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Initial complications and factors related to prehospital mortality in acute myocardial infarction with ST segment elevation

Fernando Rosell-Ortiz,[1] Francisco J Mellado-Vergel,[2] Patricia Fernández-Valle,[1] Ismael González-Lobato,[1] Manuela Martínez-Lara,[1] María M Ruiz-Montero,[1] Francisco Romero-Morales,[1] Itziar Vivar Díaz,[1] Ángel García-Alcántara,[3] Javier García del Águila[1]

[1]Empresa Pública de Emergencias Sanitarias de Andalucía. Andalusian Health Ministry, Andalucía, Spain
[2]Department of Urgencias, Hospital el Toyo, Almería, Spain
[3]Intensive Care Unit, Hospital Clínico, Málaga, Spain

Correspondence to
Dr Fernando Rosell-Ortiz, Carretera de Ronda 226, 6ª planta, Servicio Provincial 061, 04005, Almería, Empresa Pública de Emergencias Sanitarias de Andalucía. Group on Emergency Cardiac Care, Andalusian Health Ministry, Andalucía, Spain; frosell@al.epes.es

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ABSTRACT

Objective Hospital mortality in myocardial infarction ST-elevation myocardial infarction has decreased in recent years, in contrast to prehospital mortality. Our objective was to determine initial complications and factors related to prehospital mortality in patients with acute myocardial infarction with ST segment elevation (STEMI).

Methods Observational study based on a prospective continuous register of patients of any age attended by out-of-hospital emergency teams in Andalusia between January 2006 and June 2009. This includes patients with acute coronary syndrome-like symptoms whose initial ECG showed ST elevation or presumably new left bundle branch block (LBBB). Epidemiological, prehospital data and final diagnostic were recorded. The study included all patients with STEMI on the register, without age restrictions. Forward stepwise logistic regression analysis was performed to control for confounders.

Results A total of 2528 patients were included, 24% were women. Mean age 63.4±13.4 years; 16.7% presented atypical clinical symptoms. Initial complications: ventricular fibrillation (VF) 8.4%, severe bradycardia 5.8%, third-degree atrial-ventricular (AV) block 2.4% and hypotension 13.5%. Fifty-two (2.1%) patients died before reaching hospital. Factors associated with prehospital mortality were female sex (OR 2.36, CI 1.28 to 4.33), atypical clinical picture (OR 2.31, CI 1.21 to 4.41), hypotension (OR 4.95, CI 2.60 to 9.20), LBBB (OR 4.29, CI 1.71 to 10.74), extensive infarction (ST elevation in ≥5 leads) (OR 2.53, CI 1.28 to 5.01) and VF (OR 2.82, CI 1.38 to 5.78).

Conclusions A significant proportion of patients with STEMI present early complications in the prehospital setting, and some die before reaching hospital. Prehospital mortality was associated with female sex and atypical presentation, as pre-existing conditions, and hypotension, extensive infarction, LBBB and VF on emergency team attendance.

Key messages

What is already known about this subject?

- The initial complications and prognostic factors associated with in-hospital mortality in STEMI patients are well known, but the rate of complications and mortality during the out-of-hospital phase are not well documented.

What does this study add?

- In this retrospective study of the only Andalusian prehospital emergency service, among 2528 patients with STEMI or left bundle branch block, there were a significant number of complications including ventricular fibrillation (8.4%) and bradycardia (6%); 2.1% died prior to hospital arrival.
- An early and adequate prehospital management by emergency medical service (EMS) is crucial for final prognosis of these patients. Training of EMS must include both an adequate recognition of warning signs as treatment of these severe initial complications.

INTRODUCTION

Mortality rates in ST-elevation acute myocardial infarction (STEMI) have decreased significantly in recent decades.[1 2] The quantity and quality of reperfusion therapy administered are key factors in this advance,[3] although not the only ones, since decreased mortality rates have also been documented in patients not receiving reperfusion therapy.[4] Global figures on decreased rates also hide significant variability in hospital mortality between different countries and groups of patients.[5 6]

However, prehospital mortality has not decreased to the same extent in patients with STEMI, some of whom die before reaching the hospital, most without having received medical care. They are usually not included in hospital-based mortality records and, obviously, such deaths are not included in clinical trial databases.[7] Out-of-hospital attention by specific emergency medical services (EMS) has for years been a class IA recommendation in the practice guidelines of the European Society of Cardiology and the American College of Cardiology Foundation/American Heart Association.[8 9] The initial complications and prognostic factors associated with hospital mortality in STEMI are well documented,[10 11] but not for out-of-hospital mortality after contacting the emergency services. The objective of this study was to analyse the initial complications and factors related to prehospital mortality in victims of STEMI.

METHODS

Observational study. We retrospectively analysed a continuous register of cases attended by

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out-of-hospital emergency teams in Andalusia, between January 2006 and June 2009. The Andalusian population is 8.5 million, and its public health system integrates 28 hospitals with different capabilities and one prehospital emergency service, the Public Health Emergency Company (EPES). This involves ambulances with a physician on board, responsible for performing prehospital thrombolysis and/or direct transport to a cath-lab depending on hospital capabilities. The characteristics of the EPES register have been previously described.[12] Briefly, the primary objectives were to evaluate the characteristics, management and outcomes of patients with ST-elevation acute coronary syndrome (ACS) attended by EPES emergency teams. The register is used as a quality tool to evaluate the process of care and final results of assistance provided by its emergency teams. The register prospectively includes all consecutive cases of suspected ACS, regardless of age, attended in the field by EPES emergency teams and diagnosed with STEMI according to initial ECG presenting ST-segment elevation ≥1 mm in two or more contiguous leads (≥2 mm in the case of precordial leads V1-3), or new left bundle branch block (LBBB) and confirmed hospital diagnosis of STEMI. Data collection includes demographics, prehospital management, in-hospital management and status at discharge. One-month and 1-year patient follow-up are regularly performed. The register follows the STROBE Statement to evaluate data and results.[13]

For each case, we extracted demographic and clinical data including vital constants, Killip class and major complications recorded during the prehospital phase: ventricular fibrillation (VF), atrial ventricular (AV) block, symptomatic bradycardia and sustained hypotension. The clinical picture giving rise to each EMS call was classified as typical (central chest pain >20 min, with or without accompanying vegetative symptoms (nausea, vomiting, sweating) and/or radiation to the jaw, left shoulder or arm) or atypical, when chest pain was not the predominant symptom (syncope, dyspnoea, unconsciousness, atypical chest pain and ill-defined symptoms). We accessed hospital data, via electronic health records, to verify in-hospital diagnosis in patients admitted to hospital. This confirmation was not possible in those patients who died before reaching the hospital.

The study protocol was approved by the EPES research ethics committee. Patient data management was performed according to Spanish Law on confidentiality and data protection. The register is indexed by the Spanish Agency for Data Protection.

Descriptive analysis was performed with measures of central tendency for quantitative variables and frequency distributions for qualitative variables. On comparing the variable prehospital mortality, we assessed differences in the distribution of the independent variables using Student's t test for quantitative variables (age) and χ^2 or Fisher's exact test for samples with less than five values. Finally, we performed three multivariate logistic regression analyses using the forward stepwise method with prehospital mortality as the dependent variable in order to control for possible confounders. The first two regression analyses were considered necessary because a key variable, initial ECG, could yield two important but mutually exclusive results with prognostic value: the presence of LBBB or ST elevation in five or more leads. The third regression analysis included both LBBB and ST-elevation in the model.

We included those variables with a p value of <0.05 in the bivariate analysis, by forward stepwise method, including OR and 95% CIs and clinically relevant variables. Differences with a p value less than 0.05 were considered statistically significant.

Table 1 Demographic and clinical data of the study population

Variables	N (%) 2528 (100)
Male sex	1925 (76.1)
Age in years (mean±SD; median, IQR)	63.4±13.4; 64 (53–74)
Men	61.3±12.9; 61 (51.5–71)
Women	70.7±13; 73 (62–80)
Symptom duration (min) to call (median and IQR)	43 (14–113)
Symptom duration to call ≤60 min	1405 (60.9)
Cardiovascular risks factors	2.288 (90.8)
Smoker	1.029 (40.8)
Dyslipidemia	900 (35.7)
Diabetes	701 (27.8)
Hypertension	1308 (51.9)
Comorbidities	
History of angina	283 (11.4)
Previous myocardial infarction	311 (12.5)
Previous heart failure	34 (1.4)
Reason for calling: typical chest pain	2114 (83.8)
Emergency team diagnosis	
Anterior myocardial infarction	993 (39.3)
Inferior myocardial infarction	1418 (56.1)
Unspecified myocardial infarction	117 (4.6)
VF during prehospital care (one or more episodes)	213 (8.4)
Symptomatic bradycardia	147 (5.8)
Third-degree atrial ventricular block	61 (2.4)
Systolic BP ≥90 mm Hg	2174 (86.5)
Killip class I	2207 (87.7)
ST elevation in <5 leads	1937 (85.1)
LBBB on initial ECG	65 (2.6)

All values are number (N) and percentage (%) unless otherwise indicated.
LBBB, left bundle branch block; VF, ventricular fibrillation.

RESULTS

The study included 2528 patients: 1925 (76.1%) men and 603 (23.9%) women. Mean age was 63.4±3.4 years. Fifty-two patients (2.1%) died before reaching hospital.

Epidemiological and clinical variables of the study population on initial attention are summarised in table 1. Clinical presentation according to the description provided by the caller was classified as typical in 2118 (83.6%) and atypical in 410 (16.4%) cases. The atypical presentations and their relationship with prehospital mortality are described in table 2.

During EMS attendance, 213 (8.4%) patients had one or more episodes of VF requiring immediate treatment; of these, 199 (93.4%) reached hospital alive.

Table 2 Atypical clinical presentation and mortality during prehospital phase

Variables n (%)	Atypical presentation N=410	Deaths during prehospital phase N=26 (6.34)
Syncope	92 (22.4)	9 (34.6)
Atypical chest pain	87 (21.2)	3 (11.5)
Dyspnoea	78 (19.0)	5 (19.2)
Unconscious	77 (18.7)	7 (26.9)
Non-specific malaise	52 (12.7)	2 (7.7)
Dizziness	24 (5.9)	–

Table 3 Significantly different clinical and epidemiological variables between patients who were admitted and those did not reach hospital alive

Variables	Survivors 2476 (97.9%)	Non-survivors 52 (2.1%)	p Value
Age in years (mean±SD)	63.3±13.4	68.4±13.3	<0.004
Female sex	578 (23.3)	25 (38.5)	<0.001
Atypical symptom presentation	384 (15.5)	26 (50)	<0.001
Non-smoker	1448 (58.5)	44 (84.6)	<0.001
No dyslipidemia	1573 (63.5)	48 (92.3)	<0.001
Systolic BP	125.5±38.5	67.4±60.3	<0.001
Systolic BP <90 mm Hg	313 (12.6)	27 (51.9)	<0.001
Symptom duration to call (median and IQR)	43 (14–113)	17.5 (4–73)	0.009
Heart rate (mean, SD)	73±24	70.6±52	<0.001
Heart rate >100 bpm	230 (9.3)	11 (21.2)	0.014
ST elevation in ≥5 leads	325 (13.1)	13 (25)	<0.014
LBBB on initial ECG	58 (2.3)	7 (13.5)	<0.001
Killip class >I	295 (11.9)	15 (28.8)	<0.001
Previous myocardial infarction	1082 (43.7)	28 (53.8)	0.038
VF	199 (8)	14 (26.9)	<0.001
Symptomatic bradycardia	140 (5.6)	7 (13.5)	0.029
Complete atrial ventricular block	56 (2.3)	5 (9.6)	0.008

Bivariate analysis.
LBBB, left bundle branch block, VF: ventricular fibrillation.

Bivariate analysis comparing patients who reached hospital alive (survivors) versus non-survivors is shown in table 3. There were no significant differences between these groups regarding history of heart disease, angina 11.3% vs 13.7, p=0.5, infarction 12.4% vs 17.6% p=0.3, heart failure 1.4% vs 2%, p=0.5, respectively, for survivors and non-survivors, or between the time intervals call—emergency team arrival (15 (10–22) vs 13 (8.25–22.75), p=0.161, expressed as median and IQR in minutes), respectively, for survivors and non-survivors. However, the difference in clinical status and initial complications between the two groups was significant (table 3).

As mentioned, two multivariate analyses were performed according to whether initial ECG showed the presence of LBBB or ST elevation in five or more leads, which are mutually exclusive variables. In the first analysis with the variable ST elevation, 2294 patients were included, with a loss of 234 patients (9.2%), among which were the 65 (2.6%) patients with initial ECG showing LBBB. In the second analysis, with the variable LBBB, 2497 patients were included, with 31 (1.2%) cases lost. The variables associated with prehospital mortality in both logistic regression analyses are shown in tables 4 and 5. Finally, a third multivariate regression analysis was performed, shown in table 6, which included both ECG conditions (ST-elevation in ≥5 leads and LBBB).

Table 4 Multivariate logistic regression analysis

Variables	OR	95% CI	p Value
Female sex	2.71	1.42 to 5.19	0.002
Atypical clinical presentation	2.28	1.14 to 4.54	0.019
Systolic BP <90 mm Hg	4.85	2.48 to 9.48	0.000
Heart rate >100 bpm	2.54	1.18 to 5.47	0.016
VF during prehospital care	1.25	1.25 to 5.63	0.011
ST elevation in ≥5 leads	2.53	1.28 to 5.01	0.007

Factors related with prehospital mortality, including the variable ST-elevation in ≥5 leads. Total no. of patients: 2294.
VF, ventricular fibrillation.

Table 5 Multivariate logistic regression analysis

Variables	OR	95% CI	p Value
Female sex	2.36	1.28 to 4.33	0.006
Atypical clinical presentation	2.31	1.21 to 4.41	0.01
Systolic BP <90 mm Hg	4.95	2.60 to 9.20	0.000
VF during prehospital care	2.82	1.38 to 5.78	0.004
LBBB on initial ECG	4.29	1.71 to 10.74	0.002

Factors related with prehospital mortality, including the variable LBBB on initial ECG. Total no. of patients: 2497.
LBBB, left bundle branch block; VF, ventricular fibrillation.

DISCUSSION

The proportion of STEMI patients who die before reaching the hospital, after contacting the EMS, is disturbingly high. Despite a significant reduction of in-hospital STEMI mortality, to less than 10% in patients younger than 75 years,[5 14] a mortality rate slightly higher than 2% in the prehospital phase represents a major challenge in overall attendance of patients with STEMI, especially considering that there were no significant differences in EMS arrival time between survivors and non-survivors.

When atypical clinical presentation is the reason to request EMS assistance, caution should be exercised in selecting the EMS resource. The limitations of chest pain assessment in suspected ACS are well known.[15] Also important is the problem of atypical clinical STEMI presentation and its influence on the diagnosis and treatment of these patients in hospital emergency departments.[16] Emergency services should not expect typical chest pain as the definitive symptom of STEMI in all cases.

Previous cardiac events were not significant predictors of prehospital mortality; they are probably more related with medium-term and long-term mortality.[17]

A relatively unexpected finding was the high proportion of VF as a prehospital complication, significantly higher than those reported in strictly hospital series, including series with current reperfusion therapies.[18] Our study revealed some encouraging data. Of patients with STEMI, 8% presented VF and were initially saved on receiving prompt EMS attention. Finally, 90% of these patients were alive on hospital arrival.

We also found a significant proportion of other serious complications such as severe bradycardia and AV block. Hospital series data corresponding to the era of reperfusion therapy show declining trends in severe bradycardia and AV block as

Table 6 Multivariate logistic regression analysis

Variables	OR	95% CI	p Value
Female sex	2.49	1.25 to 4.97	0.009
Atypical clinical presentation	2.97	1.455 to 6.094	0.003
Systolic BP <90 mm Hg	4.74	2.359 to 9.540	0.000
VF during prehospital care	2.24	1.000 to 5.100	0.05
LBBB on initial ECG	4.53	1.140 to 18.046	0.03
ST elevation in ≥5 leads	2.64	1.260 to 5.480	0.009

Factors related with prehospital mortality, including the variable LBBB on initial ECG. Total no. of patients: 2102. LBBB, left bundle branch block; VF, ventricular fibrillation.

complications and their association with poor prognosis.[19 20] The Worcester Heart Attack Study of 2005, published 1 year before the start of our study period, indicated that complete AV block as a complication of STEMI was present in 1.9% of all patients.[20] The most recent series, from a single tertiary centre, reported an incidence of 2.7% in patients referred for primary angioplasty, although the inclusion criteria covered the first 48 h after symptom onset. AV block remains a marker of poor prognosis in 30-day mortality.[21] In our series, with a lower mean age than the above studies, complete AV block was present in 2.4% of patients. This group, along with the nearly 6% of patients with severe bradycardia, require advanced clinical management in the field during the prehospital phase.[8 9 22]

Some of the factors related to prehospital mortality, such as known cardiovascular risk factors, contribute little to EMS care in the field, but others do have greater clinical significance for onsite assistance.

According to univariate analysis, the profile of patients with increased risk of prehospital mortality was a woman aged 68 years or higher, without known cardiovascular risk factors or ischaemic heart disease, with atypical symptoms of relatively short evolution, extensive infarction or LBBB on initial ECG and electrical or hemodynamic instability.

Female sex remained a significant predictor in forward stepwise regression analysis. Different perceptions and reactions to ACS symptoms may play a role in this.[23]

The main variables associated with mortality, advanced age, Killip class >I, hypotension and tachycardia are well known since the publication of the GUSTO I study[10] and the risk of death in the first 30 days has been confirmed in clinical practice.[24] In our series, the initial complications and factors associated with mortality defined those patients at risk of immediate death. Within these variables, some of them are warning signs (atypical presentations, number of leads involved) but others could promote changes or improvements in treatment over the prehospital phase. This is the case with hypotension, one of the strongest predictors of mortality, which may require a more aggressive initial treatment.

Interestingly, some of the variables identified in this study may serve as criteria of quality regarding EMS attention. Prehospital series with low proportions of atypical presentation or initial complications may reflect selection bias in the population attended by an EMS.

It is well stated that decision on reperfusion strategy[8] and the type of hospital are key factors for final prognosis in STEMI.[25] Just before these actions, there is an important area for improvement. Mortality in the prehospital phase must be considered part of the overall mortality associated with this process.

The main limitations of the study are that it drew its data from a single database and was performed retrospectively, which limits its findings to the study population and period. However, it included a large unselected and representative sample, registered prospectively, and its results were consistent with those of recent studies performed elsewhere. The mortality rate reported here only refers to patients receiving EMS attention during the prehospital phase. The study did not include patients who died without receiving such assistance. This group of patients usually receive a generic diagnosis of cardiac arrest as the cause of death, without precise identification of the actual aetiology. Historically it is assumed that the ultimate cause of out-of-hospital cardiac arrest in four out of five cases is of cardiac origin, primarily acute ischaemic heart disease,[26 27] but the only way to obtain rigorous confirmation of this would be to perform postmortem diagnoses in population-based series.

There is also the possibility that the cause of death in some patients was not in fact due to STEMI because there are other immediately life-threatening diseases that can present ST elevation on ECG,[28] but they are exceptional and, in our opinion, would hardly affect the statistical results.

Finally, although the data on mortality are from the period 2006–2009, there have been no significant changes in international recommendations for the attention of patients since then.

In summary, STEMI mortality in patients who reach the hospital has decreased significantly in recent years, even in those not receiving reperfusion therapy. However, the initial complications of hypotension, severe bradycardia, AV block and VF are frequently observed, and the rate of prehospital death remains high. An early and adequate prehospital management by EMS is crucial for final prognosis of these patients. Training of EMS must include both an adequate recognition of warning signs as treatment of these severe initial complications.

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Competing interests None.

Patient consent Obtained.

Ethics approval The registry is registered with the Spanish Data Protection Agency. The study protocol was approved by the Ethics Committee of our institution (Empresa Pública de Emergencias Sanitarias).

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Notes