Characteristics of the Metabolic Syndrome in the Patients of IBERICAN Study (Identification of the Spanish Population at Cardiovascular and Renal Risk)

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Abstract

Objective: The main objective of this study is to know the prevalence and the clinical and epidemiological characteristics of patients with metabolic syndrome (MetS) and premorbid metabolic syndrome (pre-MetS) included in the Identification of the Spanish Population at Cardiovascular and Renal Risk (IBERICAN) study.

Materials and Methods: The IBERICAN study is an epidemiological, multicentric observational study carried out in Primary Healthcare Centers from all over Spain, in which an open cohort of subjects with/without cardiovascular risk factors (CVRF) is constituted. The MetS was defined according to the international criterion based on the presence of at least three of the five criteria of the harmonized definition.

Results: A total of 4304 patients were selected; 38.5% patients (95% confidence interval 37.0–40.0) met the MetS criteria. In both groups (MetS and pre-MetS), patients were older (62.3 ± 12.1 vs. 54.4 ± 15.2 , $P < 0.001$). The CVRF analyzed were more frequent in patients with MetS: hypertension (HT) (71.1% vs. 33.0%, $P < 0.001$), dyslipidemia (65.8% vs. 40.2%, $P < 0.001$), diabetes mellitus (DM) (38.2% vs. 6.4%, $P < 0.001$), and obesity (54.8% vs. 21.7%, $P < 0.001$), and all the cardiovascular diseases (CVDs) analyzed were more prevalent in these patients: stroke (5.1% vs. 3.6%, $P = 0.013$), heart failure (5.1% vs. 1.6%, $P < 0.001$), ischemic heart disease (9.8% vs. 5.8%, $P < 0.001$), and peripheral arterial disease (6.8% vs. 3.7%, $P < 0.001$). We observed that patients with DM were 6.36 times more likely to present MetS; patients with obesity, 3.81 times; and patients with HT, 2.66 times.

Conclusion: Patients with MetS and with pre-MetS presented higher CVRF and increased associated renal and CVD. The prognostic value of these findings must be analyzed in the longitudinal follow-up of the IBERICAN cohort.

Keywords: metabolic syndrome, cardiovascular risk, primary care

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Introduction

METABOLIC SYNDROME (MetS) is characterized by the coexistence of various cardiovascular risk factors (CVRF), including abdominal obesity, hyperglycemia, arterial hypertension (HT), and atherogenic dyslipidemia.

The importance of MetS primarily consists in its association with a higher risk of diabetes mellitus (DM) and cardiovascular disease (CVD) in patients with the syndrome.¹ This is the most widely accepted position; however, it is also true that other authors have provided results that do not show a higher cardiovascular risk (CVR) than merely the sum of the different risk factors present in the patient.^{2,3}

One of the possible causes of this discrepancy lies in the different definitions given by each Scientific Society or research group, therefore obtaining different prevalence and different associated risk according to the diagnostic criteria.³ This disparity in criteria led in 2009 to a proposal of a harmonized definition of MetS.⁴ This agreed opinion also includes the concept of premorbid metabolic syndrome (pre-MetS), which is defined as the compliance with the MetS criteria except for DM and CVD,⁵ concept that would have a great importance from the point of view of primary prevention in subjects presenting this syndrome.

Several studies have already been published in Spain following this harmonized criterion. Among them, we must mention the DARIOS study,⁶ which analyzed the data provided by studies in 10 autonomous communities and population-based studies like Di@bet.es⁷ and EN-RICA,⁸ which have described the prevalence of MetS and its components. However, none of them has analyzed the characteristics of the risk factors and CVD associated with the MetS in Primary Healthcare (PHC) clinical population.

The principal objective of this project is to know the prevalence and clinical and epidemiological characteristics of patients with MetS and pre-MetS included in the Identification of the Spanish Population at Cardiovascular and Renal Risk (IBERICAN) study. (See Supplementary Data for list of IBERICAN Study researchers; Supplementary Data are available online at www.liebertpub.com/met).

Materials and Methods

Design of the study

The IBERICAN study is an epidemiological, multicenter observational study carried out in PHC from all over Spain, in which an open cohort of subjects with/without CVRF is constituted. These patients will be monitored annually, during a period of at least 5 years, to analyze the prevalence and incidence of DM, HT, dyslipidemia, smoking, or obesity, as well as the occurrence of target organ damage (TOD) or new or recurrent cardiovascular events (CVE), in patients receiving assistance in the Spanish National Health System.

The study was approved by the ECCR of Hospital Clínico San Carlos in Madrid on February 21, 2013 (C.P. IBERICAN-C.I. 13/047-E) and is registered in <https://clinicaltrials.gov> with the number NCT02261441.

The calculation and selection of the sample have been described previously.⁹

Study variables

The MetS was defined according to the international criterion⁴ based on the presence of at least three of the five

following criteria: (1) elevated fasting blood glucose level (≥ 100 mg/dL) or receiving antidiabetic treatment with insulin or oral hypoglycemic agents; (2) elevated systolic blood pressure ≥ 130 mmHg or diastolic ≥ 85 mmHg or receiving antihypertensive medication; (3) high-density lipoprotein cholesterol (HDL-C) values < 40 mg/dL (men) or < 50 mg/dL (women); (4) triglycerides ≥ 150 mg/dL, and (5) abdominal perimeter ≥ 102 cm (men) or ≥ 88 cm (women).⁴ The pre-MetS was defined by excluding those participants with MetS who suffered DM (diagnosed previously or presenting fasting blood glucose level ≥ 126 mg/dL) and those with a history of CVE (acute myocardial infarction, angina, peripheral artery disease, or stroke).⁵

The defining parameters of MetS and pre-MetS were obtained using the habitual clinical determinations: blood pressure measurement using validated and calibrated digital devices, weight and height measurement using scales and wall measuring rods; analytical determinations were carried out in the reference clinical laboratories for each PHC center, all of them validated and controlled according to the corresponding quality criteria.

In HT, the optimal control is when blood pressure is less than 140/90 mmHg, but in patients over 80 years the optimal control is when the blood pressure is less than 150/90 mmHg; in diabetic patients, the objective is 140/85 mmHg and in patients with nephropathy or proteinuria the objective is 130/90 mmHg.¹⁰ In dyslipidemia, the optimal control was defined as the European guidelines indicate: in patients with low or moderate CVR: total cholesterol ≥ 200 mg/dL, low-density lipoprotein (LDL) ≥ 130 mg/dL, HDL < 40 mg/dL in men or < 50 mg/dL in women, or triglycerides ≥ 200 mg/dL. In patients with high CVR: cholesterol total ≥ 175 mg/dL, LDL ≥ 100 mg/dL, HDL < 40 mg/dL in men or < 46 mg/dL in women, or triglycerides ≥ 150 mg/dL. Finally, in patients with very high CVR, LDL ≥ 70 mg/dL.¹¹ In diabetic patients, we used the individual objectives proposed by Gedaps: HbA1c $< 7\%$ in patients younger than 75 years, without CVD; HbA1c $< 8\%$ in younger patients ≤ 65 years, with CVD; HbA1c $< 8.5\%$ in patients between 65 and 75 years, with CVD; and in patients over 75 years with or without CVD.¹²

The criteria used for the diagnosis and assessment of the degree of control of the different CVRF, TOD, and CVE have been defined in previous articles.⁹ Particularly, we use the definition of the European Society of Hypertension in the pulse pressure in over 65 years as TOD when the value of this pulse pressure is more than 60 mmHg in this group of patients.¹⁰ The CVR has been estimated according to the criteria established by SCORE.¹³

Statistical analysis

Qualitative variables have been defined as absolute and relative frequencies and continuous variables as mean $\pm$ standard deviation (median and interquartile range, where appropriate). Statistical tests have been carried out depending on the nature of the variables. The study of the association of categorical variables was performed using the chi-squared test (if more than 20% of cells present an expected frequency lower than 5, Fisher's exact test will be used). The bivariate analysis in the MetS was done with the rest of the sample that did not meet the diagnostic criteria; in the case of pre-MetS, it was compared with the rest of the subjects that did not meet the diagnostic criteria, but not presenting either DM or CVE. For

the comparison of continuous variables among groups of patients, Student's *t*-test was used.

The stepwise backward unconditional logistic regression method, by means of Wald chi-square, was used to determine the variables associated with MetS and pre-MetS. The candidate variables were those which showed statistical significance in the bivariate analysis: age, sex, low level of education, alcohol, CVRF (smoking, sedentary lifestyle, obesity, DM, HT, total cholesterol, family history of CVE), uric acid, creatinine, albuminuria, and estimated glomerular filtration. Two analyses were performed, one which could include the MetS defining variables and another one where these were excluded expressly.

In all the comparisons, the null hypothesis with an alpha error <0.05 was rejected. IBM SPSS version 22.0 has been used for data analysis.

Results

Description of the sample

A total of 4314 patients were selected, of which 10 (0.2%) were rejected for noncompliance with the protocol or for presenting incoherent or incomplete data, resulting in a final sample of 4304 patients (55.0% women), with an average age of 57.5 ± 14.6 years.

The three most prevalent CVRF were dyslipidemia (50.2%), HT (47.8%), and obesity (33.0%). DM was observed in 18.8% patients. Of the total sample, 25.7% presented some TOD, and the most frequent of these were pulse pressure in people over age 65 (16.8%) and albuminuria (8.0%). Of the total sample, 16.4% had a history of CVE, being ischemic heart disease (7.3%) and peripheral arterial disease (4.9%) the most frequent.

Prevalence of MetS and pre-MetS

Of the total patients, 38.5% [38.5%; confidence interval (95% CI) 37.0–40.0] met the MetS criteria, these being higher in men with 41.5% (95% CI 40.0–44.0) and 36.0% (95% CI 34.0–38.0) in women, $P < 0.0001$. Of the total sample, 21.0% (95% CI 20.0–22.0) met the pre-MetS criteria, with a similar incidence in men and women, 21.2% (95% CI 19.0–23.0) in men and 20.9% (95% CI 19.0–23.0) in women.

TABLE 1. FREQUENCY OF THE DIAGNOSTIC CRITERIA IN PATIENTS WITH METABOLIC SYNDROME

	n	Value, %
Elevated fasting blood glucose level (≥ 100 mg/dL) or receiving antidiabetic treatment with insulin or oral antidiabetics	1262	76.3
Elevated systolic blood pressure ≥ 130 mmHg or diastolic ≥ 85 mmHg or receiving antihypertensive medication	1552	93.8
HDL-C values <40 mg/dL (men) or <50 mg/dL (women)	794	48.0
Triglycerides ≥ 150 mg/dL	829	50.1
Abdominal perimeter ≥ 102 cm (men) or ≥ 88 cm (women)	1398	84.5

HDL-C, high-density lipoprotein cholesterol.

Among the 1655 patients with MetS, 93.8% met the blood pressure criterion and 84.5% the abdominal perimeter criterion (Table 1). Of the patients with MetS, 11.5% ($n=191$) met the five criteria, 29.5% ($n=488$) met four criteria, and 59.0% met three criteria. Among the patients who met four criteria, the most frequent were as follows: blood pressure (96.1%), abdominal obesity (86.1%), glycemia (84.2%), triglycerides (69.3%), and HDL (64.3%). Among the patients who met three criteria, in order of frequency were as follows: blood pressure (91.4%), abdominal obesity (80.6%), glycemia (67.6%), triglycerides (30.7%), and HDL (29.6%).

Characteristics of patients with MetS and pre-MetS

In both groups, MetS and pre-MetS, patients were older and the number of women was slightly lower (Table 2). All CVRF, except smoking and alcohol consumption, were more frequent in patients with MetS or pre-MetS. The prevalence of HT was 71.1% and 61.9%; that of dyslipidemia was 65.8% and 56.7%; that of abdominal obesity was 52.3% and 51.1%; and that of sedentary lifestyle was 37.4% and 35.5%, respectively (Table 2). Among them, arterial HT showed a poorer control and dyslipidemia better control in patients with MetS and pre-MetS, the rest of CVRF did not present statistically significant differences (Table 2). Physical and analytical values showed higher risk values in patients with MetS: higher blood pressure, weight, blood glucose, and albuminuria, as well as lower glomerular filtration rate. In contrast, LDL cholesterol values were lower (Table 3).

Target organ damage

Of the total sample, 25.7% presented some TOD, being more frequent in patients with MetS (38.3% vs. 17.8%, $P < 0.001$) and pre-MetS (27.7% vs. 13.7%, $P < 0.001$). All the individual TOD analyzed were more frequent in both groups, the most prevalent being pulse pressure in patients over age 65 (Figs. 1 and 2).

Kidney damage was analyzed independent of cardiovascular pathology. A higher prevalence of the first was observed in both groups with 13.2% in patients with MetS and 9.3% in patients with pre-MetS (Table 2). The coexistence of decreased glomerular filtration and albuminuria was more frequent both in patients with MetS (3.9% vs. 0.9%, $P < 0.001$) and in patients with pre-MetS (1.1% vs. 0.5%, $P < 0.001$).

Cardiovascular disease

Of the patients with MetS, 16.4% presented pre-existing CVD, and all the pathologies analyzed were more prevalent in these patients (Table 2). We also analyzed the prevalence of atrial fibrillation, observing that it was higher both in patients with MetS (7.6% vs. 3.7%, $P < 0.001$) and pre-MetS (3.9% vs. 2.2%, $P = 0.015$).

Cardiovascular risk

CVR was higher in patients with MetS, due to a greater percentage of patients classified as high (45.9% vs. 17.5%, $P < 0.001$) and very high risk (23.0% vs. 11.8%, $P < 0.001$). In patients with pre-MetS the percentage of patients with

TABLE 2. PREVALENCE OF CARDIOVASCULAR RISK FACTORS AND CARDIOVASCULAR DISEASE

Epidemiological data	General	MetS			p-MetS			P ^c		
		n	MetS (n = 1655)	No MetS (n = 2608)	P ^a	n	p-MetS (n = 896)		No p-MetS (n = 759)	P ^b
Age (years) (mean ± SD)	57.5 ± 14.6	4262	62.3 ± 12.1	54.4 ± 15.2	<0.001	2765	59.5 ± 12.7	53.2 ± 14.7	<0.001	<0.001
Sex, woman (%; 95% CI)	55.0	4304	51.5 (50.7–52.3)	57.2 (56.4–58.0)	<0.001	2769	55.0 (54.1–55.9)	61.2 (60.3–62.1)	0.002	0.005
Level of education (%)										
No studies	9.9	4304	14.6 (14.1–15.1)	7.0 (6.6–7.4)	<0.001	2769	11.2 (10.6–11.8)	6.0 (5.5–6.5)	<0.001	<0.001
Primary	57.3		62.7 (62.0–63.4)	52.6 (51.8–53.4)			62.1 (61.2–63.0)	52.4 (51.5–53.3)		
Higher	21.1		16.1 (15.5–16.7)	24.3 (23.6–25.0)			18.2 (17.5–18.9)	24.8 (24.0–25.6)		
University	11.7		6.2 (5.8–6.6)	15.0 (14.5–15.5)			8.1 (7.6–8.6)	16.6 (15.9–17.3)		
Cardiovascular risk factors										
Arterial HT (%)	47.8	4266	71.1 (70.4–71.8)	33.0 (32.3–33.7)	<0.001	2769	61.9 (61.0–62.8)	28.9 (28.0–29.8)	<0.001	<0.001
Good control HT (%)	57.6	2003	53.4 (52.3–54.5)	63.7 (62.6–64.8)	<0.001	1070	55.4 (53.9–56.9)	63.7 (62.2–65.2)	0.006	0.231
Dyslipidemia (%)	50.2	4263	65.8 (65.1–66.5)	40.2 (39.4–41.0)	<0.001	2769	56.7 (55.8–57.6)	37.2 (36.3–38.1)	<0.001	<0.001
Good control dyslipidemia (%)	7.9	2157	9.3 (8.7–9.9)	6.6 (6.1–7.1)	0.021	1186	6.2 (5.5–6.9)	5.8 (5.1–6.5)	0.785	<0.001
Diabetes mellitus (%)	18.8	4263	38.2 (37.5–38.9)	6.4 (6.0–6.8)	<0.001	—	—	—	—	—
Good control diabetes mellitus (%)	63.5	776	62.2 (60.5–63.9)	68.8 (67.1–70.5)	0.125	—	—	—	—	—
CVE family history (%)	16.9	3600	18.8 (18.1–19.5)	15.6 (15.0–16.2)	0.012	2767	13.5 (12.9–14.1)	12.4 (11.8–13.0)	0.415	0.001
Sedentary lifestyle (%)	30.7	4254	37.6 (36.9–38.3)	26.3 (25.6–27.0)	<0.001	2759	35.7 (34.8–36.6)	29.3 (28.4–30.2)	<0.001	0.094
Obesity by BMI (%)	33.0	4093	54.8 (54.0–55.6)	21.7 (21.1–22.3)	<0.001	2833	52.5 (51.6–53.4)	20.4 (19.6–21.2)	<0.001	0.265
Abdominal obesity (%)	28.2	4126	52.3 (51.5–53.1)	17.0 (16.4–17.6)	<0.001	2868	51.1 (50.2–52.0)	16.6 (15.9–17.3)	<0.001	0.869
Smoking (%)	18.4	4304	16.5 (15.9–17.1)	19.0 (18.4–19.6)	<0.001	2759	17.3 (16.6–18.0)	18.4 (17.7–19.1)	0.147	0.365
High alcohol consumption (%)	11.8	4257	14.5 (14.0–15.0)	12.1 (11.6–12.6)	0.026	2365	14.7 (14.0–15.4)	12.7 (12.0–13.4)	0.208	0.523
Renal disease										
RD (CKD-EPI) (%)	9.6	4077	13.2 (12.7–13.7)	7.2 (6.8–7.6)	<0.001	2739	9.3 (8.7–9.9)	5.9 (5.4–6.4)	0.002	<0.001
Cardiovascular disease										
Stroke (%)	4.2	4304	5.1 (4.8–5.4)	3.6 (3.3–3.9)	0.013					
Heart failure (%)	3.0	4304	5.1 (4.8–5.4)	1.6 (1.4–1.8)	<0.001					
Ischemic cardiopathology (%)	7.3	4304	9.8 (9.3–10.3)	5.8 (5.4–6.2)	<0.001					
Peripheral arterial disease (%)	4.9	4304	6.8 (6.4–7.2)	3.7 (3.4–4.0)	<0.001					

^aLevel of significance that compares patients with MetS to patients without MetS.^bLevel of significance that compares patients with p-MetS to patients without p-MetS.^cLevel of significance that compares patients with MetS to patients without p-MetS.

BMI, body mass index; CI, confidence interval; CVE, cardiovascular events; HT, hypertension; MetS, metabolic syndrome; p-MetS, premorbid metabolic syndrome; RD (CKD-EPI), renal disease (Chronic Kidney Disease Epidemiology Collaboration); SD, standard deviation.

TABLE 3. CLINICAL AND ANALYTICAL VARIABLES OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH METABOLIC SYNDROME AND PREMORBID METABOLIC SYNDROME

	MetS				p-MetS			
	General		MetS (n=1655)		No MetS (n=2608)		p-MetS (n=896)	
	n		n		n		n	
Physical examination								
Systolic blood pressure (mmHg)	129.1 ± 15.8	4212	135.1 ± 15.4	125.4 ± 14.8	2766	134.8 ± 15.2	124.8 ± 14.9	<0.001
Diastolic blood pressure (mmHg)	76.7 ± 10.2	4212	78.9 ± 10.4	75.2 ± 9.8	2766	79.9 ± 10.2	75.4 ± 9.9	<0.001
Pulse pressure (mmHg)	52.5 ± 12.7	4211	56.2 ± 13.1	50.2 ± 11.9	2766	54.9 ± 13.1	49.4 ± 11.7	<0.001
Heart rate (bpm)	73.2 ± 10.5	4206	74.4 ± 10.7	72.4 ± 10.2	2762	74.1 ± 10.8	72.4 ± 10.0	<0.001
Weight (Kg)	76.6 ± 15.6	4208	83.0 ± 15.4	72.1 ± 14.4	2767	82.9 ± 15.4	71.7 ± 14.1	<0.001
Height (m)	1.6 ± 0.1	4098	1.6 ± 0.1	1.6 ± 0.1	2686	1.6 ± 0.1	1.6 ± 0.1	0.309
Body mass index (Kg/m ²)	28.6 ± 5.1	4093	31.0 ± 4.8	27.0 ± 4.7	2685	30.8 ± 4.6	26.7 ± 4.5	<0.001
Waist circumference (cm)	96.2 ± 14.2	4163	104.1 ± 12.4	91.0 ± 12.9	2769	103.2 ± 11.5	90.3 ± 12.9	<0.001
Blood and urine tests								
Glycemia (mg/dL)	101.8 ± 27.7	4148	116.3 ± 33.8	92.3 ± 17.2	2769	102.2 ± 14.8	89.3 ± 9.8	<0.001
HbA1c (%)	7.0 ± 1.3	776	7.0 ± 1.3	6.8 ± 1.3	—	—	—	—
Total cholesterol (mg/dL)	196.4 ± 39.2	4136	193.1 ± 42.4	198.5 ± 36.8	2769	205.5 ± 40.5	202.1 ± 35.9	<0.001
HDL cholesterol (mg/dL)	54.8 ± 15.3	4079	47.6 ± 12.7	59.8 ± 14.9	2769	48.4 ± 12.6	60.3 ± 15.1	<0.001
LDL cholesterol (mg/dL)	118.1 ± 35.3	3944	115.4 ± 39.1	119.9 ± 32.3	2661	126.7 ± 38.1	122.7 ± 31.6	<0.001
Triglycerides (mg/dL) (median ± IQR)	124.8 ± 85.5	4121	163.7 ± 109.4	98.9 ± 50.4	2769	163.9 ± 98.7	99.1 ± 52.7	<0.001
Non-HDL cholesterol (mg/dL)	141.8 ± 38.1	4079	145.6 ± 41.1	139.1 ± 35.7	2769	157.1 ± 39.5	141.7 ± 35.2	<0.001
Uric acid	5.3 ± 1.4	3651	5.7 ± 1.5	5.0 ± 1.3	2441	5.8 ± 1.6	4.9 ± 1.3	<0.001
Creatinine (mg/dL)	0.8 ± 0.5	4120	0.9 ± 0.5	0.9 ± 0.6	2762	0.9 ± 0.4	0.8 ± 0.5	0.487
Albumin/creatinine ratio (median ± IQR)	14.1 ± 62.4	4304	23.3 ± 88.9	8.4 ± 36.2	2769	12.7 ± 44.4	8.6 ± 39.5	0.016
Estimated glomerular filtration rate by CKD-EPI	86.8 ± 24.8	4083	84.1 ± 20.1	91.6 ± 20.0	2742	87.1 ± 18.9	93.1 ± 19.6	<0.001

In general, the mean ± SD is reported.

^aLevel of significance that compares patients with MetS to patients without MetS.

^bLevel of significance that compares patients with p-MetS to patients without p-MetS.

^cLevel of significance that compares patients with MetS to patients without p-MetS.

IQR, interquartile range; LDL, low-density lipoprotein.

FIG. 1. Prevalence of target organ damage in patients with metabolic syndrome.

high CVR was greater (32.0% vs. 13.6%, $P < 0.001$), but that of very high CVR was similar (3.4% vs. 4.2%, n.s.).

Variables associated with the presence of MetS and pre-MetS

The different variables associated with the MetS and pre-MetS included in the study were adjusted simultaneously using a binary logistic regression model. Tables 4 and 5 present the resulting variables of the final model. We observed that patients with DM were 6.36 times more likely to present MetS; patients with obesity, 3.81 times; and patients with HT, 2.66 times; whereas the probability of suffering pre-MetS was 2.44 times higher in obese patients and 1.80 in hypertensive patients. It should be noted that age and sedentary lifestyle show statistically significant association, in the analyses carried out for MetS and also in pre-MetS when the definition criteria are excluded in the analysis (Tables 4 and 5).

Discussion

The results of this study show that approximately one third of the adults attending PHC present MetS and one fifth, pre-MetS.

The IBERICAN study is a study on CVR which includes a homogeneous sample, with sociodemographic and clinical characteristics very similar to the samples in other studies carried out in Spain.⁶⁻⁸ It reflects the population who attends PHC centers, showing a slight predominance of women, among whom excess weight is more frequent.

The prevalence of MetS observed in the IBERICAN study is higher than in population-based studies conducted in Spain which used the harmonized definition, such as ENRICA (22.7% for MetS and 16.9% for pre-MetS)⁸ or DARIOS (31.7% for MetS and 20% for pre-MetS).⁶ This can be explained by the fact that they are precisely population-based studies, whereas IBERICAN is a study carried out on population attending PHC. However, our study shows similar values to more recent studies, such as Di@bet.es, with a prevalence of MetS of 42% in men and 32.3% in women.⁷

At an international level, we also have prevalence data for MetS in population-based studies that used the harmonized definition. Among the most important of these, we should point out the Rotterdam study with a prevalence of 42.2% (3) and two German studies, SHIP (48.1% in men and 34.8% in women) and KORA (42.7% in men and 27.5% in women),¹⁴ all of them with similar prevalence to ours.

Obesity also deserves special attention, in this case due to its physiopathological role. In our study, the bivariate and multivariate analyses show the presence of this association, which has also been observed in other studies. Thus, the ENRICA study found a prevalence for obesity of 23%¹⁵ and 22.7% for MetS⁸; similar results were obtained in a study conducted in Europe that compared 10 population-based cohorts from different countries and that showed a prevalence of obesity varying from 11% in Italy and 26.3% in Germany, with parallel values for MetS.¹⁶ In contrast, the data from the United States indicate a prevalence of obesity of 34%¹⁷ and a prevalence of MetS of 36.1%.¹⁸ In our study, the prevalence of obesity (33.0%)⁹ and MetS (38.5%) shows

FIG. 2. Prevalence of target organ damage in patients with premetabolic syndrome.

TABLE 4. MULTIVARIATE LOGISTIC REGRESSION TO ANALYZE THE VARIABLES ASSOCIATED WITH THE PRESENCE OF METABOLIC SYNDROME

Variable	Odds ratio	95% CI	P ^a
MetS			
Diabetes mellitus	6.36	5.044–8.031	<0.001
Obesity	3.81	3.207–4.520	<0.001
HT	2.66	2.210–3.198	<0.001
Dyslipidemia	1.63	1.368–1.938	<0.001
Smoking	1.31	1.053–1.624	0.015
Sedentary lifestyle	1.27	1.060–1.514	0.009
Age	1.01	1.000–1.014	0.054
p-MetS			
Obesity	2.44	2.086–2.860	<0.001
HT	1.80	1.534–2.112	<0.001

We included the age as continuous variable.

^aWald chi-squared test.

similar results to those obtained in the United States. Further evidence of this is the increase or decrease in MetS parallel to the increase or decrease in patients' weight.¹⁹ With this information we could affirm that, regardless of the population, there is a parallel between the prevalence of obesity and MetS that goes beyond the statistical association which could involve the fact of being included in the MetS definition. The association can probably be explained by the existing interrelation among the three most frequent components of the MetS (HT, abdominal obesity, and high glycemia), with a high prevalence of obesity (36%)¹⁵ and HT (33%)²⁰ in Spain, but also a strong association of HT and hyperglycemia with obesity.²⁰ On the basis of the above, we can affirm that abdominal obesity plays a fundamental role in the development of HT and hyperglycemia and, therefore, in the genesis of MetS.

From the point of view of cardiovascular prognosis, the presence of any of the forms of CVE probably adds little, since it has been known for decades that these are high CVR patients. However, it seems logical to suggest that the MetS

should be the paradigm in primary prevention, because these are patients without CVE, but with a higher prevalence of CVRF, both classic risks and other risks of still uncertain significance, such as hyperuricemia,²¹ increased TOD,²² and kidney disease,²³ which are undoubtedly risk markers in these asymptomatic patients.

We think that IBERICAN study can contribute to answer some questions about MetS: to confirm the authentic role of MetS in the CVR, to know the individual predictive value of each criterion in prognosis, what is the key role of the obesity in the development of MetS and the rest of diagnostic components, etc. In contrast, it will also be important to analyze to what extent lifestyle habits, and the Mediterranean diet, may contribute to reduce the incidence of the MetS.²⁴

We present in our project the analysis of the data of patient inclusion in the study, which shows consistency with results published in the scientific literature. The IBERICAN study will provide far more relevant results in the analysis of the cohort's follow-up that will allow to solve these and other questions still existing in the field of CVR research and the relation of the different CVRF to the incidence of MetS and pre-MetS. Certainly, the fact that recent studies such as Di@bet.es or ours show progressively increasing prevalence rates of obesity, MetS, or DM clearly reflects the fact that CVRF are increasing in the Spanish population, which will have an impact on future CVE. This is what the IBERICAN study will analyze.

The limitations of the study have been commented on in previous publications⁹; these are basically the lack of randomization of participant physicians and patients and the selection of the sample in a clinical environment. Nevertheless, both the sample size and the rigorous methodology of the analyses grant sufficient statistical power and minimize the effect of both limitations providing robustness to the conclusions obtained.

In the light of all the above, we can conclude that both patients with MetS and with pre-MetS present higher CVRF and increased associated renal and CVE. The prognostic value of these findings must be analyzed in the longitudinal follow-up of the IBERICAN cohort.

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Author Disclosure Statement

The authors declare there are no conflicts of interest that could be perceived as prejudicing the impartiality of the research reported.

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TABLE 5. MULTIVARIATE LOGISTIC REGRESSION TO ANALYZE THE VARIABLES ASSOCIATED WITH THE PRESENCE OF METABOLIC SYNDROME EXCLUDING THE DEFINING VARIABLES OF THE SYNDROME

Variable	Odds ratio	95% CI	P ^a
Metabolic syndrome			
Level of education (low)	1.669	1.399–1.991	<0.001
Sedentary lifestyle	1.500	1.269–1.772	<0.001
Uric acid	1.334	1.262–1.411	<0.001
Age	1.030	1.023–1.036	<0.001
Albuminuria	1.003	0.996–1.010	0.044
Premorbid metabolic syndrome			
Level of education (low)	1.359	1.124–1.643	0.002
Uric acid	1.344	1.264–1.430	<0.001
Sedentary lifestyle	1.222	1.028–1.453	0.023
Sex (woman)	1.217	1.014–1.461	0.035
Age	1.011	1.003–1.018	0.007
Total cholesterol	1.008	1.005–1.010	<0.001
eGFR <60 mL/min	1.006	1.001–1.011	0.029

We included the age as continuous variable.

^aWald chi-squared test.

eGFR, estimated Glomerular Filtration Rate.

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