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CLINICAL RESEARCH

Prevalence of cardiovascular risk factors in men with stable coronary heart disease in France and Spain

Prévalence des facteurs de risque cardiovasculaire dans un échantillon d'hommes souffrant de coronaropathie stable, en France et en Espagne

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KEYWORDS

Cardiovascular risk factors;
Coronary heart disease;
Dyslipidaemia;

Summary

Background. – Cigarette smoking, raised blood pressure, unfavourable lipid concentrations, diabetes and – more indirectly – obesity, are responsible for most coronary heart disease events in developed and developing countries.

Aims. – The objective of our study was to compare prevalence, treatment and control of cardiovascular risk factors in two samples of men with stable coronary heart disease, recruited in France and Spain.

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Smoking;
Hypertension

Methods. — Standardized measurements of body mass index, systolic and diastolic blood pressures, plasma lipids, glycaemia, and smoking were collected and drug use was registered. Cross-sectional comparisons were made between French and Spanish samples.

Results. — Data from 982 individuals were analysed (420 French and 562 Spanish men). Current smoking was more frequent in Spain ($p < 0.001$), whereas hypertension and uncontrolled blood pressure were more frequent in France ($p < 0.001$). Mean concentrations of low-density lipoprotein cholesterol and triglycerides were significantly higher in France ($p < 0.001$). No significant differences were observed regarding obesity, high-density lipoprotein cholesterol and diabetes. More than 97% of participants presented with at least one of the following conditions: hypertension, dyslipidaemia, diabetes, obesity or smoking. Antiplatelet agents, calcium inhibitors, diuretics and hypoglycaemic drugs were used more frequently in France, whereas angiotensin-converting enzyme inhibitors and lipid-lowering treatments were used more frequently in Spain.

Conclusion. — Prevalence of cardiovascular risk factors is high among French and Spanish patients with stable coronary heart disease, with differences between countries regarding the distribution of the various risk factors. A great proportion of patients do not reach the recommended levels for risk factor control.

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MOTS CLÉS

Facteurs de risque cardiovasculaire ;
Maladie coronaire ;
Dyslipidémie ;
Tabagisme ;
Hypertension artérielle

Résumé

Contexte. — Le tabagisme, l'hypertension artérielle, les dyslipidémies, le diabète et plus indirectement, l'obésité sont à l'origine de la plupart des événements coronariens.

Objectifs. — Le but de ce travail était de comparer la prévalence, les traitements et le contrôle des facteurs de risque cardiovasculaire, dans une population d'hommes coronariens, recrutés en France et en Espagne.

Méthodes. — Des mesures standardisées de l'indice de masse corporelle, de la pression sanguine artérielle, des lipides plasmatiques, de la glycémie et du tabagisme ont été réalisées et les traitements médicamenteux ont été recueillis.

Résultats. — Un groupe de 982 patients de sexe masculin a été constitué (420 français et 562 espagnols). Le tabagisme actif était plus fréquent en Espagne ($p < 0,001$), l'hypertension et le non-contrôle des chiffres de pression sanguine artérielle se rencontraient plus fréquemment en France ($p < 0,001$). Les niveaux plasmatiques moyens de cholestérol-LDL et de triglycérides étaient plus élevés en France ($p < 0,001$). Aucune différence significative n'a été mise en évidence sur l'obésité, le cholestérol-HDL ou le diabète. Plus de 97% des patients présentaient une hypertension, une dyslipidémie, un diabète, une obésité ou un tabagisme. Les médicaments antiagrégants plaquettaires, inhibiteurs calciques, diurétiques et hypoglycémiantes étaient plus fréquemment utilisés en France. Les inhibiteurs de l'enzyme de conversion de l'angiotensine et les hypolipémiants étaient plus fréquents en Espagne.

Conclusion. — La prévalence des facteurs de risque cardiovasculaire est élevée parmi les patients coronariens, en France comme en Espagne, mais la répartition des facteurs de risque est différente selon le pays. Une proportion importante de patients est insuffisamment contrôlée.

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Abbreviations

ACE	angiotensin-converting enzyme
ARA II	angiotensin II receptor antagonist
BMI	body mass index
CHD	coronary heart disease
HDL	high-density lipoprotein
LDL	low-density lipoprotein

Background

Understanding the crucial role of cardiovascular risk factors has established new paradigms in the epidemiological approach to CHD. In the past decades, many potential new

precursors of CHD have been identified, such as thrombotic, inflammatory or genetic factors, infectious agents, early life exposures, oestrogen deficiency and psychosocial factors [1]. However, cigarette smoking and traditional risk factors (raised blood pressure, unfavourable lipid concentrations, diabetes and obesity [which is linked more indirectly to cardiovascular risk]), partially promoted by inappropriate diet and physical inactivity, are the most prevalent cardiovascular risk factors in both developed and developing areas of the world, and also have the highest impact on CHD incidence [2–5].

The literature has often reported that major cardiovascular risk factors can only explain half of the burden of CHD incidence, based on the observation that many individuals with significant levels of cardiovascular risk factors never

experience CHD events and, conversely, that some individuals with CHD lack any of the major cardiovascular risk factors [6–8]. However, this hypothesis is no longer supported by epidemiological studies, which show that only 15–20% of stable CHD patients lack all of the major cardiovascular risk factors [9,10]. These major modifiable risk factors are largely uncontrolled [11–14].

Populations in Southern Europe, where the incidence and mortality from CHD is low, have shown a prevalence of traditional cardiovascular risk factors close to the prevalence observed in countries characterized by much higher CHD incidence and mortality [15,16]. France and Spain are two adjacent Southern European countries that share high life expectancy [17] despite different lifestyle habits, dietary patterns and healthcare systems. Treatments and hospitalizations for acute coronary syndromes are funded entirely by the national healthcare system in each country. However, while expenditures for secondary prevention treatments and complementary tests are covered totally by the French system, with no prepayment required from patients, the Spanish healthcare system pays for secondary prevention drugs only in patients older than 65 years, whereas younger patients are partially reimbursed.

Data on cardiovascular risk factors at discharge after acute myocardial infarction have already been reported in France and Spain [14,18,19], but prevalence and long-term management of cardiovascular risk factors in individuals with stable CHD have not been studied in detail, especially with regard to lipid disorders. The aim of the present study was to compare prevalence, treatment and control of cardiovascular risk factors in two samples of men with stable CHD recruited in France and Spain.

Methods

Population setting

This analysis was designed to compare the prevalence of cardiovascular risk factors in individuals with stable CHD living in two regions of South-West Europe: France and Spain. In France, participants were recruited as part of the Génétique et Environnement en Europe du Sud (GENES) study, a case-control study designed to assess the role of gene–environment interactions in the occurrence of CHD. Participants were men living in the Toulouse area (Haute-Garonne, South-West France, bordering on Spain), a region of 1.1 million inhabitants (540,000 men). Participants were included from 2001 to 2004. For the present analysis, only cases with a history of acute myocardial infarction were taken into account. Eligible participants were French male CHD patients, aged 45–74 years, living in the area of Toulouse and hospitalized in the Toulouse University Hospital for follow-up of stable CHD. Prior acute myocardial infarction had to be documented in the medical file of the patient and be determined from evidence of new pathological Q-waves on electrocardiogram, imaging evidence of healed acute myocardial infarction or evidence of a region of loss of viable myocardium that was thinned and failed to contract, in the absence of a non-ischaemic cause. Patients with confirmed acute myocardial infarction, electrocardiogram changes or rise in cardiac enzymes

(>1.5 times the upper limit) in the past 2 months, were excluded.

In Spain, the Registre Gironi del Cor Project (REGICOR) records all acute myocardial infarctions occurring in local inhabitants in six counties in Gerona. This province is located in North-East Spain, bordering on France, with a reference population of approximately 600,000 subjects. The registry process is done prospectively, and encompasses those patients admitted to the only referral hospital in the area. In order to be eligible, subjects have to be clinically diagnosed with acute myocardial infarction. Once identified, patients are classified according to the MONItoring of trends and determinants in Cardiovascular diseases (MONICA) project algorithm, which takes into account type of symptoms, electrocardiogram findings and enzymes [20]. Selected patients were part of the definite non-fatal acute myocardial infarction group, defined as: definite electrocardiogram; or typical, atypical or inadequately described symptoms, together with probable electrocardiogram and abnormal enzymes; or typical symptoms and abnormal enzymes with ischaemic or non-codeable electrocardiogram or electrocardiogram not available [20,21]. The inclusion period lasted between 1995 and 2004, although 75% of patients were recruited after 2001. A 6-month follow-up was done to measure blood lipid concentrations in patients with stable status.

In summary, men aged 45–74 years, with stable CHD, who reported a history of acute myocardial infarction were selected in both studies for the purpose of our analysis. The sample size (420 and 562 individuals in France and Spain, respectively), allowed us to detect differences between centres in the prevalence of cardiovascular risk factors of greater than 10 percentage-points, with a statistical power of at least 87.5%. Authorization from the local ethics committees was obtained in accordance with the French and Spanish laws and the Declaration of Helsinki. All participants were informed about the aim of the study and informed consent was signed by each subject.

Questionnaires

Age and socioeconomic variables were collected through standardized interviews. Smoking status was classified as smokers (current smokers or smokers who had quit for <1 year), former smokers (those who had quit for >1 year) and non-smokers. All medications taken were also recorded. Antiplatelet agents, beta-blockers, nitrates, calcium inhibitors, ACE inhibitors, diuretics, ARA II and lipid-lowering treatments were taken into account for the purposes of the study. In the REGICOR project, information on the last two drugs was only available from 2001.

Clinical measurements

Examinations were performed by a team of trained nurses, physicians and interviewers, who used equivalent standard questionnaires and measurement methods in both surveys [20]. Anthropometrical measurements, including height and body weight were taken according to standardized procedures. BMI was determined as weight divided by height squared (kg/m^2). Participants were classified into three groups according to BMI: normal weight, $\text{BMI} < 25 \text{ kg}/\text{m}^2$;

overweight, BMI ≥ 25 and < 30 ; obese, BMI ≥ 30 . Blood pressure was measured with a periodically calibrated mercury sphygmomanometer in Spain and an automatic sphygmomanometer (OMRON 705 CP) in France. A cuff adapted to the upper arm perimeter was selected for each participant. Measurements were performed after at least a 5-minute rest. Two measurements were taken and the lower value was recorded for the analysis. The cut-off points to define hypertension followed the criteria proposed in the Second Joint Task Force of European and Other Societies on Coronary Heart Disease Prevention in Clinical Practice [22] and in the 2000 recommendations from the French Health Product Safety Agency [23]. These guidelines were chosen as they were in current use in Spain and France when the studies were carried out. The guidelines recommended identical goals and methods for cardiovascular prevention, except regarding the target goal for cholesterol, which was lower in the European guidelines than in the French guidelines, as described in the next paragraph. The following definitions were used for hypertension and its treatment and control: history of hypertension (when participants reported a previous diagnosis or treatment for hypertension); real hypertension (history of hypertension or systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg); treated hypertension (patients with a history of hypertension on drug treatment); controlled hypertension (systolic blood pressure < 140 mmHg and diastolic blood pressure < 90 mmHg among treated patients). Reference values were systolic blood pressure < 130 mmHg and diastolic blood pressure < 80 mmHg for diabetic patients.

Blood sample collection and biological analyses

In both centres, blood was withdrawn after a 10–14-hour fast, with less than 60 seconds duration, at least 2 months after acute myocardial infarction (6 months in Spain). Serum sample aliquots were stored at -80°C . Briefly, total cholesterol, glucose and triglyceride concentrations were determined enzymatically. HDL cholesterol was measured as cholesterol after precipitation of apoprotein B-containing lipoproteins with phosphotungstic-Mg⁺⁺. LDL cholesterol was calculated in both centres by the Friedewald equation whenever triglycerides were less than 3.4 mmol/L [24] (389 and 544 individuals in France and Spain, respectively). Biological measurements were performed in a core laboratory in Barcelona for Spanish participants [25] and in a core laboratory in the Toulouse University Hospital for French subjects [26]. The cut-off points to define dyslipidaemia followed the criteria used in the Second Joint Task Force of European and Other Societies on Coronary Heart Disease Prevention in Clinical Practice (LDL cholesterol ≥ 3.0 mmol/L or HDL cholesterol ≤ 1.0 mmol/L) in Spain [22], and the 2000 recommendations from the French Health Product Safety Agency (LDL cholesterol ≥ 3.4 mmol/L or HDL cholesterol ≤ 1.0 mmol/L) in France [23].

Glucose metabolism disturbances were classified as follows: history of diabetes (participants already diagnosed by a physician); impaired fasting glycaemia (fasting glycaemia ranging from 6.1–6.9 mmol/L in participants not previously

diagnosed with diabetes); real diabetes (participants with a history of diabetes or with fasting glycaemia ≥ 7 mmol/L); treated diabetes (patients with a history of diabetes under drug treatment).

Statistical analyses

Initially, the analyses were performed on the whole sample, then age-stratified analyses were done (45–59 years; 60–74 years). Continuous variables are summarized as means and standard deviations, and categorical variables are presented as proportions. Student's *t* test was used to compare means of continuous variables. A logarithmic transformation was done to compute the *p*-value for variables whose distribution departed from normal (i.e., glycaemia and triglycerides). The χ^2 -test was used to compare proportions. Statistical analysis was done with STATA software, version 9.2 (Stata Corp., College Station, TX, USA).

Results

We included 982 individuals aged 45–74 years (420 French and 562 Spanish participants). The mean age was 60 years. The proportion of smokers was higher in Spanish participants whereas French subjects had a higher proportion of former smokers (Table 1). The prevalence of obesity did not differ significantly between France and Spain (Table 1). Systolic and diastolic blood pressures were significantly higher in French participants in all age strata, and real hypertension occurred more frequently. In addition, among French subjects treated for hypertension there was significantly lower percentage of people with blood pressure below recommended levels (Table 1).

Average concentrations of total cholesterol, LDL cholesterol and triglycerides were significantly higher in French participants and the proportion of subjects with LDL cholesterol > 3.4 mmol/L was greater in France (Table 2). However, when dyslipidaemia was defined according to the guidelines used in both countries (i.e., LDL cholesterol ≥ 3.4 mmol/L in France, ≥ 3 mmol/L in Spain, or HDL cholesterol ≤ 1 mmol/L) the percentages of dyslipidaemic subjects were not significantly different between France and Spain. No significant difference was observed in HDL cholesterol concentrations. The percentage of participants with diagnosed diabetes did not differ significantly between the two countries, but diabetic participants were treated significantly more frequently in France (Table 2).

French participants were treated more frequently with antiplatelet drugs, calcium inhibitors (especially younger subjects) and diuretics. The percentages of participants receiving lipid-lowering treatment or antihypertensive drugs acting on the renin-angiotensin system (ACE-inhibitors or ARA II) were significantly higher in Spain than in France (Table 3).

Fig. 1 shows the distribution of the number of major cardiovascular risk factors per individual, among French and Spanish participants. Real hypertension, dyslipidaemia (LDL cholesterol ≥ 3.0 mmol/L [Panel A] or ≥ 3.4 mmol/L [Panel B] or HDL ≤ 1 mmol/L), real diabetes, smoking and obesity were considered. Only 2.6% of the French and 2.8% of the Spanish participants (Panel A) lacked all major cardiovascular risk factors ($< 5\%$ according to Panel B).

Table 1 Prevalence of obesity, smoking and hypertension in France and Spain, by age.

	45–59 years			60–74 years			All		
	France (n = 222)	Spain (n = 272)	p	France (n = 198)	Spain (n = 290)	p	France (n = 420)	Spain (n = 562)	p
BMI (kg/m ²)	27.2 ± 4.1	27.4 ± 4.0	0.718	27.0 ± 3.8	27.3 ± 3.8	0.370	27.1 ± 4.0	27.3 ± 3.8	0.395
Overweight and obesity			0.556			0.137			0.770
BMI < 25 kg/m ²	67 (30.2)	65 (28.3)		58 (29.3)	70 (29.2)		125 (29.8)	135 (28.7)	
25 ≤ BMI < 30 kg/m ²	100 (45.1)	115 (50.0)		106 (53.5)	111 (46.3)		206 (49.1)	226 (48.1)	
BMI ≥ 30 kg/m ²	55 (24.8)	50 (21.7)		34 (17.2)	59 (24.6)		89 (21.2)	109 (23.2)	
Smoking			< 0.001			< 0.001			< 0.001
Non-smokers	48 (21.6)	36 (13.3)		46 (23.2)	67 (23.3)		94 (22.4)	103 (18.5)	
Smokers	78 (35.1)	199 (73.7)		24 (12.1)	107 (37.2)		102 (24.3)	306 (54.8)	
Former smokers	96 (43.2)	35 (13.0)		128 (64.7)	114 (39.6)		224 (53.3)	149 (26.7)	
SBP (mmHg)	129 ± 20	112 ± 16	< 0.001	139 ± 22	115 ± 19	< 0.001	134 ± 21	114 ± 18	< 0.001
DBP (mmHg)	82 ± 11	66 ± 12	< 0.001	82 ± 10	66 ± 12	< 0.001	82 ± 10	66 ± 11	< 0.001
History of hypertension	82 (36.9)	107 (41.0)	0.362	85 (42.9)	162 (57.5)	0.002	167 (39.8)	269 (49.5)	0.003
Real hypertension ^a	133 (59.9)	114 (42.5)	< 0.001	147 (74.2)	172 (59.3)	0.001	280 (66.7)	286 (51.3)	< 0.001
Treated hypertension ^b	78 (95.1)	102 (98.1)	0.257	84 (100.0)	158 (97.5)	0.146	162 (97.6)	260 (97.7)	0.918
Controlled hypertension ^c	38 (48.7)	70 (68.6)	0.007	30 (35.7)	118 (74.7)	< 0.001	68 (42.0)	188 (72.3)	< 0.001

Results are given as mean ± standard deviation or number (%). BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

^a History of hypertension or SBP ≥ 140 mmHg or DBP ≥ 90 mmHg (≥ 130/80 mmHg in diabetic patients).

^b Patients with a history of hypertension on drug treatment.

^c SBP < 140 mmHg and DBP < 90 mmHg (< 130/80 in diabetic patients) among treated patients.

Table 2 Prevalence of dyslipidaemia and diabetes in France and Spain, by age.

	45–59 years			60–74 years			All		
	France (n = 222)	Spain (n = 272)	p	France (n = 198)	Spain (n = 290)	p	France (n = 420)	Spain (n = 562)	p
Total cholesterol (mmol/L)	5.3 ± 1.1	4.9 ± 1.0	< 0.001	5.1 ± 1.2	4.6 ± 1.0	< 0.001	5.2 ± 1.1	4.7 ± 1.0	< 0.001
Total cholesterol ≥ 4.9 mmol/L	131 (59.0)	123 (45.4)	0.003	106 (53.5)	97 (33.5)	< 0.001	237 (56.4)	220 (39.2)	< 0.001
HDL cholesterol (mmol/L)	1.1 ± 0.3	1.1 ± 0.3	0.835	1.1 ± 0.3	1.1 ± 0.3	0.094	1.1 ± 0.3	1.1 ± 0.3	0.351
HDL cholesterol ≤ 1.0 mmol/L	129 (58.1)	142 (52.4)	0.205	90 (45.5)	141 (48.8)	0.469	219 (52.1)	283 (50.5)	0.618
LDL cholesterol (mmol/L)	3.3 ± 1.0	3.1 ± 1.0	0.053	3.2 ± 1.0	2.9 ± 0.9	< 0.001	3.2 ± 1.0	3.0 ± 1.0	< 0.001
LDL cholesterol ≥ 3.0 mmol/L	116 (59.2)	139 (53.98)	0.259	109 (56.5)	119 (41.6)	0.001	225 (57.8)	258 (47.4)	0.002
LDL cholesterol ≥ 3.4 mmol/L	82 (41.8)	94 (36.4)	0.242	72 (37.3)	83 (29.0)	0.057	154 (39.6)	177 (32.5)	0.026
Dyslipidaemia ^a	147 (75.0)	196 (76.0)	0.812	127 (65.8)	195 (68.2)	0.586	274 (70.4)	391 (71.9)	0.632
Triglycerides (mmol/L)	2.2 ± 1.4	1.6 ± 0.9	< 0.001	1.7 ± 0.9	1.3 ± 0.6	< 0.001	1.9 ± 1.2	1.4 ± 0.7	< 0.001 ^e
Triglycerides ≥ 2.0 mmol/L	93 (41.9)	46 (17.0)	< 0.001	47 (23.7)	32 (11.1)	< 0.001	140 (33.3)	78 (13.9)	< 0.001
Glycaemia (mmol/L)	6.2 ± 2.4	5.9 ± 1.8	0.293	6.1 ± 2.5	6.2 ± 2.2	0.370	6.2 ± 2.5	6.1 ± 2.1	0.940 ^e
Impaired fasting glycaemia ^b	21 (11.3)	23 (10.5)	0.800	14 (8.8)	21 (9.1)	0.933	35 (10.1)	44 (9.8)	0.856
History of diabetes	43 (19.4)	60 (24.2)	0.207	62 (31.3)	73 (26.4)	0.237	105 (25.0)	133 (25.3)	0.907
Real diabetes ^c	78 (35.1)	81 (31.8)	0.436	87 (43.9)	97 (34.9)	0.046	165 (39.3)	178 (33.4)	0.060
Treated diabetes ^d	39 (90.7)	33 (68.8)	0.010	62 (100.0)	51 (76.1)	< 0.001	101 (96.2)	84 (73.0)	< 0.001

Results are given as mean ± standard deviation or number (%). HDL, high-density lipoprotein; LDL, low-density lipoprotein.

^a LDL cholesterol ≥ 3.0 mmol/L (Spain), ≥ 3.4 mmol/L (France) or HDL cholesterol ≤ 1 mmol/L.

^b Glycaemia ranging from 6.1 to 6.9 mmol/L in patients not previously diagnosed with diabetes.

^c History of diabetes or glycaemia ≥ 7 mmol/L.

^d Patients with a history of diabetes on drug treatment.

^e Computed from log-transformed values.

Table 3 Distribution of treatments in France and Spain, by age.

	45–59 years			60–74 years			All		
	France (n = 222)	Spain (n = 272)	p	France (n = 198)	Spain (n = 290)	p	France (n = 420)	Spain (n = 562)	p
	Antiplatelet agents	192 (87.2)	193 (75.7)	0.001	170 (85.9)	201 (71.8)	<0.001	362 (86.6)	394 (73.6)
Beta-blockers	150 (67.6)	190 (74.2)	0.110	120 (60.6)	162 (57.9)	0.547	270 (64.3)	352 (65.7)	0.656
Nitrates	54 (24.6)	42 (16.5)	0.029	57 (28.8)	68 (24.4)	0.280	111 (26.6)	110 (20.6)	0.031
Calcium inhibitors	45 (20.4)	18 (7.4)	<0.001	48 (24.2)	66 (24.4)	0.978	93 (22.2)	84 (16.3)	0.022
ACE-inhibitors	100 (45.1)	130 (50.8)	0.211	81 (40.9)	154 (55.0)	0.002	181 (43.1)	284 (53.0)	0.002
ARA II ^a	14 (6.4)	0 (0.0)	0.011	7 (3.5)	4 (4.9)	0.585	21 (5.0)	4 (2.3)	0.124
ACE-inhibitors or ARA II	114 (51.4)	130 (54.6)	0.482	87 (43.9)	158 (61.5)	<0.001	201 (47.9)	288 (58.2)	0.002
Diuretics	26 (11.8)	15 (5.8)	0.019	48 (24.2)	50 (17.7)	0.078	74 (17.7)	65 (12.0)	0.013
Lipid-lowering drugs ^a	155 (70.5)	144 (92.9)	<0.001	127 (64.8)	141 (78.3)	0.004	282 (67.8)	285 (85.1)	<0.001
4-drug combined therapy ^b	57 (25.1)	64 (30.2)	0.372	29 (14.7)	47 (19.2)	0.208	86 (20.6)	111 (24.3)	0.189
3-drug combined therapy ^c	99 (45.0)	106 (46.9)	0.687	70 (35.5)	77 (29.6)	0.180	169 (40.5)	183 (37.7)	0.377

Results are given as number (%). ACE, angiotensin-converting enzyme; ARA II, angiotensin II receptor antagonist.

^a Available only from 2001 to 2004 in the Spanish REGICOR study.

^b Antiplatelet and beta-blocker and lipid-lowering drug and (ACE-inhibitor or ARA II).

^c Antiplatelet and beta-blocker and lipid-lowering drug.

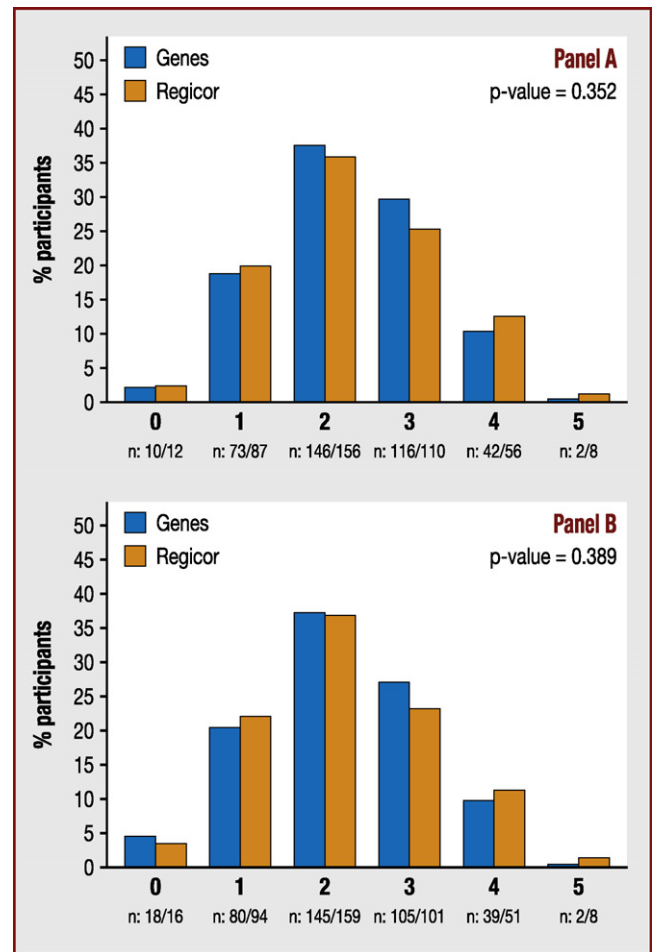


Figure 1. Number of cardiovascular risk factors per individual in France and Spain, according to the Second Joint Task Force of European and Other Societies on Coronary Heart Disease Prevention in Clinical Practice [22] (Panel A) or according to the 2000 recommendations from the French Health Product Safety Agency [23] (Panel B). *p*-values compare France and Spain. Cardiovascular risk factors taken into account: real hypertension (history of hypertension or systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg [130/80 mmHg in diabetic patients]); dyslipidaemia (LDL cholesterol ≥ 3.0 mmol/L or HDL cholesterol ≤ 1.0 mmol/L [Panel A]) or (LDL cholesterol ≥ 3.4 mmol/L or HDL cholesterol ≤ 1.0 mmol/L [Panel B]); real diabetes (history of diabetes or glycaemia ≥ 7 mmol/L; smoking; obesity (BMI ≥ 30 kg/m²). GENES, Génétique et Environnement en Europe du Sud; REGICOR, Registre Gironi del Cor.

Discussion

Our results show a high prevalence of major cardiovascular risk factors in CHD patients both in Gerona (Spain) and Toulouse (France). Indeed, 97.4% of the French and 97.2% of the Spanish participants presented with at least one of the five following conditions: hypertension, dyslipidaemia, diabetes, smoking or obesity. Previous international studies have shown that the overall pattern of cardiovascular risk factors exists irrespective of geographic origin [10,13]. Despite similarities between Toulouse and Gerona areas (two regions that are close from a geographical point of view, located in South-West Europe and characterized by

a low CHD incidence [15,16]), our study shows significant differences between the two countries regarding levels, treatment and control of cardiovascular risk factors.

The most prevalent cardiovascular risk factor was dyslipidaemia in both regions. However, the lipid profile in French participants was more unfavourable than in Spanish subjects and the use of lipid-lowering drugs was significantly lower in France. Consistent with the EUROASPIRE (European Action on Secondary Prevention by Intervention to Reduce Events) findings [11,12,14], lipid control was insufficient in the GENES and REGICOR studies: about half of the participants did not reach the European goal established in 1998 for LDL cholesterol in secondary prevention of CHD (guidelines used when patients were included) [22] and one-third remained above the threshold proposed by the 2000 French guidelines (3.4 mmol/L) [23]. The poorer control of lipids observed in French patients compared with Spanish patients is likely to be related to the less extensive use of lipid-lowering drugs in France, although the EUROASPIRE data have shown that poor lipid control may persist in CHD patients, even after a dramatic improvement in the prescription rates of lipid-lowering drugs [14].

An important finding of the study lies in the observation that more than half of the CHD patients had low HDL cholesterol (≤ 1 mmol/L). The concentrations were much lower than those described in other studies conducted among CHD-free individuals living in Gerona and Toulouse areas [25,27]. It is well known that HDL cholesterol plays a key role in the development of atherosclerosis, but raising HDL cholesterol concentration still remains difficult [28]. On the one hand, lifestyle modifications (i.e., diet, exercise, weight loss and smoking cessation) have been shown to have a favourable impact on HDL cholesterol concentration; on the other hand, evidence of the clinical efficacy of HDL-cholesterol-raising drugs is far less abundant than evidence accumulated for statins [29]. Beyond LDL cholesterol control, raising HDL cholesterol is essential to reduce residual risk in CHD patients.

Hypertension was very common in both populations. The proportion of treated patients among those who reported a previous history of hypertension was close to 100%. Nevertheless, blood pressure control remained poor, especially in French participants. This failure has been described extensively in other studies [11,12,14,19] and is generally attributed to low-dose treatment prescriptions, inadequate up-titration of doses and poor patient compliance [14], but could also be related to severe hypertension before treatment. Despite the availability of numerous antihypertensive drugs, blood pressure control is still challenging in CHD patients.

Diabetes increases markedly the risk of CHD and non-fatal recurrent coronary events in patients with clinically established CHD [30]. One-quarter of patients enrolled in the GENES and REGICOR studies were known diabetics and about an additional 10% (14% in France and 8% in Spain) had fasting plasma glucose concentrations ≥ 7 mmol/L, which could be compatible with a diagnosis of diabetes. Consequently, more than one-third of patients were potentially affected by glucose disturbances, and thus should be considered at high risk of recurrence.

According to a previous study, CHD events are attributed largely to smoking in Spanish men [31]. Although the design

of our study did not allow us to compute population-attributable risk fractions, our results show that smoking is extremely prevalent in CHD patients aged less than 60 years, with very few people achieving smoking cessation. In older age groups (60–74 years), a greater proportion of patients have quit, although 37% remained current smokers. These results highlight the need to reinforce all measures that could help patients to quit smoking permanently, in line with all current recommendations on cardiovascular prevention [32]. From a population point of view, laws aimed at forbidding smoking in public areas have been strengthened recently in France and Spain and could have a favourable impact on the prevalence of smoking in CHD patients.

No difference was found in the percentages of French and Spanish participants who were treated with a combination of the four drugs recommended in secondary prevention: statins, antiplatelet agents, beta-blockers and ACE-inhibitors. This drug combination has been shown to improve survival in high-risk patients with CHD [33] and is recommended by the European guidelines for cardiovascular prevention [22,32], although the role of ACE-inhibitors in CHD patients without a history of heart failure is still controversial [33–35]. According to a previous study, heart failure is the main determinant of the use of ACE-inhibitors in France [9].

Finally, the proportion of non-smoking CHD patients who were free of hypertension, dyslipidaemia, diabetes and obesity was very small (<3%) in both countries, suggesting that traditional risk factors remain central in the development of atherothrombosis in low-risk populations. However, our results also point out differences in the distribution, treatment and control of risk factors that should be taken into consideration to adapt prevention programmes to local characteristics. Causes of CHD are widely dependent on socioeconomic and cultural factors, which determine unhealthy lifestyles, and on healthcare systems, which determine patient management [1,32]. It is also likely that differences between France and Spain in coronary patients' risk factors reflect differences in the background population cardiovascular risk profile. Accordingly, two previous studies conducted in Spanish and French subjects recruited from the general population suggested that there are lower smoking rates and higher total cholesterol, LDL cholesterol and triglyceride concentrations in the general French population compared with the general Spanish population [25,36]. We describe in our present paper similar disparities between French and Spanish coronary patients.

Limitations

Several points should be discussed regarding our analyses and results. First, the GENES study included individuals with first or recurrent acute myocardial infarction, whereas participants in the REGICOR study were all recruited after a first acute myocardial infarction. We believe these different recruitment strategies may have contributed to observed differences in the control of risk factors between France and Spain, as patients with a history of recurrent events are likely to have a more severe risk factor profile. However, goals for cardiovascular prevention do not differ according to the number of acute events presented previously by the

patient. When necessary, in cases of poor risk factor profile, more intensive management should be provided so that every patient in a situation of secondary prevention achieves the recommended goals.

Second, the period of recruitment was slightly different in the two studies (2001–2004 for the GENES study and 1995–2004 for the REGICOR study, although participants in the REGICOR study were recruited mainly after 2001). This gap in the recruitment periods may have affected treatment patterns. For instance, the rate for the use of antiplatelet drugs was low in the Spanish sample, but should be interpreted as a mean proportion obtained from recent and older periods and reflecting the progressive implementation of the guidelines on cardiovascular prevention that were published in 1998. Even so, the use of antiplatelet drugs is very low in the Spanish sample and may be related to the inclusion of patients aged greater than 70 years, for whom antiplatelet drugs may have been underprescribed before the end of the 1990s.

Third, the elapsed time between the occurrence of the myocardial infarction and examination in the study was different in Spanish and French participants, with shorter delays in Spain. Given that drug prescription, adherence to treatment and, consequently, control of risk factors are probably better in patients who have presented recently with an acute coronary event, differences in delays may have increased differences in the management of risk factors between France and Spain. However, recommendations for smoking cessation and control of blood pressure, glycaemia and cholesterol are identical for patients with recent myocardial infarction and for those with an older history, and drug use should not vary with the time elapsed since the acute syndrome.

Conclusion

The strength of our present study lies in the comparison of two countries with different lifestyle habits, dietary patterns and healthcare systems, but relatively similar CHD incidence. Comparisons were based on extensive clinical and biological evaluations of cardiovascular risk factors. We have pointed out higher smoking rates, better blood pressure control and better lipid profiles in Spain compared with France. This may reflect differences in the background profile of risk factors in the general population. Regarding lipids, differences may also be related to the implementation of a lower recommended goal for cholesterol control and greater use of lipid-lowering drugs in Spain at the beginning of the 2000s, when most of the study recruitment took place.

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Conflict of interest

None.

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