

Management of Non-ST-Segment-Elevation Acute Coronary Syndromes in Spain. The DESCARTES (Descripción del Estado de los Síndromes Coronarios Agudos en un Registro Temporal ESpañol) Study

Héctor Bueno,^a Alfredo Bardají,^b Antonio Fernández-Ortiz,^c Jaume Marrugat,^d Helena Martí,^d and Magda Heras,^e on behalf of the DESCARTES study researchers

^aHospital General Universitario Gregorio Marañón, Madrid, Spain.

^bHospital Universitari de Tarragona Joan XXIII, Tarragona, Spain.

^cHospital Clínico San Carlos, Madrid, Spain.

^dInstitut Municipal d'Investigacions Mèdiques, Barcelona, Spain.

^eHospital Clínic, IDIBAPS, Barcelona, Spain.

Introduction and objectives. There is little information regarding the management of non-ST segment elevation acute coronary syndromes (NSTEMI) in Spain from a population-based perspective. Our objective was to study the status of clinical care in patients with NSTEMI in Spain from a representative perspective of the situation on a national level.

Patients and method. A prospective registry was used for consecutive patients with NSTEMI admitted to 52 Spanish hospitals with different cardiological facilities. Centers that fulfilled the quality control criteria for the study were randomly selected for inclusion.

Results. Between April and May, 2002, 1877 patients were recruited. Median age was 69 years, 93% had at least one risk factor and 73% had antecedents of cardiovascular disease. The electrocardiogram on admission was abnormal in 76% of the cases, and troponin levels were elevated in 53%. Twenty-seven percent of the patients were admitted to a cardiac care unit or intensive care unit. The rates of use of diagnostic techniques were: echocardiography 56%; non-invasive test for detection of ischemia 39%; coronary angiography 41%. During hospitalization, 24% underwent coronary revascularization, 88% received aspirin, 81% heparin, 37% clopidogrel, 12% glycoprotein IIb/IIIa inhibitors, 63% β -blockers, 46%

angiotensin-converting enzyme inhibitors, and 52% statins. The final diagnosis was angina in 54%, myocardial infarction in 28%, and other in 18%. Mortality was 3.7% at 28 days and 7.8% at 6 months.

Conclusions. DESCARTES is the first representative registry of NSTEMI management in Spain. It shows that despite their high-risk profile, these patients receive suboptimal medical care according to current clinical recommendations.

Key words: Acute coronary syndromes. Registry. Management.

Manejo del síndrome coronario agudo sin elevación del segmento ST en España. Estudio DESCARTES (Descripción del Estado de los Síndromes Coronarios Agudos en un Registro Temporal ESpañol)

Introducción y objetivos. Se dispone de escasa información acerca de la situación asistencial a escala poblacional de los síndromes coronarios agudos sin elevación del segmento ST (SCASEST) en España. El objetivo es conocer la situación de la atención médica a los pacientes con SCASEST en España, desde una perspectiva representativa de la realidad estatal.

Pacientes y método. Registro prospectivo de pacientes consecutivos con SCASEST ingresados en 52 hospitales españoles con distintos recursos cardiológicos, seleccionados al azar y que cumplieron con los criterios de control de calidad del estudio.

Resultados. Entre abril y mayo de 2002 se reclutó a 1.877 pacientes con una edad promedio de 69 años. El 93% tenía algún factor de riesgo y 73% antecedentes cardiovasculares. Un 76% presentaba un electrocardiograma anormal y un 53% elevación de las troponinas. El 27% fue ingresado en una unidad coronaria o de cuidados intensivos. Se estudió al 56% de los pacientes mediante ecocardiografía, al 39% mediante una prueba de

SEE EDITORIAL ON PAGES. 235-7

The annex includes a list of researchers and hospitals participating in the DESCARTES study.

The DESCARTES study was initiated by the Section for Ischemic Heart Disease and Coronary Units of the Spanish Society of Cardiology in collaboration with Bristol-Myers Squibb thru the award of an unconditional grant.

Correspondence: Dr. H. Bueno.
Servicio de Cardiología. Hospital General Universitario Gregorio Marañón.
Dr. Esquerdo, 46. 28007 Madrid. España.
E-mail: hecbueno@jet.es

Received September 24, 2004.

Accepted for publication December 9, 2004.

ABBREVIATIONS

DESCARTES: *Descripción del Estado de los Síndromes Coronarios Agudos en un Registro Temporal Español.*

CCL: cardiac catheterization laboratory.

AMI: acute myocardial infarction.

NSTE ACS: non-ST segment elevation acute coronary syndromes.

CU: coronary unit.

detección de isquemia y al 41% mediante coronariografía. En el hospital, un 88% recibió aspirina, un 81% heparina, un 37% clopidogrel, un 12% inhibidores de la glucoproteína IIb/IIIa, un 63% bloqueadores beta, un 46% inhibidores de la enzima de conversión de la angiotensina y un 52% estatinas. Se realizó revascularización coronaria en el 24% de los pacientes. El diagnóstico final fue angina en el 54%, infarto en el 28% y otros diagnósticos en el 18%. La mortalidad fue del 3,7% a los 28 días y del 7,8% a 6 los meses.

Conclusiones. DESCARTES es el primer registro representativo de la actividad asistencial en la atención a los SCASEST en España. Se demuestra que, pese a que son pacientes de alto riesgo, reciben una atención subóptima según lo recomendado.

Palabras clave: Síndrome coronario agudo. Registro. Tratamiento.

INTRODUCTION

The clinical perspective of non-ST segment elevation acute coronary syndromes (NSTE ACS) has changed greatly in recent years. The clinical concept itself has only recently been coined as a result, above all, of a better understanding of the pathophysiological processes ACS have in common. The first clinical practice guidelines on NSTE ACS management were not published until 2000¹⁻³ and were quickly revised in the light of various studies^{4,6} that added information of particular relevance to therapy. At the same time, a joint committee of the European Society of Cardiology and the American College of Cardiology⁷ proposed a controversial change in the definition of acute myocardial infarction (AMI) that was received with no little skepticism by Spanish cardiologists.⁸

The Spanish Society of Cardiology (SEC) Section for Ischemic Heart Disease perceived that the haste and magnitude of changes to the definition and to recommendations for NSTE ACS patient management might make appropriate, homogeneous medical atten-

tion more difficult. A further difficulty was the fact that the numerous specialists who participate in the diagnosis and treatment of NSTE ACS patients (emergency room physicians, cardiologists, intensivists, internists, etc) do not always apply homogeneous criteria. However, despite these peculiarities of clinical care and the fact that NSTE ACS constitutes the clinical presentation of ischemic heart disease that causes most urgent hospital admissions, little information is available about the clinical care of these patients in Spain.

To evaluate the reality of this situation, the SEC Section for Ischemic Heart Disease and Coronary Units initiated a project to describe the state of ACS in Spain thru a registry given the acronym DESCARTES. This article describes the characteristics, management and prognosis of these patients.

PATIENTS AND METHODS

Design

This prospective, observational, cohort study aimed to register all consecutive NSTE ACS patients hospitalized during April 2002 in a representative sample of Spanish hospitals, both public and private, accustomed to managing these patients.

Selection of Centers (Figure 1)

From Spanish Ministry of Health records, we compiled a list of ≥ 50 bed, non-specialist centers (i.e. hospitals specializing in pediatrics, trauma, obstetrics, etc were excluded). Using this list, we conducted a telephone survey to identify centers that received ≥ 5 NSTE ACS admissions/month. From centers that met this criterion, we made a random selection classifying centers in 3 groups according to the cardiological facilities available: *a*) centers with cardiology service, coronary unit (CU) or intensive care unit (ICU), and cardiac catheterization laboratory (CCL) where coronary interventions are performed; *b*) centers with CU or ICU, without CCL; and *c*) centers without cardiology service, CU or ICU, or CCL. The number of centers in each group was proportional to the volume of patients treated. In addition, according to the average number of admissions for each hospital type, we estimated that they admitted >50 , 20-50, or 5-19 NSTE ACS patients/month, respectively, in each group.

From these estimates, we calculated that to recruit 2000 patients in 1 month we would need to invite 66 hospitals to participate: 22 primary, 36 secondary, and 19 tertiary care centers. The projected sample size was set at some 1500 patients in order to achieve ± 0.025 precision in observed proportions of 50% (maximum standard deviation). We over-selected by 25% to compensate for possible sample loss following quality con-

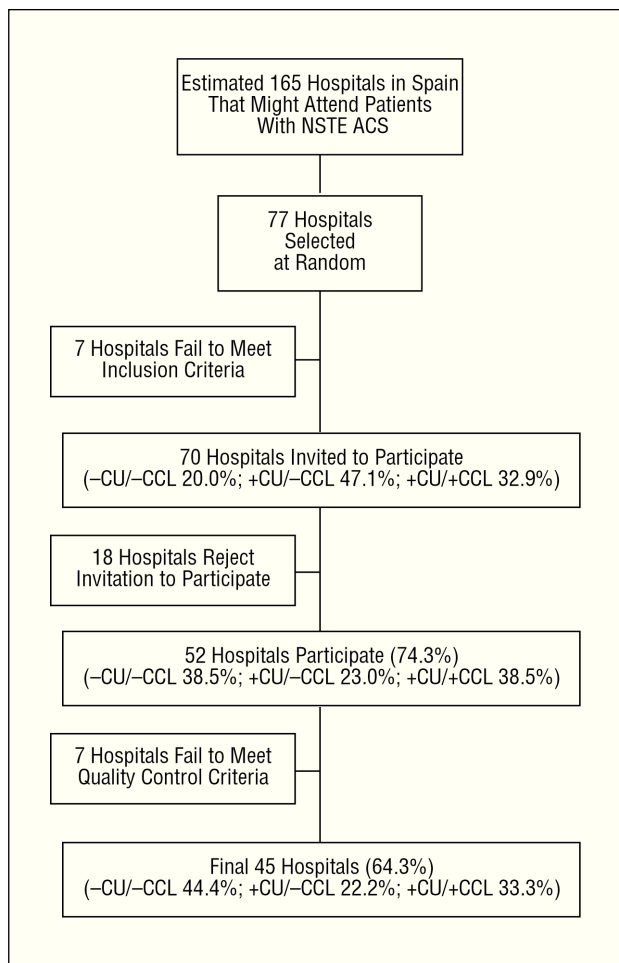


Figure 1. Flow chart showing process of selection, acceptance, and exclusion of centers and its influence on center type representativeness. CU indicates coronary care unit; CCL, cardiac catheterization laboratory; NSTE ACS, non-ST segment elevation acute coronary syndrome.

trol and increased the hospital sample by 10%-20% to compensate for centers failing to meet the minimum admissions criterion. Initially, 77 centers were invited to participate, selected at random from the list of Spanish hospitals routinely admitting ACS patients. Seven centers failed to meet minimum ± 5 ACS admissions/month criterion and declined the invitation, most of which were centers with CU or ICU, but without CCL. Of the rest, 52 (74.3%) agreed to participate, although a further 7 were later excluded for failure to fulfill quality control criteria. Final participation was 64.3% and all Spanish regions were represented except Murcia, in the south-east, and La Rioja, in the north, omitted due to the random selection procedure.

Patients

The registry included all patients hospitalized in

participating hospitals for >24 hours with symptoms that could be diagnosed as NSTEMI ACS, unless they had complete blockage of the left branch of the bundle of His-Purkinje.

Enrolment

In the month programmed for the study, April 2002, patient enrolment was lower than expected. Consequently, we extended enrolment into May, during which 39 centers contributed.

Permission

The study was approved by at least 1 ethical committee. Patients were asked to provide written informed consent before inclusion in the registry.

Variables and Data Collection

We analyzed patients' clinical, electrocardiographic, and laboratory characteristics as well as their clinical evolution in-hospital, treatment received and service or department of admission. Computer software was designed specifically for data collection with automatic encryption, compression and e-mail transmission direct to the company responsible for data management. Results were submitted continuously by each center; cases were considered closed when data on all variables had been entered on discharge.

Definitions

Definitions of variables can be found at www.scisquemica.net/PROY/descartes/descartes2.htm, the web page of the SEC Section for Ischemic Heart Disease.

Follow-up

Centralized telephone follow-up at 6 months retrospectively evaluated the appearance of major cardiovascular events: *a*) death (cause of death), and *b*) rehospitalization (cause of rehospitalization, time elapsed following the onset of each event).

Quality Control

We used an opportunist methodology based on the concentration of hospitals in large urban areas with monitors who were external to these centers. We selected 16 (30%) of the 52 centers (in Barcelona, Madrid, Valencia, and Zaragoza) and verified 10 key variables (age, gender, diagnosis on discharge, Q wave AMI, service or department of admission, electrocardiogram [ECG] on admission, diabetes, hypertension, hypercholesterolemia, smoking). Centers were warned there would be quality control without specifying which

hospitals or how many patients would be involved. In these 16 hospitals, quality control was carried out on all patients if total enrolment in the center amounted to <40 patients. In centers recruiting ≥40 patients, we selected 40 patients per center at random. Kappa index of agreement was 0.7-1 (average, 0.9). Each center provided a list of discharges during the study period and we calculated the rate of coverage (number of ACS enrolled ×100/number of ACS discharged) with a minimum 70% limit. Copies of the ECGs that qualified patients for inclusion and of ECGs performed prior to discharge were analyzed centrally.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation (SD) or as median and range if they did not fit a normal distribution. Categorical variables are given as percentages of valid responses. We constructed Kaplan-Meier survival curves and compared these using the Mantel-Cox test. Statistical analysis was performed with SPSS 11.5.

RESULTS

Between 1 April and 31 May 2002 we enrolled 2017 patients in 52 participating centers. Results from 7 centers were excluded for failure to meet established quality control criteria leaving 1877 patients. Patient numbers by hospital type were: 436 (23.2%) from the 20 centers without CU/ICU or CCL; 344 (18.3%) from the 10 centers with CU/ICU and without CCL, and 1097 (58.4%) from the 15 hospitals with CU/ICU and CCL.

Clinical characteristics of the population are in Table 1 and clinical episodes motivating admission in Table 2. Table 3 shows diagnostic and therapeutic procedures used in-hospital. During hospitalization, 94.6% of patients received antiplatelet agents and 81% heparin (of which 88% received low molecular weight heparin). Coronary angiography was performed on 41% of patients; 26% of procedures took place in the first 48 hours; significant coronary heart disease was found in 81% of studies (multivessel coronary disease in 52%, disease of the left coronary artery in 9%). Coronary revascularization, usually percutaneous procedures, was performed on 56% of patients undergoing coronary angiography.

Table 4 shows in-hospital evolution. Fifty-one patients died in-hospital (2.7%), 39 from cardiac, 2 from cerebrovascular, and 10 from other causes, including 2 unknown. Most patients received a definitive diagnosis of unstable angina (54%) or non-Q wave AMI (25%); following admission, symptoms in 18% of patients were diagnosed as of non-coronary origin. Treatment on discharge for all patients is shown in Table 4. If we exclude patients discharged with a diagnosis of chest

TABLE 1. Clinical Characteristics*

	N (% Valid)	95% CI
Age, median (percentiles 25-75) years	69 (59-76)	
Women	632 (33.7)	31.5-35.8
Cardiovascular risk factors	1742 (93.4)	92.2-94.5
Family history	499 (26.8)	24.8-28.8
Smoking		
Active	374 (20.3)	18.5-22.1
Previous	565 (30.7)	28.6-32.8
Diabetes mellitus	574 (30.9)	28.8-33.0
Insulin treatment	195 (34.1)†	30.2-38.0†
Arterial hypertension	1129 (60.9)	58.6-63.1
Dyslipidemia	968 (52.6)	50.3-54.9
Clinical history of cardiovascular illness	1366 (73.2)	71.2-75.2
Angina	952 (51.3)	49.0-53.5
Myocardial infarction	555 (29.8)	27.8-31.9
Stroke	156 (8.4)	7.1-9.6
Intermittent claudication	174 (9.4)	8.1-10.4
Heart failure	191 (10.3)	8.9-11.6
Coronary angioplasty	273 (14.7)	13.0-16.3
Surgical coronary revascularization	165 (8.8)	7.6-10.1
Previous drug treatment	1406 (75.3)	73.4-77.3
Aspirin	830 (44.6)	42.3-46.9
Ticlopidine/clopidogrel	174 (9.3)	8.0-10.7
Beta-blockers	510 (27.4)	25.4-29.4
Calcium antagonists	538 (28.9)	26.8-30.9
Nitrates	659 (35.4)	33.2-37.5
Statins	618 (33.2)	31.1-35.4
ACE inhibitors	590 (31.7)	29.6-33.8

*CI indicates confidence interval; ACE inhibitors, angiotensin converting enzyme inhibitors.

†Of the total of patients with diabetes.

TABLE 2. Characteristics of the Episode*

		95% CI
Duration of pain, min†	30 (15-120)	
Delay prior to admission, min†	120 (60-240)	
SAP on admission, mm Hg†	140 (125-160)	
DAP on admission, mm Hg†	80 (70-90)	
HR on admission, beats/min†	75 (65-90)	
Service or department of admission, n (% valid)		
Cardiology ward	883 (47.2)	44.9-49.5
Emergency	345 (18.4)	16.7-20.2
Coronary unit	321 (17.2)	15.4-18.9
General ICU	182 (9.7)	8.4-11.1
Other	140 (7.5)	6.3-8.7
Characteristics of ECG on admission, n (% valid)		
ST-segment depression	638 (34.6)	32.4-36.8
Normal repolarization	445 (24.1)	22.2-26.1
T wave inversion	368 (20.0)	18.1-21.6
Non-specific abnormalities in repolarization	299 (16.2)	14.5-17.9
ST-segment elevation (transitory)	94 (5.1)	4.1-6.1
Initial diagnosis, n (% valid)		
Unstable angina	1299 (69.7)	67.6-71.8
Non-ST elevation AMI	565 (30.3)	28.2-32.4

*ECG indicates electrocardiogram; HR, heart rate; AMI, acute myocardial infarction; CI, confidence interval; DAP, diastolic arterial pressure; SAP, systolic arterial pressure; ICU, intensive care unit.

†Median (percentiles 25-75).

TABLE 3. Diagnostic and Therapeutic Interventions During Hospitalization*

	N (% Valid)	95% CI
<i>Diagnostic procedures and results</i>		
Troponin measurement (T or I)	1531 (85.2)	83.6-86.9
Troponin elevation†	810 (53.2)	50.7-55.7
CK-MB measurement	653 (35.9)	33.7-38.1
K-MB elevation†	405 (28.1)	25.8-30.4
Echocardiogram	1035 (55.5)	53.3-57.8
LVEF<0.40†	161 (12.9)	11.0-14.7
Non-invasive tests for ischemia	733 (39.4)	37.1-41.6
Stress exercise test	548 (29.4)	27.3-31.4
Stress echocardiogram	114 (6.1)	5.0-7.2
Radioactive isotope studies	133 (7.1)	6.0-8.3
Coronary angiography	772 (41.4)	39.2-43.7
Early coronary angiography (<48 hours)	203 (11.0)	9.6-12.4
Significant coronary heart disease‡	623 (83.0)	80.4-85.8
1 vessel	223 (29.8)	26.5-33.0
2 vessels	192 (25.6)	22.5-28.8
3 vessels	207 (27.6)	24.4-30.8
Left coronary artery	69 (9.6)	7.4-11.7
Lipid profile	1452 (77.7)	75.8-79.6
Total cholesterol, mg/dL‡	190 (165-218)	
200 mg/dL total cholesterol‡	560 (40.7)	38.1-43.3
<i>Drug treatment</i>		
Antiplatelet agents	1762 (94.6)	93.6-95.6
Aspirin	1627 (87.6)	86.1-89.1
Ticlopidine	25 (1.4)	0.8-1.9
Clopidogrel	688 (37.3)	35.1-39.5
Heparin	1506 (81.3)	79.5-83.1
Glycoprotein IIb/IIIa inhibitors	220 (11.9)	10.4-13.4
Fibrinolytic agents	17 (0.9)	0.5-1.4
Beta-blockers	1160 (62.7)	60.5-64.9
ACE inhibitors	849 (46.0)	43.7-48.2
Statins	966 (52.3)	50.0-54.6
Calcium antagonists	771 (41.6)	39.3-43.8
Nitrates	1600 (85.9)	84.3-87.5
<i>Non-drug treatment</i>		
Coronary angioplasty	365 (19.9)	18.1-21.7
Surgical coronary revascularization	77 (4.2)	3.3-5.1

*LVEF indicates left ventricular ejection fraction; ACE inhibitors, angiotensin converting enzyme inhibitor; CK-MB, MB isoenzyme of creatine kinase.
 †Number (% of patients studied).
 ‡Median (percentiles 25-75).

pain of non-coronary origin, on discharge 91% were prescribed antiplatelet agents (82% aspirin, 37% clopidogrel, and 1.6% ticlopidine), 60% beta-blockers, 59% statins, and 43% angiotensin converting enzyme (ACE) inhibitors.

A complete 6 month follow-up was possible in 1762 patients (93.9%) (Table 4 and Figure 2). As suggested by the different diagnoses on discharge, 6-month mortality was highest in patients with Q wave and non-Q wave AMI (Figure 3). Differences between all possible pairs of curves were statistically significant ($P<.01$ in

TABLE 4. Evolution in-Hospital and During 6-Month Follow-up*

	N (% valid)	95% CI
Stay, days†	7 (5-12)	
<i>In-hospital complications</i>		
Recurrent/post-infarction angina	376 (20.2)	18.4-22.0
AMI/reinfarction	95 (5.1)	4.1-6.1
Heart failure	182 (9.8)	8.5-11.2
Stroke	16 (0.9)	0.4-1.3
Major bleeding	32 (1.7)	1.1-2.3
Death	51 (2.7)	2.0-3.5
<i>Definitive diagnosis‡</i>		
Unstable angina	968 (53.8)	51.5-56.1
Non-Q wave AMI	442 (24.6)	22.6-26.6
Q wave AMI	57 (3.2)	2.4-4.0
Chest pain of non-coronary/unknown origin	331 (18.4)	16.6-20.2
<i>Treatment on discharge</i>		
Antiplatelet agents	1530 (84.9)	83.3-86.6
Aspirin	1366 (76.0)	74.0-77.9
Clopidogrel	572 (32.0)	29.8-34.2
Ticlopidine	26 (1.5)	0.9-2.0
Beta-blockers	990 (55.3)	53.0-57.6
ACE inhibitors	734 (41.0)	38.7-43.3
In patients indicated	599 (50.7)	47.8-53.5
Statins	986 (55.0)	52.7-57.3
In patients indicated	936 (58.9)	56.4-61.3
<i>Follow-up</i>		
Death at 28 days	66 (3.7)	2.7-4.3
Death at 28 days to 6 months	71 (4.1)	3.2-5.1
Total deaths at 6 months	137 (7.8)	6.5-9.0
<i>Rehospitalization due to:</i>		
Any cause	257 (16.1)	14.3-17.9
Angina	80 (5.0)	3.9-6.1
Coronary revascularization	52 (3.3)	2.4-4.1
AMI	11 (0.7)	0.3-1.1
Coronary angiography	10 (0.6)	0.2-1.0
Heart failure	4 (0.3)	0.0-0.5
Other	18 (1.1)	0.6-1.6
Unknown	82 (5.1)	4.0-6.2

*AMI indicates acute myocardial infarction; ACE inhibitors, angiotensin converting enzyme inhibitor.
 †Median (percentiles 25-75).
 ‡Performed by physician responsible.

all comparisons).

DISCUSSION

The DESCARTES study is the first representative Spanish registry of routine clinical practice in NSTEMI ACS patients. The method, based on random selection proportional to hospital type defined in terms of cardiological facilities and data collection quality control, gives great reliability when results are extrapolated to the day-to-day reality of care. The DESCARTES study shows that although NSTEMI ACS patients in Spain have a high-risk cardiovascular profile only a quarter are admitted to intensive care units. Moreover, patients receive suboptimal treatment and present high

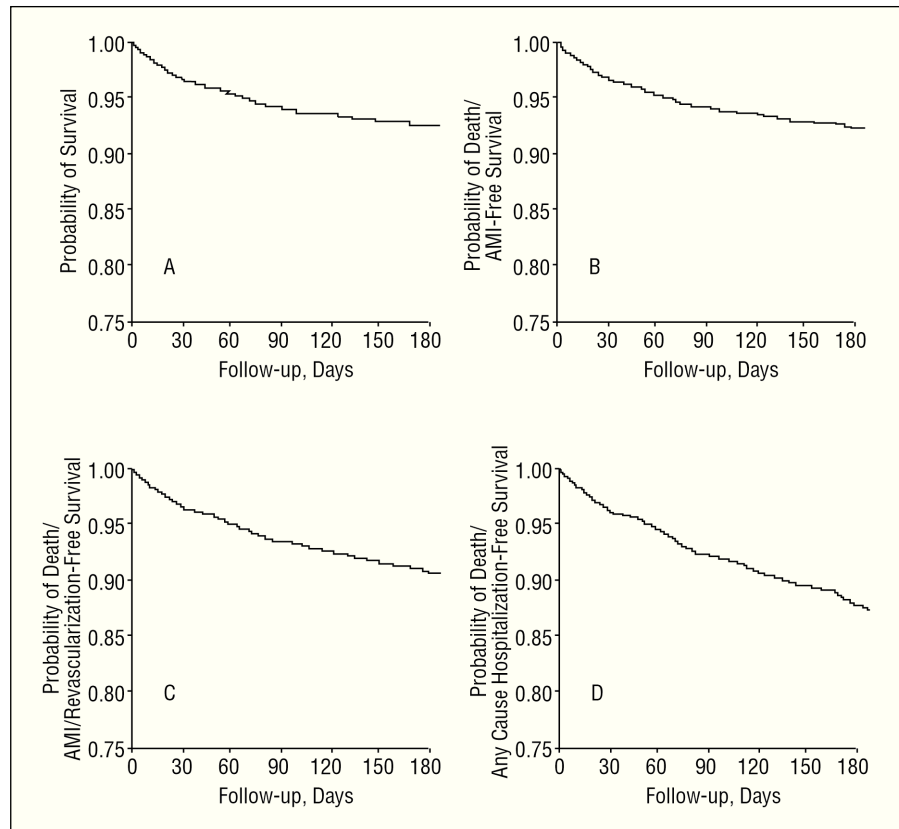


Figure 2. Survival curves at 6 months in 1877 DESCARTES patients for events: A. Death. B. Death or hospitalization for acute myocardial infarction. C. Death, hospitalization for acute myocardial infarction or coronary revascularization. D. Death or hospitalization for any cause. AMI indicates acute myocardial infarction.

6-month morbidity and mortality.

The population studied is of relatively advanced age, slightly above that reported in other European registries (64-66 years),⁹⁻¹⁵ and has a very high prevalence of risk factors, especially diabetes mellitus which is greater than in other registries.^{9-13,15} Similarly, a high proportion of patients presented a family history of cardiovascular illness, principally chest angina, and was receiving cardiovascular drug treatment. However, although almost 3 out of 4 patients were diagnosed with cardiovascular disease, fewer than half received aspirin; moreover, 27% of patients received beta-blockers when more than half had a history of angina and 29% had a history of infarction. Similarly, statin and ACE inhibitor use prior to the event was lower than would correspond to the risk level of the population studied.

In the initial ECG that led to hospitalization, 76% of patients presented anomalies in repolarization although ST-segment deviation was only found in 40%. Initial diagnosis was unstable angina in 70% and AMI in the remaining 30%. However, in discharge reports 18% were diagnosed with chest pain of non-coronary origin. These patients presented 2.6% 6-month mortality which suggests some possible diagnostic inaccuracy. Notably, although 35% presented ST-segment depression in initial ECGs and half showed some degree of myocardial necrosis marker elevation, only 1 in 4

patients with suspected NSTEMI ACS was admitted to an intensive care coronary unit. This is proportionately fewer than in the Italian registry (which, moreover, only included patients with unstable angina)⁹ or in the EuroHeart Survey,¹⁵ which reported approximately half of the patients were admitted to intensive care coronary units.

From the pharmacologic point of view, the high use of oral antiplatelet agents and heparin, generally low molecular weight heparin, stand out. We cannot draw conclusions on the 37% use of clopidogrel as its clinical indication was in transition. In the 2000 guidelines, use of clopidogrel was not contemplated except in patients contraindicated for aspirin or when associated with coronary stent implantation¹. However, the CURE study⁴ may well have influenced hospitals. Use of glycoprotein IIb/IIIa inhibitors was low and may have been indicated for coronary angioplasty rather than NSTEMI ACS; this remains unexplained although a similar low rate is reported elsewhere.^{12,13} Spanish guidelines on NSTEMI ACS in 2000,¹ unlike Spanish, European, or North American^{2,3} guidelines on antithrombotic treatment,¹⁶ described results of studies into glycoprotein IIb/IIIa inhibitors without establishing a level of recommendation and this may have influenced their use. It would be of interest to evaluate glycoprotein IIb/IIIa inhibitor use following publication of the

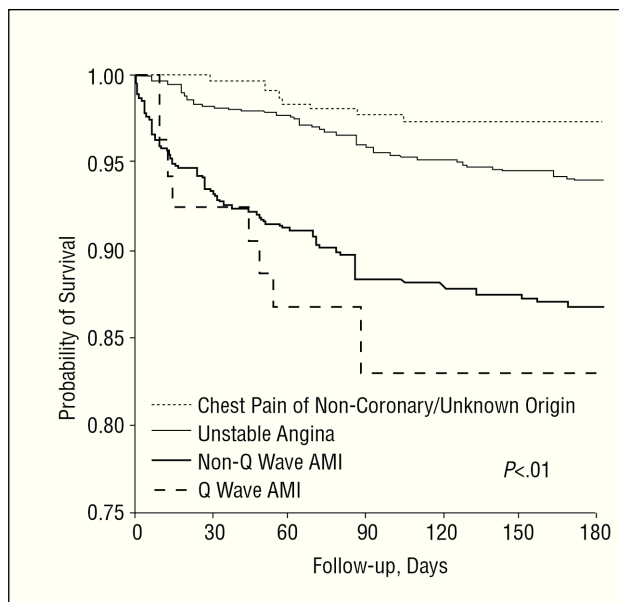


Figure 3. Six-month survival curves in 1877 DESCARTES patients in terms of diagnosis on discharge. Mantel-Cox test $P < .01$ for comparison of any pair of curves. AMI indicates acute myocardial infarction.

new recommendations. In-hospital use of beta-blockers, ACE inhibitors or statins (drugs proven to reduce mortality in NSTEMI ACS patients) was excessively low: 40%-60%. Beta-blockers and ACE inhibitor use was below that reported elsewhere.¹³⁻¹⁵

Although global use of troponins was high, the proportion of patients with troponin elevation was higher than in those finally diagnosed with AMI. The study design does not permit an explanation of this discrepancy but it would be consonant with the skepticism and/or rejection by numerous Spanish cardiologists of the new definition of AMI reported in the SEC Section for Ischemic Heart Disease survey conducted following publication of the definition.⁸

In a quarter of the population, total cholesterol levels were not determined during hospitalization. Although almost half the patients were discharged without an echocardiographic study, this proportion is greater than in other registries.^{9,15} Perhaps, this is because many patients had a prior history of cardiovascular illness and, in particular, of myocardial infarction or coronary revascularization, obviating the need for echocardiography in patients whose systolic function was already known. Non-invasive tests for ischemia were performed on 40% of patients which is more than described by other authors^{9,15} and may be due to the less selective enrolment procedure in DESCARTES. Cardiac catheterization was performed on 41% of patients, which is similar to the figure described in all but the older registries⁹⁻¹²; percutaneous coronary revascularization was performed

on just over half of patients, which is similar to that reported in other registries.¹⁰⁻¹³ It should be pointed out that almost 10% of patients undergoing coronary angiography had significant stenosis of the left coronary artery and more than 25% had stenosis of 3 coronary arteries, despite which only 4.2% of all patients underwent surgical coronary revascularization during initial hospitalization and another 3.3% were rehospitalized for revascularization during follow-up.

Representativeness of Results

One of the most important aspects of this study is the representativeness of the results. The only previous large-scale Spanish registry on NSTEMI ACS, the project for the study of prognosis in angina (known by the acronym PEPA), recruited patients from those initially admitted to 18 centers selected nationally on the single criterion of having a CCL and entailed a probable bias in attitude to diagnosis and therapy.^{10,11} The DESCARTES study uses a random, stratified selection of participating centers (based on availability of principal cardiological resources). This, together with a 67% participation of the centers selected, confers substantial external validity on results. In addition, the quality control, with 6.9% exclusions, ensures internal validity. Among the most recent European registries of NSTEMI ACS patients (Table 5),⁹⁻¹⁵ only PRAIS-UK (recruiting 1046 patients in 56 British centers during 9 months in 1998) used a similar method¹². The largest non-Spanish registries, such as EuroHeart and GRACE,^{14,15} have involved volunteer centers, making the generalization of results less reliable. The DESCARTES results can be interpreted as a reliable approximation to routine clinical care of NSTEMI ACS patients in Spain.

Implications of the Study

From a reasonably representative sample of Spanish clinical reality, DESCARTES has shown deficiencies in the care of NSTEMI ACS patients. This finding should be a stimulus to revise the clinical care of these patients and initiate qualitative improvements adapted to the clinical recommendations that, in this case, were updated a few months after the completion of the study.^{17,18} Therefore, new registries of activity should be constructed to enable us to determine whether deficiencies in care detected by DESCARTES persist or have been reduced. Similarly, the extent to which latest clinical practice guidelines are met should be determined and as should the impact of their fulfillment on patient prognosis. The errors and limitations of DESCARTES, such as overestimation in the capacity for recruitment and the decision to prolong the enrolment

TABLE 5. Characteristics of Principal European Registries of Non-ST Segment Elevation Acute Coronary Syndromes*

Study	EARISA ⁹	PEPA ^{10,11}	PRAIS-UK ¹²	ENACT ¹³	GRACE ¹⁴	EHS ACS-1 ¹⁵	DESCARTES
Year	1996	1997-98	1998	1999	1999	2000	2002
Place	Italy	Spain	United Kingdom	29 countries (Europe)	14 countries (worldwide)	25 countries (Europe)	Spain
Inclusion criteria	Final diagnosis of UA	Suspected NSTEMI ACS	Suspected NSTEMI ACS	Suspected ACS	Suspected or Dg of ACS	Diagnosis of ACS	Suspected NSTEMI ACS
Data collection	Prospective	Prospective	Prospective	Prospective	Prospective and retrospective	Prospective	Prospective
Number of cases (NSTEMI ACS)	1420	4115	1046	1431	7290	5367	1877
Number of centers	308	18	56	390	95	103	52
Enrolment period	2 weeks	13 months	9 months	3 months	21 months	9 months	2 months
Selection of participating centers	Voluntary	Voluntary (with CCL)	Random (50% response)	Voluntary	Voluntary (clusters)	Voluntary	Random (64% response)
Quality control	No	Yes	Yes	No	Yes	Yes	Yes

*UA indicates unstable angina; Dg, diagnosis; EHS-ACS, EuroHeart Survey-Acute Coronary Syndromes; CCL, cardiac catheterization laboratory; ACS, acute coronary syndrome; NSTEMI ACS, non-ST segment elevation ACS.

period, the rate of loss participating centers classified according to cardiological facilities available due to failure to meet admission or quality control criteria, or the rate of patient loss during follow-up, can facilitate improved research design and the development of similar studies in the future.

CONCLUSIONS

The DESCARTES study results show that although patients admitted to Spanish hospitals with suspected NSTEMI ACS have a high incidence of complications both in-hospital and in 6-month follow-up, some efficacious diagnostic and therapeutic measures are used less than current clinical practice guidelines recommend. Data indicate that substantial opportunities exist to improve the quality of medical care of patients with NSTEMI ACS in Spain.

REFERENCES

- López-Bescós L, Fernández-Ortiz A, Bueno H, Coma-Canella I, Lidón RM, Cequier A, et al. Guías de práctica clínica de la Sociedad Española de Cardiología en la angina inestable/infarto sin elevación de ST. *Rev Esp Cardiol*. 2000;53:815-37.
- Bertrand ME, Simoons ML, Fox KAA, Wallentin LC, Hamm CW, McFadden E, et al. Management of acute coronary syndromes: acute coronary syndromes without persistent ST segment elevation: recommendations of the Task Force of the European Society of Cardiology. *Eur Heart J*. 2000;21:1406-32.
- Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). *J Am Coll Cardiol*. 2000;36:970-1062.
- The Clopidogrel in Unstable angina to prevent Recurrent Events trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation, for the CURE investigators. *N Engl J Med*. 2001;345:494-502.
- The GUSTO IV-ACS Investigators. Effect of glycoprotein IIb/IIIa receptor blocker abciximab on outcome in patients with acute coronary syndromes without early coronary revascularisation: the GUSTO IV-ACS randomised trial. *Lancet*. 2001;357:1915-24.
- Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis A, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med*. 2001;344:1879-87.
- The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined: a consensus document of the Joint European Society of Cardiology/American College of Cardiology committee for the redefinition of myocardial infarction. *Eur Heart J*. 2000;21:1502-13.
- Bardajá A, Bueno H, Fernández-Ortiz A, Heras M. Aplicabilidad de la nueva definición de infarto de miocardio y opinión de los cardiólogos españoles. *Rev Esp Cardiol*. 2003;56:23-8.
- Maggioni AP, Schweiger C, Tavazzi L, Langiano T, Lucci D, Ramponi C, et al. Epidemiologic study of use of resources in patients with unstable angina: the EARISA Registry. *Am Heart J*. 2000;140:253-63.
- Bosch X, López de Sá E, López Sendón J, Aboal J, Miranda-Guardiola F, Bethencourt A, et al. Perfil clínico, pronóstico y variabilidad en el tratamiento del síndrome coronario agudo sin elevación del segmento ST. Datos del registro PEPA. *Rev Esp Cardiol*. 2003;56:346-53.
- Bosch X, Verbal F, López de Sá E, Miranda-Guardiola F, Bórquez E, Bethencourt A, et al. Diferencias en el tratamiento y la evolución clínica de los pacientes con síndrome coronario agudo sin elevación del segmento ST en función del servicio clínico de ingreso. *Rev Esp Cardiol*. 2004;57:283-90.
- Collinson J, Flather MD, Fox KAA, Findlay I, Rodríguez E, Dooley P, et al. Clinical outcomes, risk stratification and practice patterns of unstable angina and myocardial infarction without ST elevation: Prospective Registry of Acute Ischaemic Syndromes in the UK (PRAIS-UK). *Eur Heart J*. 2000;21:1450-7.
- Fox KAA, Cokkinos DV, Deckers J, Keil U, Maggioni A, Steg G, on behalf of the ENACT (European Network for Acute Coronary Treatment) investigators. The ENACT study: a pan-Europe-

- an survey of acute coronary syndromes. *Eur Heart J.* 2000;21:1440-9.
14. Fox KAA, Goodman SG, Klein W, Brieger D, Steg PG, Dabbous A, et al. Management of acute coronary syndromes. Variations in practice and outcome. Findings from the Global Registry of Acute Coronary Events (GRACE). *Eur Heart J.* 2002;23:1177-89.
 15. Hasdai D, Behar S, Wallentin L, Danchin N, Gitt AK, Boersma E, et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin. The Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). *Eur Heart J.* 2002;23:1190-201.
 16. Heras M, Fernández Ortíz A, Gómez JA, Iriarte JA, Lidón RM, Pérez Gómez F, et al. Guías de actuación clínica de la Sociedad Española de Cardiología. Recomendaciones para el uso del tratamiento antitrombótico en cardiología. *Rev Esp Cardiol.* 1999;52:801-20.
 17. López Bescós L, Arós Borau F, Lidón Corbi RM, Cequier Fillat A, Bueno H, Alonso JJ, et al. Actualización (2002) de las Guías de Práctica Clínica de la Sociedad Española de Cardiología en angina inestable/infarto sin elevación del segmento ST. *Rev Esp Cardiol.* 2002;55:631-42.
 18. Bertrand ME, Simoons ML, Fox KA, Wallentin LC, Hamm CW, McFadden E, et al. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. The Task Force on the Management of Acute Coronary Syndromes of the European Society of Cardiology. *Eur Heart J.* 2002;23:1809-40.

ANNEXE. Participating Centers, Principal Researchers, and Contribution to the Study

Hospital Clínico San Carlos, Madrid: A. Fernández-Ortiz (203); Hospital General Universitario Gregorio Marañón, Madrid: H. Bueno (127); Hospital Clínico Universitario Lozano Blesa, Zaragoza: F. Roncalés (121); Ciutat Sanitaria de Bellvitge, L'Hospitalet de Llobregat: E. Esplugas (110); Hospital Clínico Universitario de Valencia, Valencia: L. Fácila (96); Hospital Provincial de Navarra, Pamplona: N. Basterra (92); Hospital Miguel Servet, Zaragoza: F.J. Monzón (92); Hospital Costa del Sol, Marbella: E. González (84); Hospital San Agustín, Avilés: V.M. Rodríguez (73); Hospital de la Santa Creu i Sant Pau, Barcelona: J. García (63); Complejo Hospitalario Virgen de la Victoria, Málaga: E. de Teresa (54); Hospital Marina Baixa de Villajoyosa, Villajoyosa: I. Antorrena (49); Hospital Ramón y Cajal, Madrid: E. Asín (42); Hospital Clínic, Barcelona: M. Heras (40); Complejo Hospitalario Alarcos, Ciudad Real: L. Ruiz-Valdepeñas (37); Hospital de Palamós, Palamós: A. Gómez (37); Hospital Universitario de Girona Josep Trueta, Girona: J. Sala (36); Hospital General Yagüe, Burgos: A.J. Montón (34); Hospital Verge de la Cinta, Tortosa: Ll. Gutiérrez (32); Hospital Universitario Príncipe de Asturias, Alcalá de Henares: A. Cambroner (31); Hospital del Mar, Barcelona: J. Bruguera (31); Hospital San Eloy, Barakaldo: J.A. Novales (31); Hospital Joan XXIII, Tarragona: A. Bardají (26); Hospital Nuestra Señora de Arantzazu, Donostia: P. Marco (25); Hospital Can Misses, Ibiza: J. Seguí (25); Hospital de l'Esperit Sant, Santa Coloma de Gramanet: T. Poble (22); Hospital Comarcal de la Axarquia, Vélez: J. Zafra (22); Hospital de Sant Jaume, Calella: A. Aloy (22); Hospital de Terrassa, Terrassa: M.D. Martínez (21); Hospital Comarcal de La Selva, Blanes: A. Zamora (17); Hospital Virgen del Camino, San Lúcar de Barrameda: A. Revello (17); Hospital Comarcal Sierrallana, Torrelavega: B. Gutiérrez (16); Hospital la Inmaculada, Huerca-Overa: E. Morillo (15); Hospital de Sant Pau i Santa Tecla, Tarragona: J.C. Soriano (15); Clínica Juaneda, Palma de Mallorca: J. Soler (15); Hospital General del INSALUD, Soria: J. Martínez (12); Hospital Virgen del Puerto, Plasencia: A. Sáez (12); Clínica Santa María de la Asunción, S.A., Tolosa: J.R. Beramendi (10); Policlínico Vigo, S.A. (POVISA), Vigo: F. Noriega (10); Hospital General de Requena, Requena: L. Mainar (10); Hospital Comarcal Monforte de Lemos, Monforte de Lemos: M.L. Vázquez (9); Hospital Princesa de España, Jaén: O. Cuadra (9); Hospital José María Díaz Domínguez, Minas de Riotinto: L. García (9); Hospital de la Línea, La Línea de la Concepción: E. Rueda (9); Clínica Quirón, Barcelona: J. Riba (5); Institut Municipal d'Investigació Mèdica, Barcelona: J. Marrugat, S. Tello, and H. Martí.
