# Effect of Reactions to Symptom Onset on Early Mortality From Myocardial Infarction

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**Introduction and objectives.** A patient's social circumstances at the time when acute myocardial infarction (AMI) symptoms first appear might influence survival. Our objectives were to study the living conditions, the location where symptoms started, the type of symptoms, and the delay before action was taken in patients with AMI who survived more than one hour, and to analyze the relationship between these variables and mortality in different time periods.

**Patients and method.** Population-based observational cohort study carried out in 1997-1998. Main data source: Registre Gironí del Cor (REGICOR). Death certificates provided information on patients who died before they could be included in the register. The patients' demographic characteristics, lifestyle, clinical history, electrocardiographic abnormalities, cardiac enzyme levels, treatment, and diagnosis were recorded. Mortality before and during hospitalization, and overall mortality at 28 days were studied.

**Results.** Of the 1,097 patients included, 274 (24.97%) died before reaching hospital, 171 (15.58%) died in hospital, and 652 (59.4%) were alive at 28 days. Mortality was lower in patients who went directly to hospital (OR=0.32, 95% CI, 0.17-0.59). Mortality at 28 days was higher in those with atypical symptoms (OR=5.52, 95% CI, 2.90-10.50), and in those who lived in an institution (OR=9.47, 95% CI, 1.05-84.9).

**Conclusions.** In the absence of specially equipped ambulances, AMI patients who went directly to the hospital or who had typical symptoms had a better chance of survival both before hospitalization and at 28 days. In contrast, 28day mortality was higher in institutionalized patients.

**Key words:** Prehospital mortality. Acute myocardial infarction. Medical attention.

Received November 25, 2004. Accepted for publication September 1, 2005.

#### Impacto de la actitud frente a los síntomas en la mortalidad temprana por infarto de miocardio

Introducción y objetivos. El entorno y las circunstancias del paciente en el inicio de los síntomas del infarto agudo de miocardio (IAM) pueden condicionar su supervivencia. El objetivo es estudiar los aspectos relativos a la convivencia, las características y el retraso en las primeras acciones tomadas por los pacientes con IAM que sobrevivieron más de 1 h y analizar su relación con la mortalidad en distintos períodos.

Pacientes y método. Se ha realizado un estudio de cohortes de base poblacional entre 1997 y 1998. La principal fuente de información ha sido el Registre Gironí del Cor (REGICOR) y, para los fallecidos antes de acceder a monitorización, los boletines estadísticos de defunción. Se estudiaron las características demográficas, los hábitos y los antecedentes, los síntomas, las alteraciones electrocardiográficas, el valor de las enzimas miocárdicas y los procedimientos terapéuticos y diagnósticos. Se analizó la mortalidad prehospitalaria, intrahospitalaria y global a los 28 días.

**Resultados.** Se analizaron 1.097 casos: 652 (59,4%) supervivientes a 28 días, 171 muertes en hospitales (15,58%) y 274 muertes prehospitalarias (24,97%). Los pacientes que fueron directamente al hospital presentaron menor mortalidad (*odds ratio* [OR] = 0,32; intervalo de confianza [IC] del 95%, 0,17-0,59). Hubo mayor mortalidad a los 28 días entre los que tenían síntomas atípicos (OR = 5,52; IC del 95%, 2,90-10,50) y/o vivían institucionalizados (OR = 9,47; IC del 95%, 1,05-84,9).

**Conclusiones.** En ausencia de un servicio de ambulancias medicalizadas, los pacientes con un IAM que se dirigen directamente a un hospital y/o presentan síntomas típicos sobreviven en mayor proporción a los 28 días y en la fase prehospitalaria de la enfermedad, y los institucionalizados presentan una mayor mortalidad a los 28 días.

**Palabras clave:** Mortalidad prehospitalaria. Infarto agudo de miocardio. Asistencia sanitaria.

This study was financed with the following grants: Fondo de Investigación Sanitaria (FIS 97/0920) and the HERACLES network (FIS G03/045).

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### ABBREVIATIONS

AMI: acute myocardial infarction.ACE: angiotensin converting enzyme.REGICOR: Registre Gironí del Cor (Heart Register of Girona).

## INTRODUCTION

In Spain, approximately 40% of individuals who have an acute myocardial infarction (AMI) die before reaching the hospital, whilst mortality in hospitalized patients is approximately 12%.<sup>1</sup>

Interventions to reduce mortality in AMI patients are generally hospital-based. The use of fibrinolysis and acetylsalicylic acid has led to an estimated 26% reduction in AMI-related mortality in Spain<sup>2</sup> and primary angioplasty has improved prognosis in individuals who reach the hospital.<sup>3</sup> The benefits from these interventions are maximized when applied as early as possible after symptom onset.<sup>4</sup>

Several aspects of a patient's social circumstances at the time of symptom onset may affect survival, and little is known about some delays in help-seeking, delays which could be appropriate targets for public health interventions.<sup>5</sup>

The aim of the present study was to investigate patients' living conditions, the patient's location when symptoms began, the delay before the first actions were taken after symptom onset, and the type of action taken, in patients with AMI surviving for more than 1 hour after symptom onset, and to analyze the relationship between these aspects and mortality at 28 days.

## PATIENTS AND METHODS

This was a population-based, prospective, cohort study carried out in the province of Gerona, in northeastern Spain. The reference population, which consisted of 266 000 people aged over 35 according to the 1996 census, was drawn from 6 counties in the province. All consecutive patients up to 85 years of age with a probable or definite diagnosis of AMI based on World Health Organization (WHO) standard criteria were included.<sup>6</sup> This is the first populationbased study of this type to be performed in Spain.

Patients were drawn from 2 groups: those who died before they could receive cardiac monitoring or defibrillation, and all those with a diagnosis of AMI admitted to any of the 7 hospitals in the study area during 1997 and 1998. Patients who died within an hour of symptom onset were excluded from the study. The primary data source was the Registre Gironí del Cor (REGICOR), which provides a complete register of all AMIs within the study area. Patients who died before they could receive cardiac monitoring were identified primarily from death certificates. Death certificates which included any of the WHO ICD-9 diagnostic codes 410 to 414 were selected. For these patients, certifying clinicians and, when considered necessary, patients' relatives were contacted and asked to complete a structured questionnaire on the actions taken after symptom onset. The questionnaire covered aspects such as calling a general practitioner, calling an ambulance or using own transport to go to the hospital, initial care, and the journey to hospital transfer. Data were also collected on the time elapsed (in minutes) between symptom onset and the first request for medical attention, the arrival of a clinician or other health care personnel, the arrival of medical transport, and the time when monitoring commenced. Surveys of family members and certifying clinicians did not take place until 1999-2000 due to a delay in obtaining the death certificates. Data for patients admitted to the hospital were obtained on admission by questioning the patient or family members.

Variables analyzed included place of residence, gender, age, living conditions, the patient's location when symptoms first appeared, the location where AMI was treated, as well as the patient's habits and antecedents, including smoking, hypertension, diabetes, hypercholesterolemia, and previous ischemic heart disease. Patients were classified as "definite" AMI, "possible" AMI, or "insufficient" data (when it was not possible to precisely determine the cause of death), on the basis of symptoms, electrocardiographic abnormalities, and cardiac enzyme levels. Standard criteria<sup>6</sup> were used to define these categories and to classify patients. Patients were classified by expert staff (epidemiologists and cardiologists) who received studyspecific training.

Data was also collected on the therapeutic and diagnostic procedures applied, including use of fibrinolysis, antiplatelet treatment, angiotensin converting enzyme (ACE) inhibitors, beta-blockers, cardiac catheterization, and coronary revascularization.

Overall mortality at 28 days, prehospital and inhospital mortality were analyzed.

## **Statistical Analysis**

The  $\chi^2$  test was used to compare prehospital and inhospital mortality between groups in a bivariate analysis. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated for 28-day mortality, and the relationships between pre- and inhospital mortality and living conditions, patients' or family members' first reactions, and symptoms were investigated using logistic regression models adjusted for demographic, clinical and co-morbidity variables which had been found to be significantly associated with mortality and other variables of interest in the bivariate analysis (potential confounders). The significance level in all analyses was set at 5%, and analyses were performed using SPSS 12.0.

#### RESULTS

A total of 1276 consecutive patients were diagnosed with AMI during the study period. Of these, 179 died within the first hour after symptom onset, leaving 1097 cases for analysis. Six hundred and fifty two patients were still alive at 28 days, 171 patients died in the hospital, and 274 patients died before reaching the hospital. In the latter 2 groups, death occurred more than 1 hour after symptom onset.

Table 1 shows patients' demographic and clinical characteristics, and the procedures used, for groups based on overall, prehospital and in-hospital mortality. All comparisons are relative to the group of patients who were alive after 28 days. Significant associations for the 3 types of mortality were as follows:

– Overall mortality at 28 days was positively associated with age, and was also higher in women, or when acute pulmonary edema/cardiogenic shock, recurrent AMI, and severe arrhythmias were present. Mortality was lower in current smokers, in patients with a history of angina, and in patients who received thrombolytic treatment, antiplatelet treatment, angiography, angioplasty, and surgery within 28 days.

– Prehospital mortality was positively associated with age, being female and with having a previous AMI. Mortality was lower in patients who had previously had angina.

– In-hospital mortality was higher in patients with previous angina or AMI, as well as in patients with acute pulmonary edema/cardiogenic shock, recurrent AMI, and severe arrhythmias. As with overall mortality, mortality was lower in current smokers and patients who received thrombolysis, antiplatelet treatment, angiography, angioplasty, and surgery within 28 days.

Table 2 shows the relationship between context, circumstances and the first reactions to AMI symptom onset, and overall, prehospital and in-hospital mortality. All comparisons are relative to the group of patients who were still alive after 28 days. Significant associations with the 3 types of mortality were as follows:

- Overall mortality at 28 days was associated with living conditions, and was higher in patients who lived alone or who were institutionalized. The patient's

TABLE 1. Epidemiological and Clinical Characteristics of 1097 Consecutive Patients With Acute Myocardial Infarction Surviving More Than 1 Hour From Symptom Onset. Data for Different Mortality Sub-Groups Compared With Survivors at 28 Days\*

	Overall, 28 Days (n=445)	Mortality		Survivors at 28 Days
		Prehospital (n=274)	In-hospital (n=171)	Survivors (n=652)
Age, years				
<65	20.4% <sup>a</sup>	23.0%†	16.4%†	43.70%
65-75	33.50%	31.40%	36.80%	36.70%
76-85	46.10%	45.60%	46.80%	19.60%
Women	31.2%\$	32.8%‡	28.70%	23.80%
Hypertension	56.00%	46.80%	62.2%\$	52.20%
Diabetes	31.30%	28.80%	32.90%	29.40%
Current smokers	16.7%†	27.40%	10.1%†	36.00%
Previous angina	54.50%	39.0%\$	63.7%‡	50.10%
Previous AMI	27.90%	29.4%†	26.9%†	14.80%
Characteristics on admission				
Anterior AMI	36.40%	-	37.70%	34.00%
APE/cardiogenicshock	73.3%†	-	73.6†	11.10%
Angina	11.6%\$	-	18.20%	19.30%
Recurrent AMI	5.2%\$	-	7.8%†	1.70%
Severe arrythymia	47.7%†	-	47.9%†	9.40%
Management				
Thrombolysis	4.2%†	-	7.0%†	35.50%
Antiplatelets	44.2%†	-	72.9†	94.40%
Angiography at 28 days	5.9%†	-	7.9%†	24.50%
Angioplasty 28 days	0.4%‡	-	0.6%‡	4.10%
Surgery at 28 days	1.1%\$	_	0.6%‡	6.20%

\*AMI indicates acute myocardial infarction; APE: acute pulmonary edema. †*P*<.0001. ‡*P*<.001. \$*P*<.01.

TABLE 2. Living Conditions, Location, and Time of Symptom Onset, Characteristics of and Delay in First Actions Taken After Symptomon Set in 1097 Consecutive Patients With Acute Myocardial Infarction Surviving More Than 1 Hour After Symptomon Set and the Irrelation With Different Types of Mortality Compared With Survivors at 28 Days

	Overall, 28 Days (n=445), % (n)	Prehospital (n=274), % (n)	In-hospital (n=171), % (n)	Survivors (n=652)
Living conditions				
Living alone	7.8* (9)	12.3* (8)	2.0 (1)	7.40%
With relatives	79.3 (92)	67.7 (44)	94.1 (50)	91.20%
Institutionalized (residences)	12.9 (15)	20.0 (13)	3.9 (2)	1.30%
Location of symptom onset				
Home	78.2* (93)	73.8* (48)	83.3‡ (47)	70.60%
Street	5.9 (7)	4.6 (3)	7.4 (4)	11.80%
Work	0.8 (1)	1.5 (1)	0 (0)	11.10%
Other places	15.1 (18)	20.0 (13)	9.3 (6)	6.50%
Time of day	- \ -/	\ -/		
Morning	44.4 (40)	40.0 (20)	50.0 (21)	40.10%
Afternoon/evening	21.1 (19)	18.0 (9)	25.0 (10)	26.60%
Night	34.4 (31)	42.0 (21)	25.0 (12)	33.20%
Patient/family members' first read				
Call physician/ambulance	67.8* (59)	85.0* (34)	53.2‡ (27)	30.50%
Go directly to hospital	32.2 (27)	15.0 (6)	46.8 (23)	69.50%
Symptoms	( )		()	
Typical	51.9* (126)	28.4* (21)	62.1* (44)	86.90%
Atypical	48.1 (117)	71.6 (53)	37.9 (73)	13.10%
Time from symptom onset to read				
<1 h	65.9 (27)	53.3 (8)	73.1 (19)	58.70%
1-3 h	9.8 (4)	20.0 (3)	3.8 (1)	15.50%
>3 h	24.4 (10)	26.7 (4)	23.1 (6)	25.70%
Time from symptom onset	()		2011 (0)	2011 0 / 0
to doctor's arrival\$				
<1 h	85.2 (23)	80.0 (16)	100 (8)	79.20%
1-3 h	3.7 (1)	5.0 (1)	0 (0)	8.30%
>3 h	11.1 (3)	15.0 (3)	0 (0)	12.50%
Time symptom onset/transport	11.1 (0)	10.0 (0)	0 (0)	12.0070
<1 h	88.0 (22)	75.0 (6)	94.1 (16)	72.70%
1-3 h	8.0 (2)	25.0 (2)	0 (0)	9.10%
>3 h	4.0 (1)	0 (0)	5.9 (1)	18.20%

\*P<.0001. †P<.001. ‡P<.01. \$Symptoms, reaction: n=265. IISymptoms, arrival doctor: n=84; symptoms, arrival transport: n=80.

location when symptoms first appeared was also important, with mortality increasing when symptom onset began at home or elsewhere (primarily in institutions). Calling a doctor or an ambulance was also associated with higher mortality. Presence of typical symptoms was associated with lower mortality.

- Prehospital mortality. Statistically significant associations were the same as for overall mortality at 28 days.

- In-hospital mortality. The patient's location at symptom onset, the patient's/family member's first actions and the presence of atypical symptoms were associated with increased mortality.

Table 3 shows the results of the logistic regression analysis after adjusting for several confounders.

Atypical symptoms and living in an institution were independently associated with higher mortality at 28 days. Going directly to the hospital was associated with lower mortality. Results for prehospital and in-hospital mortality were similar, except in institutionalized patients. Only the presence of atypical symptoms was independently associated with in-hospital mortality.

#### DISCUSSION

The results of this observational study suggest that, of the different aspects studied here, having typical symptoms and going directly to the hospital are the most important determinants of improved survival in AMI patients. It is likely that the time taken by the patient to associate the pain experienced with a serious

	Total 28-day, OR (95% CI)	Prehospital, OR (95% CI)	In-hospital, OR (95% CI)
Living conditions			
Living alone	1	1	1
With other family members	2.77 (0.53-14.39)	1.40 (0.13-15.50)	2.86 (0.33-24.62)
Institutionalized	9.47 (1.05-84.9)	20.75 (0.95-454.11)	9.90 (0.40-242.64)
Patient/family member's first reaction	· · · · ·		· · · · ·
Call doctor/ambulance	1	1	1
Go directly to hospital	0.32 (0.17-0.59)	0.11 (0.03-0.40)	0.48 (0.23-1.03)
Symptoms	· · · · ·		, , , , , , , , , , , , , , , , , , ,
Typical	1	1	1
Atypical	5.52 (2.90-10.50)	14.68 (5.19-41.06)	3.87 (1.70-8.83)

\*OR indicates odds ratio; CI, confidence interval.

Model for total 28-day mortality adjusted for gender, age, smoking habit, and previous AMI.

Model for prehospital mortality adjusted for gender, age, angina, and previous AMI.

Model for in-hospital mortality adjusted for gender, age, hypertension, smoking, angina, and previous AMI.

illness, to decide to call an ambulance or request medical attention at home, and possible delays in accessing medical care, are largely responsible for these results. In 1997-1998, when this study was performed, the current care plan, which includes the use of paramedic ambulances, had not been fully implemented in Gerona province. In 1997, the results of a hospital register analysis suggested that the prehospital delay detected was in part due to the functioning of the health care system and in part due to the characteristics of the patients studied. That study indicated that the great majority of patients arrived at the hospital after calling their doctor and in their own vehicle.<sup>7</sup>

As shown by the IBERICA study,<sup>8</sup> the epidemiology of ischemic heart disease in the study area is similar to that in other parts of Spain, in which it was observed that the difference in mean incidence rates for Gerona and for Spain as a whole did not exceed 15%. The proportion of out-of-hospital mortality is also similar in all areas, at around 30%. The sociodemographic, clinical and treatment characteristics of patients in the present study also coincide with those in the literature, in studies of both out-of-hospital and in-hospital mortality.<sup>8-11</sup>

Patients who died within an hour of symptom onset (n=179, or 65% of the 274 patients who died before reaching the hospital) were excluded principally because the suddenness of death left little opportunity for diagnosis and treatment. This criterion for excluding patients also concurs with the most frequently used definitions of sudden death.<sup>12</sup> The difficulty of interviewing relatives and the fact that there are often no witnesses to the death also usually means that there are fewer details available of the actions taken after symptom onset. In this study, the majority of those who died before reaching the hospital died within an hour of symptom onset,

although the remaining 35% still constitutes a substantial proportion of these patients, and this is precisely the type of patient in which attitudemodifying interventions in the patient's immediate circle might be beneficial. A sensitivity analysis which included patients who reached the hospital but who died within an hour of symptom onset (n=179) did not produce any changes in the data in tables 2 and 3.

Making defibrillators available in public places is still a controversial issue in Spain, although recent studies in 24 regions of the USA have confirmed that when defibrillators are made available in this way, and when availability is coupled with the provision of community volunteers who are trained in their use, survival can increase amongst patients experiencing an AMI in a public place.<sup>13</sup> In the present study, in the majority of patients who died early, symptom onset occurred in the place of residence, and not in a public place; in such cases, the prompt arrival of a paramedic ambulance is decisive, as defibrillation is the most frequently needed intervention in these cases.<sup>14,15</sup>

In this group of patients, recognition of the urgency of the situation and the actions taken by patients, family members, caregivers and health care services, might be presumed to lead to quicker access to resources, which in turn could lead to a reduction in mortality.<sup>16</sup> However, in studies in the United States over the last decade, no improvement in the delay between AMI symptom onset and medical helpseeking has been observed, with the delay remaining close to 2 h.<sup>17</sup>

In the present study, the majority of people who died in places other than the street, work or at home were in institutions (results not shown). This finding is difficult to interpret without data on co-morbidity, particularly psychiatric co-morbidity, in institutionalized patients. Although a recently published study using representative data from the Community of Madrid suggested that people living in residences for the elderly had, in general, a high degree of autonomy and a low need for care,<sup>18</sup> other studies indicate that these facts may have more to do with less efficient services.<sup>19</sup>

In Spain, people living alone or those who go to the hospital by their own means have better survival rates. Living alone may mean that patients need to rely more on their own resources and to seek help quickly, leading to lower mortality. Some studies have suggested that people who take longer to seek help do not attach sufficient importance to symptoms.<sup>20</sup> In other countries, it has been observed that time from symptom onset to cardiac monitoring increases when people travel to the hospital using their own transport as opposed to going by ambulance.<sup>21</sup> Recent guidelines on the management of AMI patients with an elevated ST segment (American College of Cardiology/American Heart Association) recommend that patients with chest pain should use ambulances or medical transport, as this has been shown to improve survival and lead to earlier reperfusion. It should be noted that 1 out of every 300 patients with chest pain who are taken to the hospital in a private vehicle suffers a heart attack during the transfer journey.<sup>17</sup>

The time between symptom onset and the first actions taken (n=265), the arrival of a clinician (n=84), and the arrival of an ambulance (n=80) were not significantly related with prehospital mortality. The large number of missing responses to these questions is one of the study's main limitations, although the responses to these questions were used in only one part of the study, and were not included in the explanatory model of mortality. It has also been found that even when it is possible to obtain exhaustive information on the length of delay, the data is highly subjective and subject to recall bias, particularly when there is a delay in collecting the data. In the present study, these data were collected 1.5-2 years after the event.<sup>22</sup>

Prehospital mortality occurring more than one hour after symptom onset accounted for over 30% of overall mortality at 28 days (274 of 624 deaths). Even a small reduction in prehospital mortality could have a substantial impact on overall AMI-related mortality. However, educational campaigns to encourage patients to make prompt use of health care services when AMI symptoms appear have been shown to have an uncertain impact, and there appears to be a need for more individualized health care education or campaigns which focus on particular groups, such as the elderly or those with additional co-morbidities<sup>23,24</sup>.

Future studies should continue to analyze the factors associated with AMI-related prehospital mortality as this remains an important public health challenge, despite the inauguration of primary care centers with defibrillators and the increased availability of and in improvements in, paramedic ambulances. Qualitative studies, such as those performed in the United Kingdom,<sup>25,26</sup> could also provide more information on the motives behind the delays and on the nature of the delays themselves.

This study has shown that, in the absence of paramedic ambulances, patients with AMI who go directly to the hospital and those with typical symptoms show greater survival at 28 days and reduced prehospital mortality. Being institutionalized, on the other hand, is associated with increased mortality at 28 days.

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