Original article

Effect of Opening a New Catheterization Laboratory on 30-Day and 2-Year Survival Rates in Myocardial Infarction Patients

Daniel Bosch,[a] Rafel Masia,[a] Joan Sala,[a] Joan Vila,[b] Rafel Ramos,[c] Roberto Elosua,[b,d] Isaac Subirana,[b,d] Magda Heras,[e] Juan Sanchis,[f,g] María Grau,[b] Ramon Brugada,[a,h] Jaume Marrugat,[b,*] and the REGICOR investigators[◇]

[a] *Department of Cardiology, Hospital Universitari Dr. Josep Trueta, Girona, Spain*
[b] *Cardiovascular Genetics and Epidemiology Research Group, Inflammatory and Cardiovascular Disorders Research Program, Institut Municipal d'Investigació Mèdica (IMIM), Barcelona, Spain*
[c] *Unitat de Recerca d'Atenció Primària, IDIAP JGol, Girona, Spain*
[d] *CIBER Epidemiologia y Salud Pública, Barcelona, Spain*
[e] *Department of Cardiology, Hospital Clinic Universitari de Barcelona, Barcelona, Spain*
[f] *Department of Cardiology, Hospital Clinic Universitari de Valencia, Valencia, Spain*
[g] *Departamento de Medicina, Universidad de Valencia, Valencia, Spain*
[h] *Medical School, University of Girona, Girona, Spain*

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ABSTRACT

Introduction and objectives: To determine the effect of opening an on-site diagnostic catheterization facility on 30-day and 2-year mortality rates in patients with myocardial infarction (MI).
Methods: The study included 1539 consecutive MI patients aged 25–74 years who were recruited before and after the catheterization laboratory opened in 1998: during 1995–1997 and 1999–2003, respectively.
Results: The 641 consecutive MI patients recruited in 1995–1997 had worse 30-day mortality than the 898 recruited between 1999–2003 (11.2% versus 6.35%, respectively; P = .001). The number of coronary angiographies and percutaneous coronary interventions (PCIs) carried out was greater in the second period (19.4% versus 3.3%, and 54.8% versus 23.0%, respectively; P < .001). Two-year survival curves were significantly better in the second period for all-cause and cardiovascular death. The adjusted odds ratio for death at 30 days was 0.58 (95% confidence interval [CI] 0.36–0.95) for the second period compared with the first and the adjusted hazard ratio for cardiovascular death at 2 years for patients still alive at 30 days was 0.62 (95%CI 0.39–0.99). After adjustment for the prescription of statins, angiotensin-converting enzyme inhibitors, beta-blockers and antiplatelet drugs at discharge, the effect observed at 2 years was no longer significant.
Conclusions: Opening a new on-site diagnostic catheterization unit significantly increased the 30-day survival of MI patients. However, the increase in 2-year survival of 30-day survivors observed was largely explained by the implementation of better secondary prevention.

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Impacto de la apertura de un nuevo laboratorio de hemodinámica sobre la supervivencia a 30 días y a 2 años en los pacientes con infarto de miocardio

RESUMEN

Introducción y objetivos: Determinar la contribución de la apertura de un nuevo laboratorio de cateterismo diagnóstico en el centro a la modificación de la mortalidad a 30 días y a 2 años en pacientes con infarto de miocardio (IM).
Métodos: Se incluyó en el estudio a 1.539 pacientes consecutivos con IM, de 25-74 años de edad, en los periodos 1995-1997 y 1999-2003, antes y después de la apertura de un laboratorio de cateterismo, que tuvo lugar en 1998.
Resultados: Los 641 pacientes consecutivos con IM del periodo 1995-1997 tuvieron una mortalidad a 30 días peor que la de los 898 pacientes reclutados en el periodo 1999-2003 (el 11,2 frente al 6,35%; p = 0,001). El número de angiografías coronarias e intervenciones coronarias percutáneas (ICP) aumentó en el segundo periodo (el 19,4 y el 3,3%, y el 54,8 y el 23%; p < 0,001). Las curvas de supervivencia a los 2 años fueron significativamente mejores en el segundo periodo tanto en lo relativo a las muertes por todas las causas como en lo referente a las muertes cardiovasculares. La *odds ratio* ajustada de la

mortalidad a 30 días fue 0,58 (intervalo de confianza [IC] del 95%, 0,36-0,95) y la razón de riesgos ajustada de la mortalidad cardiovascular a los 2 años para los pacientes que habían sobrevivido a los 30 días fue 0,62 (IC del 95%, 0,39-0,99) para el segundo periodo en comparación con el primero. Al introducir un ajuste adicional relativo a la prescripción de estatinas, inhibidores de la enzima de conversión de la angiotensina, bloqueadores beta y antiagregantes plaquetarios al alta, el efecto observado a los 2 años dejaba de ser significativo.

Conclusiones: La apertura de una nueva sala de cateterismos diagnósticos local aumentó significativamente el número de supervivientes a 30 días, pero no el de supervivientes a dos 2 de aquellos que habían sobrevivido 30 días, lo que puede explicarse suficientemente por una mejor prevención secundaria en este segundo periodo de de tiempo.

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Abbreviations

AMI: acute myocardial infarction
CVD: cardiovascular disease
PCI: percutaneous coronary intervention
MI: myocardial infarction
ACS: acute coronary syndrome
CABG: coronary artery bypass graft

INTRODUCTION

Although mortality rates are lower in Spain than in northern Europe, cardiovascular disease (CVD) remains the principle cause of death in the country. Consequently, it is generally accepted that increased aging of the population and better survival after a first event will result in a rising workload for departments of cardiology.[1–3]

Evidence from clinical trials and retrospective studies show that coronary angiography and coronary angioplasty improve both the management of patient with acute coronary syndrome (ACS) and the outcomes obtained.[4] However, the use of coronary angiography in patients with myocardial infarctions (MI) can vary between 15% and 50% without affecting morbidity and mortality at 6 months, provided that urgent indications are dealt with quickly.[5] On the other hand, when its use varies substantially between centers (e.g. 6% to 93%), there is a significant effect on mortality.[6] Having a cardiac catheterization laboratory on site is the critical factor that determines the use angiography and angioplasty.[5,7,8] Therefore, the opening a new diagnostic coronary catheterization unit in a center that previously had to refer all its patients to a distant tertiary hospital provides a good opportunity for a prospective analysis of the benefits of an on-site unit.

The objective of the present study was to determine whether the availability of a new diagnostic cardiac catheterization facility in a tertiary hospital had an effect on 30-day and 2-year cardiovascular mortality rates in consecutively admitted patients with MI. Given that it has been shown over the last decade that the use of new therapies such as thrombolysis,[9] antiplatelet drugs,[9,10] beta-blockers,[11] angiotensin-converting enzyme (ACE) inhibitors,[12] and statins,[13] has improved the prognosis of ACS patients who present with ST-elevation leading to MI, a second objective of the study was to determine whether the patient's drug regime at discharge contributed to any differences in outcome observed.

METHODS

Patients

The Girona Heart Registry (*Registre Gironí del cor*; REGICOR) was established in 1978 and contains the records of all consecutive patients with MI aged 25 to 74 years who live in the Girona catchment area.[14]

Time periods

We included patients registered during two distinct time periods during the era of invasive cardiology: 641 from 1995–1997 and 898 from 1999–2003. The diagnostic catheterization laboratory opened in early 1998; we omitted this start-up year from the analysis.

Measurements and Patient Management

The following patient data were collected prospectively: age, sex, smoking status, history of hypertension, diabetes and angina, type of acute coronary syndrome, and final ECG MI findings. Disease severity was determined from the degree of ventricular dysfunction (e.g. acute pulmonary edema or cardiogenic shock) and the presence of ventricular arrhythmias (e.g. fibrillation or tachycardia) that required immediate treatment. Treatment variables, such as the use of thrombolysis, antiplatelet drugs, coronary angiography, percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery, were also recorded. Prescription of antiplatelet drugs, statins, ACE inhibitors, and beta-blockers at discharge was noted to assess the potential influence of drug treatment on 2-year outcomes.

Patients were treated according to the guidelines in force at the time, which did not differ substantially in the two periods studied.[15,16] Consequently, in these two periods, the use of coronary angiography was restricted to patients with heart failure, ventricular dysfunction, post-acute myocardial infarction (AMI) angina and residual ischemia.

Definitions

The MI was categorized as Q-wave, non-Q-wave or unclassifiable MI from the discharge ECG if a patient presented with chest pain lasting more than 20 minutes on admission and had exhibited characteristic ECG changes in serial recordings. To standardize diagnoses over the two time periods studied, any abnormal increase in creatine kinase level was taken into account. The troponin level was not considered because the marker had not been introduced at the time of the earlier study period.

The diagnosis of re-infarction was based on the occurrence of typical ECG changes, defined using the same criteria as for the initial MI, along with a second increase in creatine kinase level following the peak associated with the MI present at first admission.

Criteria for post-MI angina were the recurrence of angina symptoms with ECG changes 24 hours to 30 days after MI symptom onset, without an increase in cardiac enzyme levels.

Unstable angina during follow-up (i.e. 30 days to 2 years after MI symptom onset) was diagnosed from the recurrence of angina symptoms accompanied by ECG changes in serial recordings, with an increase in cardiac enzyme levels below the limit previously described for MI diagnosis. The definition of MI used during follow-up was the same as for the first MI.

Follow-up

Patients still alive after 30 days were followed up by telephone 2 years later and data on the cohorts were crosschecked with the official Catalan Department of Health mortality register. Data were also obtained by reviewing the hospital medical records of all patients reported to have been hospitalized for an apparent cardiac condition.

The principal end-points were 30-day and 2-year cardiovascular mortality. We also recorded all-cause mortality (during the acute phase, that is in the first 30 days after symptom onset, all deaths were considered to be of cardiac origin), new MIs and admission for unstable angina.

Sample Size and Statistical Analyses

Our study was sufficiently powered (i.e. 86%) such that a hazard ratio (HR) for mortality ≤ 0.65 for the second period found in a two-sided test would be statistically significant ($P < .05$). It was assumed that 2-year mortality would be $>15\%$ in the first period, that the first/second ratio would be 40%, and that the correlation of the time period variable with potential confounders would be <0.3.

Differences between the time periods and between patients who did or did not experience an event within 30 days or, among 30-day survivors, within 2 years were assessed using a chi-squared test for categorical variables and Student's t test for continuous variables, or the non-parametric equivalents, as appropriate.

The adjusted odds ratio (OR) for an event within 30 days in the second time period was calculated using a logistic model, and the HR for mortality at 2 years in 30-day survivors was estimated using a Cox model. Any demographic, comorbidity, clinical or severity variables associated with an, at least, marginally significant difference (i.e. $P \leq .15$) on bivariate analysis between the time periods or between patients who did and did not experience events at 30 days or 2 years and any variables that were considered important on the basis of clinical judgment were included as potential confounders (e.g. sex, age and diabetes). Severity variables (i.e. acute pulmonary edema or cardiogenic shock), which could be interpreted as intermediate mechanisms of death, were included in separate models along with the above-mentioned variables. The final model for the 2-year follow-up of 30-day survivors included statin, ACE inhibitor, antiplatelet and beta-blocker prescription at discharge.

Survival curves were derived using the Kaplan–Meier method and compared using Mantel–Cox statistics. Calculations were carried out using the R statistical package.

RESULTS

During 1995–1997, there were 3345 admissions to the cardiology service, of which 919 were for an AMI. Of these, 783 were for a first AMI in individuals resident in our catchment area. During 1999–2003, there were 4629, 1332 and 1108 cases, respectively.

The demographic characteristics and cardiovascular risk factors of patients admitted during 1995–1997 and 1999–2003 are shown in Table 1. Patients in the more recent period were younger, were more likely to be current smokers, and more often had a diagnosis of hypertension, hypercholesterolemia, or non-Q-wave MI. The proportion who underwent thrombolysis or CABG surgery was similar, but the number of coronary catheterizations and PCIs increased with the availability of the on-site catheterization laboratory. Delays in performing coronary angiography, PCI and CABG surgery were significantly shorter in the second time period. The proportion taking statins, ACE inhibitors, beta-blockers and antiplatelet drugs at discharge was higher in the second period.

The proportion of patients who died or developed post-infarction angina by 30 days was significantly lower in the second period. The proportion with complications remained at a similar level (Table 2).

Follow-up for mortality at 2 years was completed in all patients (the cause of death was unknown in 6, or 0.4%) who survived the acute phase for 30 days: 569 patients in the first time period and 841 in the second. In total, 499 patients (87.7%) in the first period were still alive after 2 years compared with 777 (92.4%) in the second. All-cause and CVD mortality 2 years after discharge was significantly lower in the second period (Table 2).

Follow-up for readmission due to MI or unstable angina was completed in 455 of the 499 surviving patients (91.2%) from the first period and in 755 of the 777 (97.2%) from the second period (Table 2).

Overall all-cause mortality from admission to 2 years was 22.2% and 13.5% in the first and second time periods, respectively ($P < .001$), and cardiovascular mortality was 18.6% and 10.9%, respectively ($P < .001$).

Table 3 shows the demographic, clinical and treatment characteristics and risk factors for patients who did or did not die of cardiovascular disease within 30 days for both time periods combined. Patients who experienced this type of event were older, were more frequently female, and were less frequently smokers or hypercholesterolemic. In addition, they received thrombolysis less often, were in a poorer Killip class, underwent more angiographic procedures, and more often had anterior MI and unclassifiable ECG findings.

Table 4 shows the demographic, clinical and treatment characteristics and risk factors for MI patients who were still alive at 30 days and who did or did not die of cardiovascular disease within 2 years. Patients who experienced an event were significantly older, were more frequently female, diabetic or smokers, more often had unclassifiable ECG findings, and more often belonged to the second time period, although the difference for the last parameter was only marginally significant. They were also more likely to have received ACE inhibitors and less likely to have received beta-blockers or to have undergone thrombolysis or coronary angiography (i.e. during admission; they generally underwent many more angiographies after discharge than those still alive).

Table 5 shows the characteristics of patients who did or did not undergo coronary angiography, regardless of PCI, in the two study periods. The use of coronary angiography in patients with non-ST-elevation ACS was higher in the second period.

Adjusted Risk of Death at 30 Days and 2 Years

Fig. 1 shows the ORs for death at 30-day follow-up for the second time period as the number of factors for which adjustment was made in the logistic models increased (Fig. 1, Panel A). The risk of death in this period was significantly lower, regardless of the level of adjustment. The Cox model showed that the HR for cardiovascular death at 2-year follow-up in 30-day survivors was

Table 1

Demographic and Clinical Characteristics of Myocardial Infarction Patients, by Period of Admission Without and With an On-Site Catheterization Laboratory (1995-1997 and 1999-2003)

	1995–1997	1999–2003	*P*-value
Patients, n	641	898	
Age, years[*]	63.7 (11.9)	60.7 (10.9)	<.001
Percentage women	22.0%	20.3%	.411
Risk factor history			
Hypertension	46.5%	52.2%	.029
Diabetes	27.3%	26.0%	.568
Hypercholesterolemia	41.2%	52.0%	<.001
Current smokers	35.9%	43.6%	.003
ECG myocardial infarction findings			
Non-Q-wave	16.5%	26.7%	
Inferior	42.7%	37.0%	
Anterior	35.7%	31.7%	
Unclassifiable	5.0%	4.6%	<.001
Type of acute coronary syndrome			
ST-elevation	82.5%	74.4%	
Non-ST-elevation	12.3%	20.8%	
Unclassifiable	5.2%	4.8%	<.001
Procedure used during the first 30 days			
Thrombolysis	41.5%	40.2%	.612
Coronary angiography	19.4%	54.8%	<.001
Days to coronary angiography[**]	15.0 (10.0–24.5)	9.00 (5.0–13.0)	<.001
Percutaneous intervention	3.3%	23.0%	<.001
Days to percutaneous intervention[**]	21.0 (14.0–33.0)	10.5 (5.0–17.0)	<.001
Coronary artery bypass graft surgery	5.5%	8.4%	.054
Days to coronary artery bypass graft surgery[**]	29.0 (22.5–51.0)	23.0 (15.5–33.5)	.015
Drug treatment at discharge			
Calcium antagonists	20.1%	19.0%	.606
Statins	13.6%	66.2%	<.001
Angiotensin-converting enzyme inhibitors	29.0%	52.6%	<.001
Beta-blockers	32.4%	57.1%	<.001
Antiplatelet drugs	86.7%	91.7%	.002
Nitrates	30.9%	22.9%	<.001

[*] Mean (standard deviation).
[**] Median (first quartile–third quartile) for patients undergoing the procedure.

Table 2

Proportion of Myocardial Infarction Patients Experiencing a Major Event Within 30 Days of Symptom Onset and Within 2 Years in 30-Day Survivors, by Period of Admission Without (1995–1997) and With (1999–2003) an On-Site Catheterization Laboratory

	1995–1997	1999–2003	*P*-value
Events within 30 days, n	641	898	
Cardiovascular death	11.2%	6.35%	.001
Reinfarction	3.25%	3.64%	.697
Post-myocardial infarction angina	22.4%	15.1%	<.001
Killip class III–IV	17.2%	14.3%	.115
Events within 2 years in 30-day survivors	569	841	
All-cause death	12.3%	7.61%	.003
Cardiovascular death	8.29%	4.78%	.008
Myocardial infarction	6.59%	7.81%	.475
Unstable angina	4.43%	2.79%	.115
Coronary catheterization	4.21%	8.10%	.014
Percutaneous intervention	1.55%	4.65%	.008
Coronary artery bypass graft surgery	0.23%	0.27%	1

Killip class III–IV: acute pulmonary edema or cardiogenic shock.

significantly lower in the second period (Fig. 1, Panel B) after adjustment for age, sex, hypertension, dyslipidemia, smoking, diabetes, ECG MI findings, acute pulmonary edema or cardiogenic shock, and thrombolysis (Fig. 1, Panel B, model 2). However, this effect was confounded by statins, ACE inhibitors, beta-blockers and antiplatelet drugs being prescribed at discharge (Fig. 1, Panel B, model 3). The HR for all-cause death among 30-day survivors was 0.73 (95% confidence interval [CI] 0.50–1.06), 0.72 (95% CI 0.50–1.05) and 0.89 (95% CI 0.56–1.42) for the second period for the three models adjusted as indicated in Fig. 1, Panel B.

Fig. 2 shows survival curves from admission to 2 years for the two time periods: for cardiovascular death in Panel A and for all-cause death in Panel B. In both cases, the survival rate was significantly better at 2 years for the 1999–2003 time period, when a catheterization laboratory was available on site.

Table 3

Demographic, Clinical and Treatment Characteristics and Risk Factors for Patients Who Did or Did Not Die of Cardiovascular Disease Within 30 Days, for the Two Time Periods Combined

	Death		
	No	Yes	P-value
Patients, n	1410	129	
Period 1999-2003	59.6%	44.2%	.001
Age, years*	61.3 (11.4)	69.6 (9.24)	<.001
Percentage women	20.1%	31.0%	.004
Risk factor history			
Hypertension	49.3%	55.7%	.174
Diabetes	25.9%	33.3%	.079
Hypercholesterolemia	48.8%	32.2%	.001
Current smokers	42.0%	21.7%	<.001
ECG myocardial infarction findings			
Non-Q-wave	23.3%	14.0%	
Inferior	40.4%	27.9%	
Anterior	32.8%	40.3%	
Unclassifiable	3.6%	17.8%	<.001
Type of acute coronary syndrome			
ST-elevation	77.9%	76.0%	
Non-ST-elevation	18.4%	5.4%	
Unclassifiable	3.7%	18.6%	<.001
Thrombolysis	42.1%	25.2%	<.001
Killip class III–IV	11.0%	68.1%	<.001
Coronary angiography at admission	42.7%	10.5%	<.001
Antiplatelet drugs at admission	97.5%	80.8%	<.001

Killip class III–IV: acute pulmonary edema or cardiogenic shock.
* Mean (standard deviation).

Table 4

Demographic, Clinical and Treatment Characteristics and Risk Factors for Myocardial Infarction Patients Who Were Alive at 30 Days and Who Did or Did Not Die of Cardiovascular Disease Within 2 Years, for the Two Time Periods Combined

	Cardiovascular death		
	No	Yes	P-value*
Patients, n	1317	87	
Period 1999–2003	60.5%	46.0%	.008
Age, years†	60.7 (11.2)	69.9 (9.52)	<.001
Percentage women	19.2%	33.3%	.001
Risk factor history			
Hypertension	48.8%	54.1%	.317
Diabetes	24.5%	47.7%	<.001
Hypercholesterolemia	48.8%	49.4%	.914
Current smokers	43.3%	22.6%	<.001
ECG myocardial infarction findings			
Non-Q-wave	23.1%	26.4%	Reference
Inferior	40.9%	31.0%	.155
Anterior	33.0%	31.0%	.569
Unclassifiable	3.0%	11.5%	.002
Type of acute coronary syndrome			
ST-elevation	78.2%	73.6%	
Non-ST-elevation	18.6%	14.9%	
Unclassifiable	3.2%	11.5%	<.001
Thrombolysis	43.9%	16.3%	<.001
Killip class III–IV	9.0%	41.9%	<.001
Treatment prescribed at discharge			
Statins	49.8%	27.8%	<.001
Angiotensin-converting enzyme inhibitors	45.0%	57.0%	.030
Beta-blockers	53.1%	19.0%	<.001
Antiplatelet drugs	94.3%	89.3%	.062
Coronary angiography within initial 30 days	43.8%	25.6%	.001
Coronary angiography within 30 days to 2 years	6.0%	15.4%	<.001

Killip class III–IV: acute pulmonary edema or cardiogenic shock.
* Estimated by Cox regression analysis.
† Mean (standard deviation).

Table 5

Characteristics of Patients Who Did or Did Not Undergo Coronary Angiography in the Two Study Periods, Irrespective of Percutaneous Intervention

	1995–1997			1999–2003			
	Coronary angiography			Coronary angiography			
	No	Yes	P-value[a]	No	Yes	P-value[b]	P-value[c]
Patients, n	508	122		400	485		
Age, years[d]	64.3 (12.2)	61.9 (10.2)	.052	61.2 (11.2)	60.3 (10.7)	.212	.116
Percentage women	22.0%	21.3%	.86	17.0%	22.7%	.036	.746
Risk factor history							
Hypertension	45.5%	50.0%	.372	46.9%	57.1%	.003	.158
Diabetes	26.5%	29.2%	.548	25.1%	26.7%	.585	.589
Hypercholesterolemia	40.7%	43.0%	.645	47.7%	55.8%	.018	.012
Current smokers	37.1%	32.0%	.289	46.3%	41.1%	.132	.064
ECG myocardial infarction findings							
Non-Q-wave	15.9%	18.9%		18.0%	34.6%		
Inferior	44.3%	37.7%		47.2%	28.7%		
Anterior	34.1%	41.8%		31.0%	32.2%		
Unclassifiable	5.71%	1.64%	.091	3.75%	4.54%	<.001	.001
Type of acute coronary syndrome							
ST-elevation	82.1%	83.6%		81.8%	68.5%		
Non-ST-elevation	12.0%	14.8%		14.5%	26.6%		
Unclassifiable	5.91%	1.64%	.126	3.75%	4.95%	<.001	.004
Thrombolysis	38.7%	50.8%	.014	45.6%	35.4%	.002	.002
Killip class III–IV	17.6%	15.6%	.601	14.1%	14.2%	.991	.693

Killip class III–IV: acute pulmonary edema or cardiogenic shock.

Note: data on coronary angiography were not available for 11 patients in the first period and 13 in the second.

[a] no coronary angiography versus coronary angiography for the first time period
[b] no coronary angiography versus coronary angiography for the second time period
[c] no coronary angiography versus coronary angiography for both time periods combined
[d] mean (standard deviation)

DISCUSSION

The results of this 2-year follow-up cohort study of patients admitted to the same tertiary hospital during two distinct time periods, without and with a diagnostic catheterization laboratory on site, show that the availability of the facility resulted in the increased use of invasive strategies, a shorter delay before treatment, and lower 30-day mortality, which persisted at 2 years. The improvement observed at 2 years principally stemmed from the results obtained within the initial 30 days following admission, combined with the increased prescription of statins, ACE inhibitors, beta-blockers and antiplatelet drugs at discharge. The shorter delay before treatment and increased use of all the diagnostic and therapeutic procedures made available by the catheterization laboratory indicate that the overall management of MI patients during the acute phase may well be the reason for the observed benefit.

Although the easy availability of invasive cardiac care facilities is associated with an increase in their use, their influence on outcomes is not clear, especially when a simultaneous increase in the use of drug treatment is taken into account.[17–20] The RESCATE study compared treatment and outcomes over the same time period in a number of Spanish hospitals with and without on-site catheterization laboratories and found that those with a catheterization laboratory performed more procedures, with a shorter treatment delay. However, no difference in mortality was found at 6 months.[5] Another study compared treatment and outcomes during the same period at two hospitals with markedly different rates of catheterization use and found that survival at 28 days was significantly better in the hospital with higher use.[6] A study of the records of 19 hospitals in Seattle found no difference in mortality despite differences in the rates of use of coronary angiography and coronary angioplasty.[17] In a French study, the lower mortality associated with admission to a hospital with on-site angioplasty facilities was attributed to greater use of evidence-based medical treatment.[21] A post hoc analysis of the Gusto-IIb trial database showed that, despite a higher rate of interventions in the United States compared with Canada, 1-year mortality was comparable.[22] Most of these studies date from the time before the widespread use of primary angioplasty.

It is known that the use of primary angioplasty was relatively low in Spain during the period studied. The figures reported in our study are consistent with those recorded by Spanish national registries early in the decade.[23,24]

Study Advantages and Potential Limitations

One particularly positive feature of this study was that the evaluation was carried out at a single hospital, thereby avoiding any variability in patient management between centers.

Although the on-site catheterization laboratory first became operational in 1998, initially only diagnostic coronary angiography was carried out. Patients were referred to other tertiary hospitals for angioplasty procedures. This enabled us to evaluate the contribution the catheterization laboratory made to the reduction in the 2-year event rate independent of the use of angioplasty, despite the fact that the total number of procedures carried out in our case may have been lower than that recommended by current criteria.

In our study, we took into account the treatment prescribed at discharge (this treatment is practically free for the general population in Spain), but we had no information on compliance or on any side effects during the 2-year follow-up period. This may have introduced some unknown biases that would clearly not have operated in favor of the study hypothesis because currently available data suggest that the medication compliance of MI patients has not changed in the past 10 years.[25]

One limitation of the study is that it did not consider drug use at admission. We observed an increase in the use of beta-blockers (from 30% in 1993 to 83% in 2003) and ACE inhibitors (from 36% in 1996 to 74% in 2003). The use of thrombolysis (45% in 1993 and
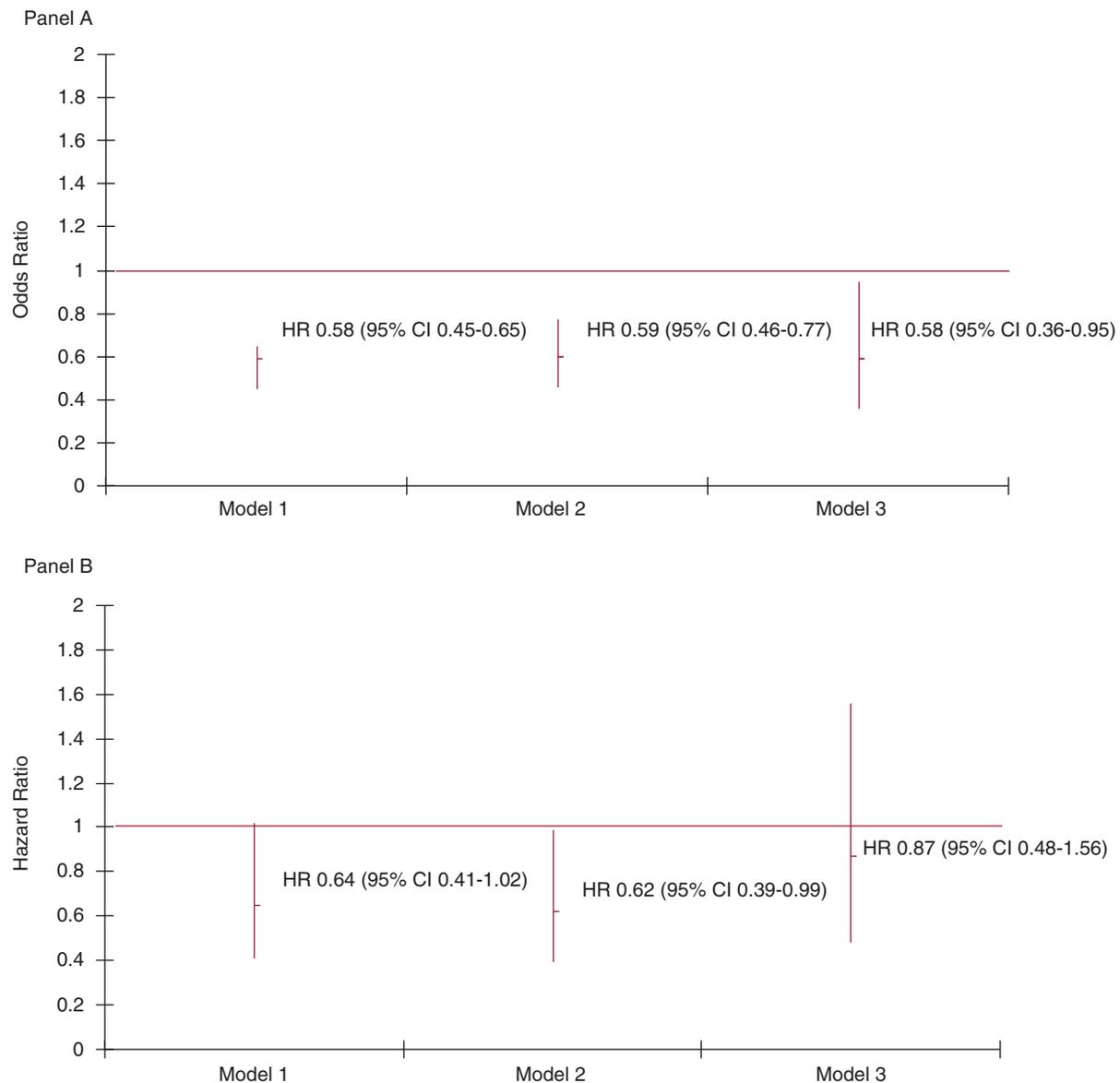
Figure 1. Adjusted hazard ratio (HR) for death at 30 days (Panel A) and for cardiovascular death at 2 years in 30-day survivors (Panel B) in the period of hospital admission with an on-site catheterization laboratory (i.e. 1999–2003) compared with the period without (i.e. 1995–1997). CI: confidence interval; HR: hazard ratio.
Panel A
Model 1: adjusted for age, sex, hypertension, dyslipidemia, smoking, diabetes and ECG myocardial infarction findings.
Model 2: adjusted as for Model 1 with the addition of acute pulmonary edema and cardiogenic shock.
Model 3: adjusted as for Model 2 with the addition of thrombolysis and antiplatelet drug use on admission.
Panel B
Model 1 adjusted for age, sex, hypertension, dyslipidemia, smoking, diabetes, ECG myocardial infarction findings, acute pulmonary edema and cardiogenic shock.
Model 2: adjusted as for Model 1 with the addition of thrombolysis.
Model 3: adjusted as for Model 2 with the addition of the prescription of statins, angiotensin-converting enzyme inhibitors, beta-blockers and antiplatelet drugs at discharge.

37% in 2003) and platelet inhibitors (94% in 1993 and 98% in 2003) has remained stable over the past 15 years, according to REGICOR data (unpublished findings). The Spanish MI registry also showed a decrease in 28-day mortality (from 14.2% to 11.3%; $P < .001$) and 1-year mortality (from 18.5% to 16.4%; $P < .001$) between 1995 and 2000 which was associated with the increased use of both reperfusion techniques and medical treatment.[26] Consequently, some undetermined part of the beneficial effect of the "time period" on 30-day mortality might have been due to these changes.

Moreover, ejection fraction was not taken into account because it was not documented systematically during the first time period.

The increase observed in the prevalence of hypertension, diabetes, and hypercholesterolemia may have been due to changes in diagnostic criteria that occurred at the end of 1990 s.[27-29]

The variation in treatment received by these patients, which resulted from the different treatment guidelines in force during the two time periods, could have resulted in some variation in the use of coronary angiography.

Finally, our analysis of the effect of coronary angiography and PCI was limited by the difference in survival during the acute phase (i.e. in the first few hours after symptom onset). Therefore, the models were not adjusted for these variables because that could
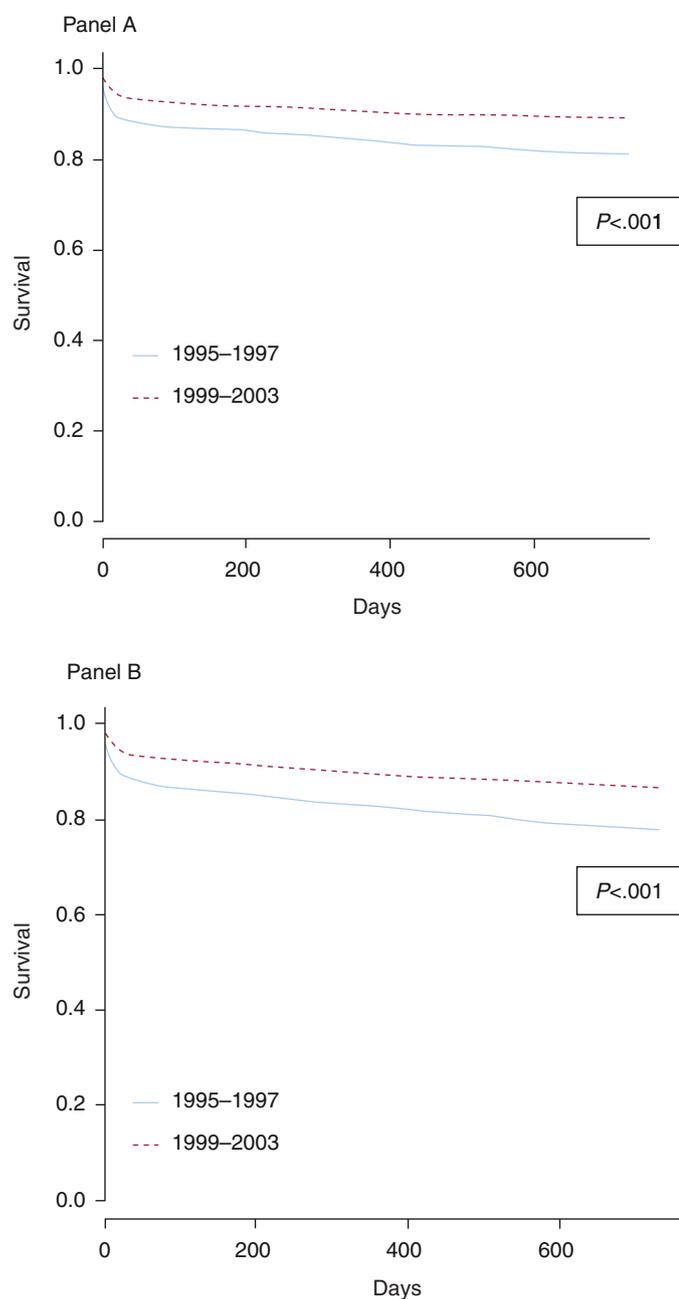
Figure 2. Survival curves for death from coronary heart disease (Panel A) and all causes (Panel B) from admission to 2 years, for both time periods.

have led to their actual effect being overestimated due to reverse causality. The hypothesis under analysis was restricted to the effect of the availability of a catheterization laboratory (i.e. the "time period" effect).

CONCLUSIONS

The opening of a new catheterization unit in a tertiary hospital was associated not only with an increase in the number of coronary catheterizations and PCIs carried out in MI patients, but also with a reduction in the time delay before these procedures were implemented.

The greater availability of this facility increased its use and broadened the range of indications for referral.

The result was lower cardiovascular mortality at 30 days, which was maintained at 2 years. Lower mortality persisted after hospital discharge and was combined with the effect of more intensive secondary prevention with statins, ACE inhibitors, beta-blockers and antiplatelet drugs, which were prescribed at discharge.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Marrugat J, Elosua R, Martí H. Epidemiología de la cardiopatía isquémica en España: estimación del número de casos y de las tendencias entre 1997 y 2005. Rev Esp Cardiol. 2002;55:337–46.
2. Gil M, Martí H, Elosua R, Grau M, Sala J, Masia R, et al. Análisis de la tendencia en la letalidad, incidencia y mortalidad por infarto de miocardio en Girona entre 1990 y 1999. Rev Esp Cardiol. 2007;60:349–56.
3. Marrugat J, Elosua R, Aldasoro E, Tormo MJ, Vanaclocha H, Segura A, et al. Regional variability in population acute myocardial infarction cumulative incidence and mortality rates in Spain 1997 and 1998. Eur J Epidemiol. 2004;19:831–9.
4. Mehta SR, Cannon CP, Fox KA, Wallentin L, Boden WE, Spacek R, et al. Routine *vs.* selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. JAMA. 2005;293:2908–17.
5. Marrugat J, Sanz G, Masiá R, Valle V, Molina L, Cardona M, et al. Six-month outcome in patients with myocardial infarction initially admitted to tertiary and nontertiary hospitals. RESCATE Investigators. Recursos Empleados en el Síndrome Coronario Agudo y Tiempos de Espera. J Am Coll Cardiol. 1997;30:1187–92.
6. Marrugat J, Ferrières J, Masià R, Ruidavets J, Sala J. Differences in use of coronary angiography and outcome of myocardial infarction in Toulouse (France) and Gerona (Spain). The MONICA-Toulouse and REGICOR investigators. Eur Heart J. 2000;21:740–6.
7. Van de Werf F, Gore JM, Avezum A, Gulba DC, Goodman SG, Budaj A, et al. Access to catheterisation facilities in patients admitted with acute coronary syndrome: multinational registry study. BMJ. 2005;330:441.
8. Bueno H, Bardají A, Fernández-Ortiz A, Marrugat J, Martí H, Heras M. 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). Rev Esp Cardiol. 2005;58:244–52.
9. Baigent C, Collins R, Appleby P, Parish S, Sleight P, Peto R. ISIS-2: 10 year survival among patients with suspected acute myocardial infarction in randomised comparison of intravenous streptokinase, oral aspirin, both, or neither. The ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. BMJ. 1998;316:1337–43.
10. Sabatine MS, Cannon CP, Gibson CM, López-Sendón JL, Montalescot G, Theroux P, et al. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. N Engl J Med. 2005;352:1179–89.
11. The GISSI Collaborative Group Randomised trial of intravenous atenolol among 16 027 cases of suspected acute myocardial infarction: ISIS-1. First International Study of Infarct Survival Collaborative Group. Lancet. 1986; 2:57–66.
12. Pfeffer MA, Braunwald E, Moyé LA, Basta L, Brown Jr EJ, Cuddy TE, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. N Engl J Med. 1992;327:669–77.

13. The Scandinavian Simvastatin Survival Study group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet. 1994;344:1383–9.
14. Sala J, Marrugat J, Masiá R, Porta M. Improvement in survival after myocardial infarction between 1978-85 and 1986-88 in the REGICOR study. (Registre GIroní del COR) registry. Eur Heart J. 1995;16:779–84.
15. Acute myocardial infarction: pre-hospital and in-hospital management. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J. 1996; 17:43–63.
16. Bertrand ME, Simoons ML, Fox KA, 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.
17. Every NR, Larson EB, Litwin PE, Maynard C, Fihn SD, Eisenberg MS, et al. The association between on-site cardiac catheterization facilities and the use of coronary angiography after acute myocardial infarction. Myocardial Infarction Triage and Intervention Project Investigators. N Engl J Med. 1993;329:546–51.
18. Alter DA, Naylor CD, Austin PC, Tu JV. Long-term MI outcome at hospitals with or without on-site revascularization. JAMA. 2001;285:2101–8.
19. Krumholz HM, Chen J, Murillo JE, Cohen DJ, Radford MJ. Admission to hospitals with on-site cardiac catheterization facilities: Impact on long-term cost and outcomes. Circulation. 1998;98:2010–6.
20. Van Brabandt H, Camberlin C, Vrijens F, Parmentier Y, Ramaekers D, Bonneux L. More is not better in the early care of acute myocardial infarction: a prospective cohort analysis on administrative databases. Eur Heart J. 2006;27:2649–54.
21. Labarere J, Belle L, Fourny M, Genès N, Lablanche JM, Blanchard D, et al. Outcome of myocardial infarction in hospitals with percutaneous coronary intervention facilites. Arch Intern Med. 2007;167:913–20.
22. Fu Y, Chang WC, Mark D, Califf RM, Mackenzie B, Granger CB, et al. Canadian-American differences in the management of acute coronary syndromes in the GUSTO IIb trial: one-year follow-up of patients without ST-segment elevation. Circulation. 2000;102:1375–81.
23. Ferreira-González I, Permanyer-Miralda G, Marrugat J, Heras M, Cuñat J, Civeira E, et al. Estudio MASCARA (Manejo del Síndrome Coronario Agudo. Registro Actualizado). Resultados globales. Rev Esp Cardiol. 2008;61:803–16.
24. Arós F, Loma-Osorio A, Vila J, López-Bescós L, Cuñat J, Rodríguez E, et al. Efecto de la asociación de bloqueadores beta e inhibidores de la enzima de conversión en la supervivencia al año tras sufrir un infarto agudo de miocardio. Resultados del registro PRIAMHO II. Rev Esp Cardiol. 2006;59:313–20.
25. Gislason GH, Rasmussen JN, Abildstrom SZ, Gadsboll N, Buch P, Friberg J, et al. Long-term compliance with beta-blockers, angiotensin-converting enzyme inhibitors, and statins after acute myocardial infarction. Eur Heart J. 2006;27:1153–8.
26. Heras M, Marrugat J, Arós F, Bosch X, Enero J, Suárez MA, et al. Reducción de la mortalidad por infarto agudo de miocardio en un periodo de 5 años. Rev Esp Cardiol. 2006;59:200–8.
27. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. Seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure. Hypertension. 2003; 42:1206–52.
28. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 1997; 20:1183-97.
29. Wood D, De Backer G, Faergeman O, Graham I, Mancia G, Pyörälä K. Recommendations of the Second Joint Task Force of European and other Societies on Coronary Prevention. Eur Heart J. 1998;19:1434–503.