## **Brief report**

# Cardiovascular Risk Factors and Lifestyle Associated With Premature Myocardial Infarction Diagnosis

Eva Andrés,<sup>a,\*</sup> Montserrat León,<sup>b</sup> Alberto Cordero,<sup>c</sup> Rosa Magallón Botaya,<sup>d</sup> Purificación Magán,<sup>e</sup> Emilio Luengo,<sup>b</sup> Eduardo Alegría,<sup>e</sup> and José A. Casasnovas<sup>b</sup>

<sup>a</sup> Unidad de Investigación-Epidemiología Clínica, Hospital Universitario 12 de Octubre, CIBER de Epidemiología y Salud Pública, Madrid, Spain

<sup>b</sup> Unidad de Investigación Cardiovascular, Instituto Aragonés de Ciencias de la Salud (I + CS), Zaragoza, Spain

<sup>c</sup> Departamento de Cardiología, Hospital Universitario de San Juan, San Juan de Alicante, Alicante, Spain

<sup>d</sup> Unidad de Investigación en Atención Primaria, Spain

<sup>e</sup> Departamento de Cardiología, Policlínica Gipuzkoa, San Sebastián, Guipúzcoa, Spain

Article history: Received 15 April 2010 Accepted 19 September 2010 Available online 19 April 2011

Keywords: Myocardial infarction Lifestyle Risk factors Prognosis Gender

Palabras clave: Infarto de miocardio Estilo de vida Factores de riesgo Pronóstico Sexo

#### ABSTRACT

Young and old patients with acute myocardial infarction have different risk factor profiles, clinical presentation, angiographic findings and prognosis. In the present study we investigated the clinical profile of patients aged <46 years with acute myocardial infarction.

© 2010 Sociedad Española de Cardiología. Published by Elsevier España, S.L. All rights reserved.

# Factores de riesgo cardiovascular y estilo de vida asociados a la aparición prematura de infarto agudo de miocardio

#### RESUMEN

Los pacientes jóvenes diagnosticados de infarto agudo de miocardio tienen diferente perfil de riesgo cardiovascular, presentación clínica, hallazgos angiográficos y pronóstico que los demás pacientes. En este estudio se analizan las características y la evolución de los pacientes diagnosticados de infarto agudo de miocardio con edad < 46 años.

© 2010 Sociedad Española de Cardiología. Publicado por Elsevier España, S.L. Todos los derechos reservados.

#### **INTRODUCTION**

Atherothrombotic cardiovascular disease is one of the major causes of death in the world.<sup>1</sup> The cardiovascular risk profile of young patients diagnosed with acute myocardial infarction (AMI) differs from the rest of the population, as does clinical presentation, angiographic results and coronary disease prognosis.<sup>2</sup> Premature coronary disease mainly affects men and exhibits a high prevalence of specific cardiovascular risk factors such as family history of ischemic heart disease, hyperlipidemia or tobacco use. In young patients, the mortality rate from AMI is lower, suggesting they constitute a group of patients with chronic ischemic heart disease who should be submitted to stringent secondary prevention measures.

A family history of coronary disease associates strongly with the appearance of premature AMI, indicating that a substantial hereditary factor exists.<sup>3,4</sup> On the other hand, the analysis of

\* Corresponding author: Unidad de Investigación-Epidemiología Clínica, Hospital Universitario 12 de Octubre, CIBER de Epidemiología y Salud Pública, Avda. de Córdoba s/n, 28041 Madrid, Spain.

E-mail address: eandres@h120.es (E. Andrés).

cardiovascular risk factors in young patients has identified a high prevalence of tobacco use.<sup>5,6</sup> Moreover, although it has not been demonstrated clearly, substance abuse associates with cardiovas-cular disease in young patients.

#### **METHODS**

This ecological study was conducted in the autonomous region of Aragón (northeastern Spain), using the region's Minimum Basic Data Set (CMBD) from January 2000 to December 2007. In 2000, the autonomous region had a population of approximately 1 200 000 inhabitants. The CMBD database is coordinated on a regional basis and collects all data on hospitalization in the public sector healthcare system. It includes both administrative data (age, sex, and in-hospital stay or death) and clinical data, all of which hospitals must report. The inclusion criteria were AMI as principle diagnosis, using International Classification of Disease (ICD-9) criteria, and admission via Emergency Room. From secondary diagnoses, we deduced the presence of cardiovascular risk factors or a family history of cardiovascular disease, as well as data on substance use (tobacco, alcohol and drugs).

We defined premature AMI as that occurring in patients aged <46 years. Patient characteristics were analyzed by sex and by premature or non-premature AMI. Continuous variables are expressed as mean (95% confidence interval [CI]) and quantitative variables as percentages. The nonparametric Mann Whitney U test was used to contrast the existence of significant differences in quantitative variables and chi squared to compare qualitative variables.

We used logistic regression to compare premature and nonpremature AMI, validating the model with the Hosmer-Lemeshow test and ROC curves. Premature AMI prognosis was studied in terms of readmission and mortality using the survival model proposed by Wang, which generalizes the Cox model and permits the construction of models that take account of correlations between events (in the case of readmission).<sup>7</sup>

### RESULTS

We included 12 096 hospitalizations in the period 2000-2007, of which 8606 were men (71.15%). In the sample, 685 hospitalizations were for premature AMI (5.66%), 613 (89.49%) in men. The prevalence of men was significantly greater in the premature AMI group than in non-premature AMI: 89.49% vs. 70.05% (*P* < .001). Among patients with premature AMI, women showed lower prevalence of obesity, dyslipidemia and tobacco use (Table 1). We found no differences in the frequency of the different revascularization procedures.

In non-premature AMI, we found differences in all risk factors except previous angina. In women, we found greater prevalence of high blood pressure, obesity and diabetes mellitus. However, tobacco use was much more frequent in men and this difference was greater than that found in the premature AMI group. We should highlight the high level of substance abuse among patients diagnosed with premature AMI, with a 76.78% prevalence of smoking; 12.41% of regular alcohol consumption; and 7.59% use of other drug types. However, these percentages were lower in the non-premature AMI group: 24.46%, 3.49% and 0.11%, respectively. In both groups, substance use was greater among men. In contrast, the other coronary risk factors were more prevalent in nonpremature AMI, except for dyslipidemia (50.21% vs. 35.79%; *P* < .001) and atherosclerosis (31.67% vs. 27.63%; *P* = .022).

Logistic regression (Table 2) shows statistically significant associations with premature AMI for all the variables analyzed except previous angina. Premature AMI associated with greater prevalence of obesity (odds ratio [OR] = 1.7 [1.34-2.16]), dyslipidemia (OR = 1.37 [1.15-1.62]) and substance abuse: drug use (OR = 22.7 [11.16-44.45]), current tobacco use (OR = 6.35 [5.23-7.71]) and alcohol consumption (OR = 1.6 [1.19-2.15]).

In relation with prognosis of infarction, the in-hospital premature AMI mortality rate was much lower (2.77% vs. 13.65%; P < .001). However, when analyzed by sex, it was greater among women than men (9.72% vs. 1.96%; P < .001). When analyzing probability of readmission, we found differences in the two groups. Specifically, probability of readmission in the nonpremature AMI group was 12.53%; in the premature AMI group it was 3.1% (*P* < .05).

#### DISCUSSION

The main results of our study are the differences found in cardiovascular risk factors in premature AMI when compared with other age groups. These differences are heightened when men and women are analyzed independently. Moreover, the role of lifestyle in the young population, in terms of the use of toxic and other

Characteristics of Acute Myocardial Infarction in Patients Aged <46 Years and in II Other Patients, by Sex	farction in Patients Ageo	l <46 Years and in 11 Other P	atients, b	y Sex					
Variables	Premature infarction (n=685)	Non-premature infarction (n = 11 411)	Р	Prem	Premature infarction		Non-pre	Non-premature infarction	
				Men (n=613)	Women (n=72)	Ρ	Men (n= 7993)	Women (n=3418)	Ρ
Age	39.99 (39.89-40.38)	71.35 (71.14-71.56)	<.001 <sup>a</sup>	40.06 (36.65-40.46)	39.4 (37.91-40.89)	.788 <sup>a</sup>	69.07 (68.82-69.32)	75.93 (75.56-76.3)	<.001 <sup>a</sup>
Tobacco use (%)	76.78 (73.61-79.95)	24.46 (23.67-25.24)	<.001 <sup>b</sup>	78.62 (75.37-81.88)	61.11 (49.57-72.64)	.001 <sup>b</sup>	32.75 (31.72-33.78)	5.06 (4.32-5.79)	<.001 <sup>b</sup>
Alcohol consumption (%)	12.41 (9.93-14.88)	3.49 (3.15-3.83)	<.001 <sup>b</sup>	13.86 (11.12-16.6)	0	.001 <sup>b</sup>	4.85 (4.38-5.32)	0.32 (0.01-0.51)	<.001 <sup>b</sup>
Drug use (%)	7.59 (5.6-9.57)	0.11 (0.05-0.17)	<.001 <sup>b</sup>	7.83 (5.69-9.96)	5.56 (0.13-10.97)	.491 <sup>b</sup>	0.16 (0.07-0.25)	0	.048
High blood pressure (%)	21.75 (18.65-24.85)	47.72 (46.81-48.64)	<.001 <sup>b</sup>	22.18 (18.88-25.48)	18.06 (8.95-27.15)	.422 <sup>b</sup>	43.35 (42.26-44.43)	57.96 (56.3-59.61)	<.001 <sup>b</sup>
Diabetes mellitus (%)	6.86(4.96 - 8.75)	28.09 (27.27-28.92)	<.001 <sup>b</sup>	6.68 (4.7-8.67)	8.33 (1.79-14.87)	.601 <sup>b</sup>	24.1 (23.17-25.04)	37.42 (35.79-39.04)	<.001 <sup>b</sup>
Obesity (%)	16.35 (13.57-19.12)	$10.91\ (10.34-11.49)$	<.001 <sup>b</sup>	17.45 (14.44-20.46)	6.94 (0.92-12.95)	.023 <sup>b</sup>	9.49(8.85-10.13)	14.25 (13.07-15.42)	<.001 <sup>b</sup>
Dyslipidemia (%)	50.21 (46.46-53.97)	35.79 (34.91-36.67)	<.001 <sup>b</sup>	52.69 (48.72-56.65)	29.19 (18.41-39.92)	<.001 <sup>b</sup>	37.45 (36.39-38.51)	31.91 (30.35-33.48)	<.001 <sup>b</sup>
Artery disease (%)	1.75 (0.76-2.73)	8.92 (8.4-9.45)	<.001 <sup>b</sup>	1.63 (0.61-2.63)	2.78 (0-6.66)	.483 <sup>b</sup>	9.72 (9.07-10.37)	7.08 (6.21-7.94)	<.001 <sup>b</sup>
History of ischemic heart disease (%)	2.62 (1.42-3.82)	12.7 (12.09-13.31)	<.001 <sup>b</sup>	2.44 (1.22-3.67)	4.17 (0-8.89)	.388 <sup>b</sup>	10.64 (9.97-11.32)	17.52 (16.24-18.8)	<.001 <sup>b</sup>
Atherosclerosis (%)	31.67 (28.18-35.17)	27.63 (26.81-28.45)	.022 <sup>b</sup>	30.99 (27.32-34.66)	37.5 (26.04-48.95)	.262 <sup>b</sup>	30.91 (29.9-31.92)	19.95 (18.61-21.29)	<.001 <sup>b</sup>
Angina (%)	2.33 (1.2-3.46)	1.47 (1.25-1.69)	.073 <sup>b</sup>	2.61 (1.34-3.87)	0	.165 <sup>b</sup>	1.43 (1.17-1.69)	1.55 (1.13-1.96)	.65 <sup>b</sup>
Angioplasty (%)	25.54 (22.27-28.82)	16.83 (16.14-17.52)	<.001 <sup>b</sup>	26.59 (23.08-30.09)	16.67 (7.84-25.48)	.068 <sup>b</sup>	18.91 (18.05-19.77)	11.97 (10.87-13.05)	<.001 <sup>b</sup>
Catheterization (%)	37.22 (33.59-40.85)	22.96 (22.18-23.73)	<.001 <sup>b</sup>	36.7 (32.87-40.53)	41.67 (30-53.33)	.41 <sup>b</sup>	25.75 (24.78-40.53)	16.44 (15.19-17.68)	<.001 <sup>b</sup>
Derivation + revascularization (%)	0.29 (0-0.69)	1.14(0.95-1.34)	.037 <sup>b</sup>	0.32 (0-0.77)	0	.771 <sup>b</sup>	1.38 (1.13-1.64)	0.59 (0.33-0.84)	<.001 <sup>b</sup>
<sup>a</sup> Mann-Whitney U test.									

Chi-squared

#### Table 2

Logistic Regression Taking as Dependent Variable the Existence or not of Premature Myocardial Infarction

Premature infarction	OR (95% CI)	Р
Sex	0.79 (0.6-1.06)	.112
Diabetes mellitus	0.3 (0.22-0.41)	<.001
High blood pressure	0.39 (0.32-0.47)	<.001
Obesity	1.72 (1.35-2.18)	<.001
Dyslipidemia	1.36 (1.15-1.62)	<.001
Arterial disease	0.23 (0.13-0.42)	<.001
History of ischemic heart disease	0.35 (0.21-0.58)	<.001
Atherosclerosis	0.63 (0.49-0.82)	<.001
Angina	1.79 (1.01-3.2)	.052
Tobacco use	6.05 (4.95-7.4)	<.001
Alcohol consumption	1.6 (1.19-2.15)	.02
Drug use	22.7 (11.6-44.45)	<.001
Angioplasty	0.98 (0.74-1.3)	.931
Catheterization	2.15 (1.62-2.84)	<.001
Derivation + revascularization	0.32 (0.08-1.31)	.118

CI, confidence interval; OR, odds ratio.

Pseudo-R<sup>2</sup>, 24.97%; c-statistic (area under ROC curve), 0.8508.

substances that influence the appearance of premature infarction, seems decisive.

Age has a linear relation with the appearance of cardiovascular disease, and mortality is greater among older patients because they present more risk factors and coronary complications.<sup>2,8</sup> In contrast, the economic, social and medical impact of premature AMI is very high, as it generates and increases the number of patients with chronic coronary disease who are at greater risk of undergoing new coronary events, need repeat revascularization, and are at risk of heart failure, atrial fibrillation or stroke.<sup>1</sup> Consequently, prevention of AMI in the population is very important, but especially in the young population, which should be the fundamental objective of the healthcare authorities and the medical community. The results presented here show that the principle factors associated with premature appearance of AMI are associated with lifestyle and social behavior. Specifically, we have identified obesity and substance abuse as decisive in premature AMI. In comparison with other age groups, the distribution of classic risk factors is very similar in patients < 46 years, except for tobacco use, alcohol consumption and the use of other drugs. Therefore, our results indicate a destabilizing effect of these risk factors, triggering the appearance of AMI at a younger age. Indirectly, the high rate of catheterization and other related procedures could reflect the same perception on the part of specialists attending this type of patient.

Sex-related differences in cardiovascular disease have roused growing interest in the last decade<sup>9</sup> and our results show there are practically no differences in the classic risk factors with respect to premature infarction. In contrast, as age increases, differences between the sexes appear in terms of classic risk factors such as high blood pressure, diabetes mellitus and obesity, and we find a greater prevalence of these among women. In a wide-ranging sample of the working population, we found obesity had the most noticeable effect on women in the presence of cardiovascular risk factors.<sup>10</sup> The results of the impact of obesity in premature infarction add information relevant to cardiovascular disease prevention, as many earlier studies have shown.<sup>11,12</sup>

The results of this study indicate that if restrictions on tobacco use, alcohol consumption and drug use were more severe, we would significantly reduce the prevalence of AMI in the young population. Due to the huge cost of coronary disease in the developed world, healthcare authorities should develop new information policies aimed at changing habits among the young population to achieve the primary objective of preventing this type of disease at an early age.

The principle limitation of our study lies in the data collection because the CMBD is a defined database and does not permit us to obtain or analyze potentially relevant parameters such as family history of ischemic heart disease, waist circumference or readmission to hospitals in other autonomous regions.

#### **CONFLICTS OF INTEREST**

None declared.

#### REFERENCES

- Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson TB, Flegal K, et al.; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics 2009 update: A report of the American Heart Association Statistics Committee and Stroke Statistics Subcommitee. Circulation. 2009;119:480–6.
- Devlin G, Gore JM, Elliott J, Wijesinghe N, Eagle KA, Avezum A, et al.; GRACE Investigators. Management and 6-month outcomes in elderly and very elderly patients with high-risk non-ST-elevation acute coronary syndromes: the Global Registry of Acute Coronary Events. Eur Heart J. 2008;29:1275–82.
- Pineda J, Marín F, Roldán V, Valencia J, Marco P, Sogorbe F. Premature myocardial infarction: clinical profile and angiographic findings. Int J Cardiol. 2007;125:127–9.
- Lluís-Ganella C, Lucas G, Subirana I, Sentí M, Jiménez-Conde J, Marrugat J, et al. Efecto aditivo de diferentes variantes genéticas en el riesgo de cardiopatía isquémica. Rev Esp Cardiol. 2010;63:925–33.
- Krupski WC. The peripheral vascular consequences of smoking. Ann Vasc Surg. 1994;5:291–304.
- Wolfe MW, Vacek JL. Myocardial infarction in the young. Chest. 1998;94: 926–30.
- Wang MC, Chang SH. Nonparametric estimation of a recurrent survival function. J Am Stat Assoc. 1999;94:146–53.
- Pfisterer M; Trial of Invasive versus Medical therapy in Elderly patients Investigators. Long-term outcome in elderly patients with chronic angina managed invasively versus by optimized medical therapy. Four-year follow-up of the randomized Trial of Invasive versus Medical therapy in Elderly patients (TIME). Circulation. 2004;110:1213–8.
- 9. Cordero A, Alegría E. Sex differences and cardiovascular risk. Heart. 2006;92: 145-6.
- Cordero A, León M, Andrés E, Ordoñez B, Laclaustra M, Grima A, et al. Gender differences in obesity related cardiovascular risk factors in Spain. Prev Med. 2009;48:134–9.
- Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al.; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364:937–52.
- Zhang C, Rexrode KM, Van Dam RM, Li TY, Hu FB. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of followup in US women. Circulation. 2008;117:1658–67.