acid. Vasc Health Risk Manag. 2010;6:525–39.
- Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004;350:1495–504.
- 38. Shepherd J, Barter P, Carmena R, Deedwania P, Fruchart JC, Haffner S, et al. Effect of lowering LDL cholesterol substantially below currently recommended levels in patients with coronary heart disease and diabetes: The Treating to New Targets (TNT) study. Diabetes Care. 2006;29:1220–6.
- 39. Deedwania P, Barter P, Carmena R, Fruchart JC, Grundy SM, Haffner S, et al.; Treating to New Targets Investigators. Reduction of low-density lipoprotein cholesterol in patients with coronary heart disease and metabolic syndrome: analysis of the Treating to New Targets study. Lancet. 2006;368:919–28.
- 40. Ascaso JF, Fernández-Cruz A, González Santos P, Hernández Mijares A, Mangas Rojas A, Millán J, et al. Significance of high density lipoprotein-cholesterol in cardiovascular risk prevention: recommendations of the HDL Forum. Am J Cardiovasc Drugs. 2004;4:299–314.
- Bruckert E, Baccara-Dinet M, McCoy F, Chapman J. High prevalence of low HDL cholesterol in a pan-European survey of 8545 dyslipidaemic patients. Curr Med Res Opin. 2005;21:1927–34.

- Bruckert E, Baccara-Dinet M, Eschwege E. Low HDL cholesterol is common in European type 2 diabetic patients receiving treatment for dyslipidaemia: data from a pan-European survey. Diabet Med. 2007;24:388–91.
- Austin MA, King MC, Vranizan KM, Krauss RM. Atherogenic lipoprotein phenotype. A proposed genetic marker for coronary heart disease risk. Circulation. 1990;82:495–506.
- Reaven GM, Chen YD, Jeppesen J, Maheux P, Krauss RM. Insulin resistance and hyperinsulinemia in individuals with small, dense low density lipoprotein particles. J Clin Invest. 1993;92:141–6.
- 45. Kathiresan S, Otvos JD, Sullivan LM, Keyes MJ, Schaefer EJ, Wilson PW, et al. Increased small low-density lipoprotein particle number: a prominent feature of the metabolic syndrome in the Framingham Heart Study. Circulation. 2006; 113:20–9.
- 46. Athyros VG, Mikhailidis DP, Kakafika Al, Karagiannis A, Hatzitolios A, Tziomalos K, et al. Identifying and attaining LDL-C goals: mission accomplished? Next

target: new therapeutic options to raise CHDL levels. Curr Drug Targets. 2007;8:483-8.

- Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14 719 initially healthy American women. Circulation. 2003;107:391–7.
- Farin HM, Abbasi F, Reaven GM. Comparison of body mass index versus waist circumference with the metabolic changes that increase the risk of cardiovascular disease in insulin-resistant individuals. Am J Cardiol. 2006;98: 1053–6.
- Ahnve S, Angelin B, Edhag O, Berglund L. Early determination of serum lipids and apolipoproteins in acute myocardial infarction: possibility for immediate intervention. J Intern Med. 1989;226:297–301.
- Henkin Y, Crystal E, Goldberg Y, Friger M, Lorber J, Zuili I, et al. Usefulness of lipoprotein changes during acute coronary syndromes for predicting postdischarge lipoprotein levels. Am J Cardiol. 2002;89:7–11.