Relationship Between Metabolic Syndrome and Ischemic Heart Disease Mortality in Spain

Montserrat León Latre,[a] Eva M. Andrés,[a] Alberto Cordero,[b] Isaac Pascual,[a] Cristina Vispe,[c] Martín Laclaustra,[d] Emilio Luengo,[a] and José Antonio Casasnovas[a]

[a]Unidad de Investigación Cardiovascular, Instituto Aragonés de Ciencias de la Salud, Zaragoza, Spain
[b]Departamento de Cardiología, Hospital Universitario de San Juan, Sant Joan d'Alacant, Alicante, Spain
[c]Servicio de Prevención de Administración General, Gobierno de Aragón, Zaragoza, Spain
[d]Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain

Morbidity and mortality due to ischemic heart disease (IHD) is subject to wide geographic variation both between and within countries. The aim of this study was to determine whether geographic variations exist in the prevalence of metabolic syndrome in the Spanish working population or in its relationship with IHD mortality. We analyzed clinical and laboratory data obtained during health check-ups carried out in Spanish workers (n=17 837) during 2003.

The prevalence of metabolic syndrome was 17% in men and 6.5% in women. However, there was a heterogeneous distribution across the different regions studied. The prevalence in southern and western regions (eg, in men: 22.15% in Extremadura and 20.6% in Galicia) was double that observed in central and northern zones (eg, in the País Vasco and Castilla y León). This research indicates that there is a significant association between IHD mortality and the prevalence of metabolic syndrome in workers from different Spanish regions.

Key words: *Metabolic syndrome. Ischemic heart disease. Mortality.*

Relación entre el síndrome metabólico y la mortalidad por cardiopatía isquémica en España

La mortalidad y morbilidad de la cardiopatía isquémica siguen una distribución geográfica heterogénea entre diferentes países e incluso dentro de cada país. El objetivo del presente estudio es analizar si hay diferencias en la distribución geográfica del síndrome metabólico en la población laboral española y su relación con la mortalidad por cardiopatía isquémica. Analizamos datos clínicos y analíticos (n=17.837) procedentes de los exámenes de salud realizados a trabajadores durante el año 2003.

La prevalencia del síndrome metabólico es del 17% en varones y el 6,5% en mujeres. Sin embargo, su distribución es heterogénea en las diferentes comunidades estudiadas. Las regiones del sur y el oeste muestran prevalencias (Extremadura, 22,15%; Galicia, 20,6% en varones) que duplican las de las zonas del centro y el norte: País Vasco y Castilla y León. Nuestro trabajo señala una asociación significativa entre la mortalidad por cardiopatía isquémica y la frecuencia de síndrome metabólico en trabajadores de las diferentes provincias españolas.

Palabras clave: *Síndrome metabólico. Cardiopatía isquémica. Mortalidad.*

INTRODUCTION

Recent years have seen the publication of studies investigating the prevalence of metabolic syndrome (MS) in different parts of Spain.[1-3] However, their results cannot be easily compared owing to the type of samples selected and the different methods used in each.

Metabolic syndrome is a risk factor for diabetes mellitus and ischemic heart disease (IHD).[4,5] The existence of geographic heterogeneity with respect to cardiovascular disease-related mortality and morbidity between and even within countries is well known.[6] The aim of the present work was to describe the distribution of the prevalence of MS in the working population of Spain, and to determine whether any relationship exists between this distribution and IHD mortality rates.

METHODS

Study sample

This study involved a cross-sectional, epidemiological investigation of Spanish workers

TABLE 1. General Characteristics of the Population Examined

	Men (n=13 693)		Women (n=4069)	
	Mean (SD)	Median	Mean (SD)	Median
Age, y	41.86 (10.01)	41	38.91 (9.43)	37
Weight, kg	80.75 (12.35)	80	62.62 (11.07)	61
Height, cm	172.63 (6.97)	173	161.27 (6.43)	161
Body mass index	27.08 (3.76)	26.75	24.1 (4.23)	23.3
Systolic blood pressure, mm Hg	125.36 (15.24)	120	113.52 (14.54)	110
Diastolic blood pressure, mm Hg	77.91 (10.22)	80	69.93 (9.58)	70
Total cholesterol, mg/ dL	207.7 (41.69)	206	195.96 (38.65)	193
LDL	133.43 (36.53)	132	123.89 (34.58)	121.4
HDL, mg/ dL	48.97 (10.9)	48	56.76 (14.06)	54.2
Triglycerides, mg/ dL	130.79 (103.04)	103	76.71 (42.76)	66
Glucose, mg/ dL	92.1 (20.54)	89	84.5 (13.32)	84.5

HDL indicates high density lipoproteins; LDL, low density lipoproteins.
$P<.0001$ for all variables..

recruited during health check-ups performed by the prevention services of FREMAP in the year 2003. The initial sample included 118 138 workers, of which 17 837 (13 768 men and 4069 women) were eligible for inclusion. After eliminating those initial subjects with computer-illegible data, the sample size was 69 860 patients. Of the remainder, those with all the variables required to make a diagnosis of MS were finally selected. All these subjects were between 25 and 64 years of age. The most important limiting variable for making this final selection of workers was the high density lipoprotein cholesterol (HDL-C) concentration; this datum was only available for one quarter of the initial population. An analysis was made of the randomness of the presence or absence of high density lipoprotein data, which showed the missing data were random and uniformly distributed across the provinces included in the study.

The mean values of the variables studied (Table 1) for the sample of workers included in and excluded from the study were compared after dividing them in terms of the presence or absence of HDL-C data, and glucose and triglyceride data, both in general and by sex. No significant differences were detected. The methods used in the collection of physical examination data and for the collection of samples for biochemical analysis are described elsewhere.[7,8]

Statistical Analysis

Continuous variables were described in terms of the mean, standard deviation, and median. Dichotomous variables were described in terms of proportions. Standardized estimates of proportions were recorded along with their 95% confidence intervals (95% CI). The adjustment of prevalences and means was undertaken using a standard European population for the age range 25-64 years, with subdivisions by decades as in previous analyses. Standardized statistical information was prepared for each region and province (in this case for men only), excluding those for which a sample of <100 workers was available. For the provincial level analysis a total of 13 305 workers was available. Adjusted confidence intervals were obtained by calculating the variance for each stratification of proportions, later adjusting for the weight of each of the groups used in the stratification procedure. The IHD-related mortality rates adjusted for sex and age for each province were obtained from the *Centro Nacional de Epidemiología* (National Epidemiology Center).[9] The association between the prevalence of MS and IHD-related mortality was determined by calculating the Spearman non-parametric rho coefficient.

RESULTS

Table 1 shows the characteristics of the workers studied. The men showed high values for all the variables studied except HDL-C. The raw prevalence of MS was 13.4% (15.9% in men and 5.2% in women).

Table 2 shows the prevalence of MS in each region according to sex and age; significant differences were seen between men and women (*P*<.05) in all regions. The maximum prevalence of MS was seen among men in Extremadura (22.15%; 95% CI, 21.7-22.5) and Galicia (20.6%; 95% CI, 20.2-20.9), and in women in Castilla-La Mancha (10.4%; 95% CI, 10.1-10.6) and Extremadura (9.1%; 95% CI, 8.1-10.2). Both sexes showed low prevalences in the País Vasco and Castilla-León. Figure 1 shows the significant positive correlation between the provincial figures for IHD-related mortality, adjusted for age and sex, and the standardized prevalence of MS (R=0.414; *P*=.04).

TABLE 2. Prevalence of Metabolic Syndrome (MS) Adjusted by Age and Sex for Each Region

|	Men		Women	
	No.	MS, % (95% CI)	No.	MS, % (95% CI)
Andalucia	2268	15.2 (14.9-15.4)	677	6.5 (6.3-6.7)
Aragón	480	14.5 (14.1-15)	158	7.9 (7.6-8.2)
Castilla-La Mancha	2741	17.8 (17.5-18)	1164	10.4 (10.1-10.6)
Castilla-León	1578	14.3 (14-14.5)	527	4 (3.9-4.1)
Cataluña	987	18.6 (18.1-19)	249	7.3 (7.1-7.6)
Extremadura	563	23.7 (22.7-24.6)	107	9.1 (8.1-10.2)
Galicia	2492	20.6 (20.2-20.9)	505	6.2 (6-6.4)
Madrid	232	15.5 (14.7-16.3)		
País Vasco	1272	13.7 (13.5-14)	333	5.8 (5.5-6)
Levante	945	17.3 (16.8-17.7)	248	10.5 (9.9-11.1)
Raw total		15.9		5.2
Standardized total	13 693	16.9 (16.7-17)	4069	6.5 (6.4-6.7)
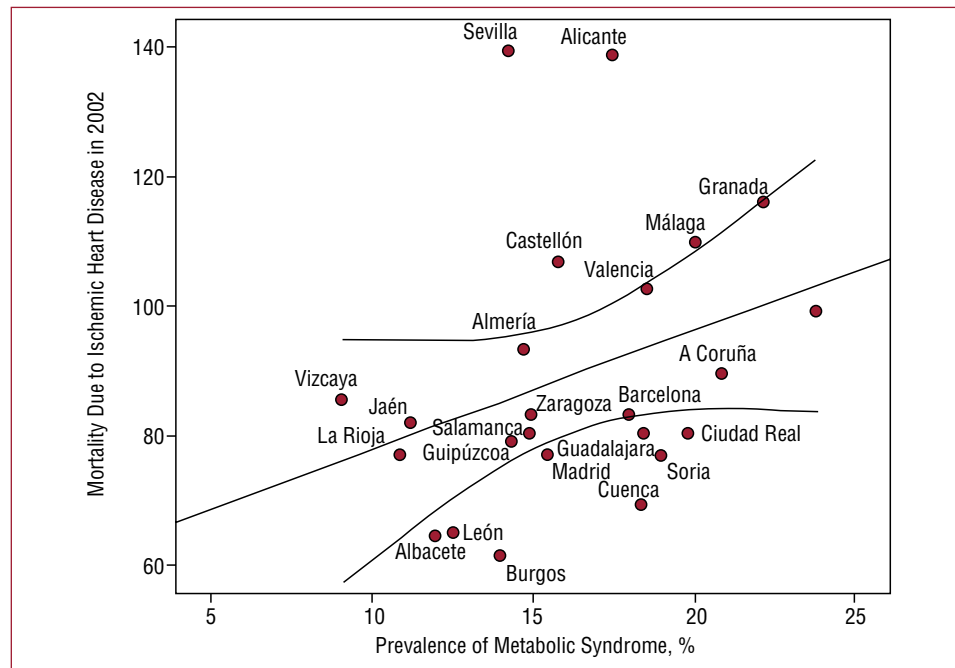
Figure. Association between prevalence of metabolic syndrome (MS) in Spanish provinces (%) and mortality related to ischemic heart disease.

DISCUSSION

The prevalence of MS was found to be similar to that published for other samples of Spanish workers. However, its distribution was not homogeneous across regions. In addition, it correlated with IHD-related mortality. The southern regions of the country showed a greater prevalence of MS, reaching up to twice that seen in the center and north. This north-south/southwest pattern agrees with that described by other authors for hypertension, diabetes, and obesity in Spain, both in adults and children.[10-12] The presence of MS might be determined by the greater prevalence of overweight in these regions, which would also lead to an increase

in other risk factors and eventually increased IHD-related morbidity and mortality. This would appear to be borne out by recently published data that show the south of Spain to be losing its position as one of the areas of Europe with the lowest IHD-related mortality; in fact the area now has higher values than the rest of Europe.[6]

The present results indicate a significant relationship between IHD-related mortality in workers and the frequency of MS in the different provinces. Unfortunately, the results refer to an association between cardiovascular risk in 2003 and IHD-related mortality in 2002.

Sadly, data for the preceding 10 years on the prevalence of MS are unavailable – such

information would be very useful for establishing the relationship between MS and current IHD-mortality. However, those data that do exist suggest that the prevalence of cardiovascular risk factors has not diminished in recent years. In addition, the same geographical differences as detected in the present work have been previously reported.

The present work suffers from a number of limitations. No other factors (eg, socioeconomic factors, physical activity, diet, use of tobacco) that might have influenced the results were controlled. Further, the selection of the provinces was neither random nor weighted; rather, those that could supply information for >100 workers were included. The present results could, however, allow one to design new studies to determine the influence of genetic or acquired (dietetic, physical activity, etc) factors on MS in the different regions. Knowledge of these differences is important for deciding upon the best preventive strategy to be followed in each area.

ACKNOWLEDGMENTS

REFERENCES

1. Álvarez EE, Ribas L, Serra L. Prevalencia del síndrome metabólico en la población de la Comunidad Canaria. Med Clin (Barc). 2003;120:172-4.
2. Martínez-Larrad MT, Fernández-Pérez C, González-Sánchez JL, López A, Fernández-Álvarez J, Riviriego J, et al. Prevalencia del síndrome metabólico (criterios del ATP-III). Estudio de base poblacional en áreas rural y urbana de la provincia de Segovia. Med Clin (Barc). 2005;125:481-6.
3. Calbo JM, Terrancle DJI, Fernández P, Rodríguez MJ, Martínez V, Santisteban Y, et al. Prevalencia de síndrome metabólico en la provincia de Albacete (España). Rev Clin Esp. 2007;207:64-8.
4. Wilson PW, D'Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation. 2005;112:3066-72.
5. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol. 2007;49:403-14.
6. Müller-Nordhorn J, Binting S, Roll S, Willich SN. An update on regional variation in cardiovascular mortality within Europe. Eur Heart J. 2008;29:1316-26.
7. Alegria E, Cordero A, Laclaustra M, Grima A, León M, Casasnovas JA, et al. Prevalencia de síndrome metabólico en población laboral española: registro MESYAS. Rev Esp Cardiol. 2005;58:797-806.
8. Cordero A, Laclaustra M, León M, Grima A, Casasnovas JA, Luengo E, et al. Prehypertension Is Associated With Insulin Resistance State and Not With an Initial Renal Function Impairment A Metabolic Syndrome in Active Subjects in Spain (MESYAS) Registry Substudy. Am J Hypertens. 2006;19:189-96.
9. Morbilidad provincial por cardiopatía isquémica por sexo. España 2002 [cited Sep 11, 2008]. Available from: http://www.isciii.es/htdocs/centros/epidemiologia/epi_cardio_tabla4.jsp
10. Villar Álvarez F, Banegas Banegas JR, Donado Campos J, Rodríguez Artalejo F. Las enfermedades cardiovasculares y sus factores de riesgo en España: hechos y cifras. INFORME SEA 2007. España: Equipo Creativo; 2007.
11. Aranceta-Bartrina J, Serra-Majem L, Foz-Sala M, Moreno-Esteban B. Prevalencia de obesidad en España. Med Clin (Barc). 2005;125:460-6.
12. Pérez-Rodrigo C, Aranceta Bartrina J, Serra Majem L, Moreno B, Delgado Rubio A. Epidemiology of obesity in Spain. Dietary guidelines and strategies for prevention. Int J Vitam Nutr Res. 2006;76:163-71.