**ORIGINAL ARTICLE**

**Ischemic Heart Disease**

Management of Myocardial Infarction in Spain in the Year 2000. The PRIAMHO II Study

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**Introduction and objectives.** Hospital registries are useful tools to measure the degree of implementation of new treatments and clinical practice guidelines.

**Patients and method.** The hospital registry described here was developed in the prospective PRIAMHO II study, which involved a random selection of Spanish hospitals with a coronary intensive care unit and external quality control. This study investigated patients admitted to the coronary care unit with acute myocardial infarction. Demographic and clinical characteristics were recorded, as well as the management, clinical course and survival after 28 days and one year.

**Results.** From May 15 to December 15 2000 we included in the registry 6,221 patients from the 58 hospitals that complied with the quality control requirements (71.6% of all participating hospitals). Acute mortality was 9.6%; 28-day and one-year mortality were 11.4% and 16.5%, respectively. Of the patients with ST elevation-myocardial infarction of less than 12 hours’ duration, 71.6% were reperfused and 89.3% received fibrinolysis with a median door-to-needle time of 48 minutes. Ejection fraction was measured in 81% of the patients, and 43% were tested for inducible ischemia. About nine-tenths (91%) of the patients were discharged on least one antiplatelet drug, 56% on a beta blocker, 45% on an ACE inhibitor, and 45% on a lipid-lowering agent, with a coefficient of variation between hospitals greater than 25% for the last three drugs.

**Conclusions.** The percentage of patients with ST elevation treated with reperfusion should increase, as it probably will thanks to the increasing use of primary angioplasty. The door-to-needle time was longer than the recommended interval. In-hospital risk stratification was good but nonsystematic for the evaluation of ejection fraction, and unsatisfactory for inducible ischemia testing. At discharge the percentages of patients receiving beta blockers, ACE inhibitors and statins were not optimal, and there were wide variations in prescribing practices between hospitals.


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Tratamiento del infarto agudo de miocardio en España en el año 2000. El estudio PRIAMHO II

**Introducción y objetivos.** Los registros hospitalarios son útiles para conocer el grado de aplicación de las nuevas evidencias y recomendaciones de las guías de práctica clínica.

**Pacientes y método.** El estudio PRIAMHO II es un estudio prospectivo con una selección aleatoria de los hospitales españoles con unidad coronaria y control de calidad externo. Se incluyó a los pacientes con infarto agudo de miocardio ingresados en la unidad coronaria. Se recogieron las características clínicas, el tratamiento y la evolución hospitalaria, así como la supervivencia a los 28 días y al año.

**Resultados.** Del 15 de mayo al 15 de diciembre de 2000, 6.221 pacientes fueron registrados en los 58 hospitales que cumplieron los controles de calidad (el 71.6% de los seleccionados).
ABBREVIATIONS

AMI: acute myocardial infarction.
ACE: angiotensin-converting enzyme.
PRIAMHO II: Acute Myocardial Infarction Hospital Registry Project II.
ACS: acute coronary syndrome.
CICU: Coronary Intensive Care Unit.
CK-MB: creatine kinase myoglobin isoenzyme.

INTRODUCTION

In the coming decades cardiovascular disease will continue to be the most frequent cause of death and disability in industrialized countries. Acute coronary syndrome (ACS), specifically acute myocardial infarction (AMI), is the main cause of death in hospitalized patients and is a considerable healthcare burden. Acute myocardial infarction-related mortality is 50% in Spain and estimates for the next decade predict a 10% increase in the incidence of this disease.

Various drugs and therapeutic procedures of proven efficacy have recently been incorporated into the management of patients with ACS. Medical societies have responded to this problem with the publication of practical clinical guidelines for ACS with and without ST segment elevation. These are updated continuously in an effort to close the gap between scientific evidence and clinical practice, and to reduce variations in the use of the available therapeutic options. In this connection, hospital registries have proved to be a useful instrument to monitor the fulfillment of these objectives and to determine the extent to which new evidence and recommendations are actually applied in daily practice.

The Proyecto de Registro de Infarto Agudo de Miocardiocoratorio Hospitalario II (Acute Myocardial Infarction Hospital Registry Project II; PRIAMHO II), completed 5 years after the PRIAMHO I study, is a multicenter hospital registry of patients with a diagnosis of AMI in coronary intensive care units (CICU), compiled jointly by 58 Spanish hospitals. The main objective of the registry was to elucidate the clinical characteristics, management and evolution of AMI patients seen in Spanish hospitals, as well as the 28-day and 1-year survival rates in these patients. This article presents the overall results of the study.

PATIENTS AND METHOD

PRIAMHO II is a cohort study with a hospital registry of AMI and 1-year follow-up period. Data were recorded prospectively for all consecutive AMI patients who required CICU admission in 58 (71.6%) of the 81 hospitals selected randomly from among 165 Spanish hospitals that treat AMI patients, are equipped with a CICU and either belong to or are contracted by the public healthcare system. Enrollment took place between 15 May and 15 December 2000. Seven hospitals declined to participate and were substituted by others with similar characteristics. The random selection of hospitals was stratified according to the number of beds (<200, 200-500, and >500).

Quality control

As in the PRIAMHO I study, the centers had to fulfill the following conditions at the end of the enrollment process for their data to be included in the study: a) coverage: registry of at least 70% of the patients with AMI identified in the hospital discharge list for a mean period of three months; b) rigor: registry of more than 75% of the patients with AMI in the CICU, identified by the same procedure; c) concordance: mean Kappa index higher than 70% between the data recorded and those obtained by an external auditor after assessing ten variables per patient in a random sample of 20% of the patients registered per hospital, and d) one-year follow-up: knowledge of the vital status of more than 90% of the patients registered and residing in the hospital’s catchment area (Table 1).

Only 5 hospitals of the 63 that agreed to initiate data
collection and successfully completed the pilot phase during the first month of enrollment failed to meet one or more of these requirements, leaving a total of 58 hospitals with valid data for the registry (Figure 1).

Data were compiled on the patient’s demographic characteristics, clinical history and complications, and on the diagnostic and therapeutic procedures used during the CICU and hospital ward stays, and treatment at discharge. All variables had been predefined and their recording and coding were standardized. Fibrinolysis or primary angioplasty, beta blockers, antiplatelet agents, ACE inhibitors and lipid-lowering drugs were considered the index (study) treatments.

In each center, data were recorded using a dedicated software program that automatically checked the internal consistency and interactively flagged any errors. The study’s coordinating center handled the data follow-up, quality control, statistical analyses and logistic support.

Patients were followed up by the coordinating center through either a personal or telephone interview, or by the local researcher. Minimum follow-up time of the survivors was one year. All deaths occurring in the first 28 days after AMI were considered related to this event. After this period, the different causes of death were noted.

Diagnosis of myocardial infarction

The diagnosis of AMI was based on the presence of at least three criteria derived from the initial classification of the World Health Organization:\textsuperscript{9}

1. Clinical presentation: typical symptoms of pain, oppression and/or local discomfort in the anterior thorax, left arm and/or jaw of more than 20 minutes’ duration, with or without sweating or nausea and without evidence of a non-cardiac cause. Atypical presentations were also taken into consideration, including other less common locations of pain, shock, syncope, left ventricular dysfunction and/or intermittent symptoms of less than 20 minutes duration.

2. Electrocardiographic data: Q-wave AMI, defined as the appearance of a Q-wave $\geq$30 ms in 2 or more contiguous leads\textsuperscript{10}; posterior AMI, defined as an R/S $\geq$1 in V1-V2.

3. Enzyme analysis data: in the absence of revascularization treatment, three criteria were applied: a) total creatinine kinase (CK) elevation $>$twice the normal limit; b) CK myoglobin isoenzyme (MB-CK) elevation $>$6% of the total, and c) MB-CK activity or mass elevation $>$25 U/L or $>$7 ng/mL, respectively,\textsuperscript{11} all of the above obtained from serial determinations showing an enzyme curve.

Indication for reperfusion

The requirements for reperfusion were an ST segment elevation of at least 1 mm in at least 2 of the limb leads or an ST elevation of at least 2 mm in 2 or more contiguous precordial leads. A depressed ST segment in V1-V3 was considered a mirror image of the posterior plane.

The contraindications for fibrinolysis were those included in the AMI management guidelines.\textsuperscript{3}

Statistical analysis

| TABLE 1. Characteristics of the hospitals participating in the PRIAMHO II study |
|---------------------------------|---------|
| Mean hospital size, bed capacity| 540     |
| Hospital size, bed capacity     |         |
| <200                            | 6 (10.4%) |
| 200-500                         | 27 (46.5%) |
| >500                            | 25 (43.1%) |
| Mean CICU size, bed capacity    | 8       |
| Total population attended 17 300 000 |         |
| Number of hospitals with interventional cardiology | 25 (43.1%) |
| Coverage                        | 87%     |
| Rigor                           | 96%     |
| Patients followed at one year   | 93%     |

CICU indicates coronary intensive care unit.
The results for continuous variables are expressed as the mean and standard deviation (SD) or as the median and range in variables with a non-normal distribution. Categorical values are expressed as percentages. The SPSS statistical package was used for all calculations. The coefficient of variation (100×standard deviation/mean) was used to report between-hospital variation.

### RESULTS

#### TABLE 2. Patient demographics, clinical history and main ECG findings (initial and final)

<table>
<thead>
<tr>
<th>Total group (n=6221)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean±SE</td>
<td>65.4±12.8</td>
</tr>
<tr>
<td>Women, %</td>
<td>25.3</td>
</tr>
<tr>
<td><strong>Cardiovascular risk factors</strong></td>
<td></td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>29.4</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>44.1</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>40.3</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>46.1</td>
</tr>
<tr>
<td><strong>History of coronary disease</strong></td>
<td></td>
</tr>
<tr>
<td>Previous infarction, %</td>
<td>15.7</td>
</tr>
<tr>
<td>Previous revascularization, %</td>
<td>8.5</td>
</tr>
<tr>
<td><strong>Initial ECG alteration</strong></td>
<td></td>
</tr>
<tr>
<td>ST segment elevation, %</td>
<td>66.3</td>
</tr>
<tr>
<td>Depressed ST segment, %</td>
<td>17.3</td>
</tr>
<tr>
<td>LBBB, %</td>
<td>3.1</td>
</tr>
<tr>
<td>Non-specific alterations, %</td>
<td>13.3</td>
</tr>
<tr>
<td><strong>Final ECG</strong></td>
<td></td>
</tr>
<tr>
<td>Non-Q wave, %</td>
<td>34.4</td>
</tr>
</tbody>
</table>

LBBB indicates left bundle branch block; ECG, electrocardiogram.

The results for continuous variables are expressed as the mean and standard deviation (SD) or as the median and range in variables with a non-normal distribution. Categorical values are expressed as percentages. The SPSS statistical package was used for all calculations.

The coefficient of variation (100×standard deviation/mean) was used to report between-hospital variation.

### Reperfusion treatment in acute myocardial infarction with ST segment elevation

Among AMI patients with an indication for reperfusion (elevated ST segment or left bundle branch block of less than 12 hours; duration), 71.6% received some type of treatment (43% of the total population; Table 3). Fibrinolysis was the most frequently used therapy (89.3% of reperfused patients, 38.2% of the total population). The median time interval between onset of symptoms and reperfusion treatment was 175 minutes, with a median door-to-needle time of 48 minutes and a door-to-balloon time of 80 minutes.

### Clinical evolution

There were no complications in 54.2% of the CICU patients and 90% of the hospital ward patients (Table 4). Coronary intensive care unit mortality was 9.6%, increasing to 11.4% at 28 days. More than 30% of the patients in the CICU had some degree of heart failure and 17.2% had acute pulmonary edema or cardiogenic shock. Some 15.3% of the patients experienced postinfarction angina and 3.1% had reinfarction during hospitalization. Median hospital stay was 10 days 7-13 with three days spent in the CICU and six in the hospital ward (Table 4).

### Diagnostic and therapeutic procedures

In addition to the patients who underwent primary angioplasty, less than 31% of the patients had coronary angiography (Table 5). Echocardiography was the most frequently used examination, both in the CICU (34.1%) and the hospital ward (60.3%). Mean ejection fraction after 48 hours was determined in 80.8% of the patients in the subacute phase, with a mean value of 51.3% (SD=12%). In these patients,
11.4% had ejection fractions lower than 40%. Less than half (42.6%) of the patients who survived after the CICU stay underwent inducible ischemia testing at least once.

**Pharmacological treatment**

More than 92% of the patients received aspirin during their CICU stay. At discharge, this percentage decreased to 84.3% (Table 6), whereas the use of other antiplatelet agents increased. A total of 90.6% of the patients were discharged on at least one antiplatelet drug. The percent use of beta-blockers, ACE inhibitors, calcium antagonists and nitrates increased slightly from CICU admission to hospital discharge, whereas the use of lipid-lowering drugs decreased from 19.9% to 44.9%. Oral anticoagulant use was not recorded.

**Follow-up**

Overall mortality at one year of follow-up was 16.5%, including 17.2% among patients with ST-elevation AMI and 15.1% among those with non-ST elevation AMI.

**Variations in treatments**

The use of aspirin was the only index treatment that did not show wide variations among the participating hospitals (Figure 2). The coefficient of variation for the use of fibrinolysis and reperfusion was at the 25% cut-off for being considered excessive, whereas variability for beta-blockers, ACE inhibitors, and lipid-lowering drugs exceeded this value.

**DISCUSSION**

Among the 165 hospitals in Spain with CICUs, 58 (35.2%) were selected randomly to participate in the PRIAMHO II study. The information obtained from this sample is undoubtedly representative of AMI management in Spain in 2000, and the sample is larger than the total of 24 hospitals included in PRIAMHO I.5

**Characteristics of the PRIAMHO II registry**

**TABLE 4. Clinical evolution during hospitalization**

<table>
<thead>
<tr>
<th></th>
<th>CICU</th>
<th>Hospital ward</th>
</tr>
</thead>
<tbody>
<tr>
<td>No complications, %</td>
<td>54.2</td>
<td>89.8</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, %</td>
<td>9.6</td>
<td>1.8a</td>
</tr>
<tr>
<td>Maximum Killip class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I, %</td>
<td>69.5</td>
<td></td>
</tr>
<tr>
<td>II, %</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td>III, %</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td>IV, %</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>ICC</td>
<td>—</td>
<td>4.1</td>
</tr>
<tr>
<td>Re-AMI, %</td>
<td>2.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Post-AMI angina, %</td>
<td>9.4</td>
<td>5.9</td>
</tr>
<tr>
<td>Primary ventricular fibrillation, %</td>
<td>5.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Sustained ventricular tachycardia, %</td>
<td>3.0</td>
<td>0.4</td>
</tr>
<tr>
<td>Advanced AV block, %</td>
<td>6.3</td>
<td>—</td>
</tr>
<tr>
<td>Atrial flutter/fibrillation, %</td>
<td>8.1</td>
<td>—</td>
</tr>
<tr>
<td>Mechanical complication, %</td>
<td>2.6</td>
<td>—</td>
</tr>
<tr>
<td>Mean stay</td>
<td>3 (2.3)b</td>
<td>6 (4.9)b</td>
</tr>
</tbody>
</table>

AV indicates atrioventricular; AMI, acute myocardial infarction; CHD, congestive heart disease; CICU, coronary intensive care unit.

aIncludes mortality up to 28 days.
bMedian and 25th and 75th percentiles.
Two of the characteristics of PRIAMHO II are not typical of this type of registry: random selection of the participating hospitals and quality control by external auditing. Alpert has particularly recommended random selection of hospitals to improve the quality of the data. Nevertheless, the National Registry of Myocardial Infarction from the USA, the European Society of Cardiology ACS Registry, and the multinational Global Registry of Acute Coronary Events (GRACE) do not comply with this condition. The Swedish Registry of Cardiac Intensive Care (RISK-HIA) included 75% of the hospitals, and therefore did not require randomizing.

With respect to quality control, the GRACE registry has proposed an audit of all participating hospitals over a three-year cycle, and a review of 4.6% of the cases in the Swedish study yielded a concordance level of 94%. In the US registry, quality control was based on internal control integrated into the software, and in the European registry, “auditing was performed in only a minority of the centers.” We have no data for the German Myocardial Infarction Registry (MIR) with regard to quality control.

Clinical evolution of patients with acute myocardial infarction

In Spain, AMI-associated mortality is 9.6% in the acute phase and 11.4% at 28 days, rates that confirm the trend toward a reduction in mortality in absolute numbers observed in the Registro de Infartos de la Sección de Cardiopatía Isquémica y Unidades Coronarias (Infarct Registry in the Ischemic Heart Disease Section and Coronary Units; RISCI) between 1995 and 1999.

The incidence of severe complications in the year 2000 is comparable to that observed in similar studies in our setting in previous years. The rate of reinfarction in PRIAMHO II was 3.1%, as compared to 2.8% and 2.7% reported in the Investigación, Búsqueda Específica y Registro de Isquemia Coronaria Aguda (Research, Specific Search and Registry of Acute Coronary Ischemia; IBERICA) study and the RISCI registry, respectively. Similar results were found for the Killip III-IV grades in the CICU, supporting the findings of Rohlfs et al who reported stable levels of reinfarction in the Registro Gerundense del Corazon (Gerona Heart Registry; REGICOR) for 1978 to 1997.

The fact that mortality has decreased, but the rate of severe complications has remained stable suggests an improvement in patient management.

Management of acute myocardial infarction in Spain

The number of patients with ST segment elevation who receive reperfusion treatment and the time to reperfusion are basic aspects of AMI management. In PRIAMHO II, 71.6% of the patients were treated in less than 12 hours. This figure is similar to the 70% reported in the USA in 1999 in the NRMI 2 and 3 studies, and in the GRACE registry and higher than the 56% in the European ACS registry. In contrast, the percentage of primary angioplasties recorded in our registry is lower than in other registries, including the Portuguese dataset.

Interval before arrival in the emergency room (median, 109 minutes) and the interval between onset of symptoms and the start of revascularization treatment (175 minutes) are virtually the same as those recorded in the RISCI study and in the ARIAM project.

Door-to-needle time decreased from 50 to 48 minutes.
between PRIAMHO I and II, a figure well above the maximum of 30 minutes recommended by current guidelines. The lack of change in these delays is worrisome, although this is a complex issue involving several factors such as health education, the organization of the emergency system and intrahospital coordination.

In addition to the clinical parameters, prognostic stratification in the acute phase of AMI is based on the determination of ventricular function and residual ischemia. Among the patients who survived the CICU phase, ventricular function was determined in 81% and inducible ischemia testing was done in 43%. These figures are higher than those reported in other registries. The guidelines recommend routine determination of ventricular function, whereas it has been suggested that the study of residual ischemia can be reserved for non-complicated AMI.

Coronary arteriography is indicated less often in AMI patients in Spain than in neighboring countries. Whereas in Spain this examination is indicated in 31% of the patients, other similar registries report figures higher than 50%. The hospital stay, however, is longer in Spain (median, 10 days) than in Europe (median, 8 days) and the United States (median, 4.3 days), although hospital mortality is no lower.

The PRIAMHO II secondary prevention data show progress with respect to the Prevención Secundaria del Infarto de Miocardio en España (Secondary Prevention of Myocardial Infarction in Spain; PREVESE II) study conducted in 1998 with 2054 Spanish patients. Among AMI survivors, prescription of antiplatelet drugs at discharge was high in both studies, and prescription of ACE inhibitors was similar (from 46% to 45%). PRIAMHO II, however, shows an 11% increase in the use of beta-blockers (from 45% to 56%) and a 14% increase in lipid-lowering drugs (from 31% to 45%). Despite the increase, beta-blockers are still underused in our hospitals as compared to prescription for more than 70% of the patients reported in other registries. ACE inhibitors are also prescribed more frequently in other countries, with the highest figure (61%) appearing in the European ACS registry. These differences are not seen for antiplatelet drugs and statins.

In PRIAMHO II a surprising degree of variation between hospitals was found for the use of treatments with a universal indication, such as primary reperfusion, aspirin, beta-blockers and ACE inhibitors. Recommendations in medical society guidelines are classified according to the grade of scientific evidence and clinical efficacy. Application of these measures in daily practice for the cases noted above should not pose problems, since the indications were class IA. Nevertheless, our results contradict this assumption and are difficult to explain. It should be mentioned that programs to improve healthcare quality have achieved figures of 90%-98% in the use of reperfusion, aspirin, beta-blockers and ACE inhibitors at a single center, and somewhat lower figures (75%-90%) in national programs.

Limitations of the study

The new definition of AMI from the European Society of Cardiology and the American College of Cardiology was published in September 2000, coinciding with the final part of our study. Thus, it could not be included in the selection criteria for participating patients.

Our registry is limited to AMI patients with and without ST segment elevation admitted to the CICU, but does not include AMI patients seen in the hospital ward, who account for more than 10% of all patients and in whom mortality is higher. Therefore, AMI-related mortality may be higher than recorded in this study.

CONCLUSIONS

Early mortality and one-year mortality rates have decreased with respect to 1995 figures, although the incidence of severe complications is similar. Nevertheless, this study has revealed areas requiring improvement. The percentage of patients with ST-elevation AMI who receive perfusion treatment should increase, and delays in the use of this treatment should be reduced. Primary angioplasty and coronary arteriography are used less frequently in Spain than in other countries in our geographical area. Prognostic stratification in the subacute phase does not include routine study of ventricular function and is ineffectual for the detection of residual ischemia. Pharmacological secondary prevention has improved, but the use of beta-blockers and ACE inhibitors is suboptimal.

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REFERENCES

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ANNEX. Organizational structure of the PRIAMHO II study

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