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European Heart Journal: Acute Cardiovascular Care 2012 1: 192 originally published online 2 July 2012

DOI: 10.1177/2048872612453923

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Mortality and ST resolution in patients admitted with STEMI: the MOMI survey of emergency service experience in a complex urban area

European Heart Journal: Acute Cardiovascular Care
1(3) 192–199

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DOI: 10.1177/2048872612453923

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Abstract

Background: Since 2001, the urban area of Milan has been operating a network among 23 cardiac care units, the 118 dispatch centre (national free number for medical emergencies), and the county government health agency called Group for Prehospital Cardiac Emergency.

Methods and results: In order to monitor the network activity, time to treatment, and clinical outcome, a periodic survey, called MOMI², was repeated two or three times a year. Each survey lasted 30 days and was repeated in comparable periods. Data were stratified for hospital admission mode. We collected data concerning 708 consecutive ST-elevation myocardial infarction (STEMI) patients (male 72.6%; mean age 64.4 years). In these six surveys, we observed a high rate of primary percutaneous coronary intervention (73.2%) and a mortality rate of 6.3%. Using advanced statistical models, we identified age, Killip class, and the symptom onset-to-balloon time as most relevant prognostic factors. Nonparametric test showed that the modality of hospital admittance was the most critical determinant of door-to-balloon time. 12-lead ECG tele-transmission and activation of a fast track directly to the catheterization laboratory are easy action to reduce time to treatment.

Conclusions: The experience of the Milan network for cardiac emergency shows how a network coordinating the community, rescue units, and hospitals in a complex urban area and making use of medical technology contributes to the health care of patients with STEMI.

Keywords

ECG, myocardial infarction, primary angioplasty, statistics, survey, tests

Received: 7 May 2012; accepted: 8 June 2012

Introduction

When the American College of Cardiology/American Heart Association (ACC/AHA) set the gold standard of a door-to-balloon time of 90 minutes for the performance of primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) in 2006, the goal appeared to be very ambitious right from the start.^{1,2} At that time, performance was far below expectations: in the NRMI study, door-to-balloon time was over 120 minutes in nearly 50% of cases.² However, it was understood that cardiologists had to rise to the occasion in view of the compelling mortality data obtained from the GUSTO-IIb and NRMI studies.^{3,4}

Since then, it has been shown that door-to-balloon time is associated with adjusted risk of in-hospital mortality continuously and should therefore be as short as possible, i.e.

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even shorter than the 90-minute benchmark.⁵ In 2009, the ACC/AHA endorsed this conclusion.⁶

Extensive studies have analysed the factors influencing door-to-balloon time and have led to the formulation of a number of strategies designed to reduce it, including activation of the catheterization laboratory (CathLab) while the patients is en route to the hospital, having a central page operator, setting standards for the time staff takes to reach the CathLab, and having an attending cardiologist always on site.⁷ Some of these strategies, such as always having a cardiologist on site, are expensive and may not be feasible in all hospitals.² In 2008, the European Society of Cardiology guidelines for STEMI recommended an efficient ambulance service, planned in such a way that the ambulance could be a place for initial diagnosis, triage, and treatment. In particular, it recommended that ambulances should be equipped with a 12-lead ECG and that ambulance staff should be able either to interpret it or transmit it to experienced staff.⁸

In the county of Milan, in the north of Italy, the coordination of emergency resources servicing 2.9 million inhabitants plus 1 million of daily commuters was centralized in 2001. It consists of a network connecting a hub that receives incoming calls (about 2000 calls/day), variously equipped ambulances, and 23 receiving hospitals, all with cardiology departments and intensive cardiac care units (ICCU), 19 with a 24-hour CathLab service able to perform primary PCI.

In 2006, we started to collect data from the hospitals through five 30–60-day periods named “Month Monitoring Myocardial Infarction in Milan” (MOMI²), an observational study gathering main patient characteristics and other prehospital and in-hospital factors on in-hospital mortality and ST resolution in patients with STEMI.

Methods

Data collection

The data related to all in-patients with STEMI were collected during predefined 30–60-day periods: MOMI^{2.1}, 1–30 June 2006; MOMI^{2.2}, 15 November–15 December 2006; MOMI^{2.3}, 1–30 June 2007; MOMI^{2.4}, 15 November–15 December 2007; MOMI^{2.5} 1–30 June 2008.

Hospital staff filled in a MOMI² standardized electronic case report form and sent it by email to the Biometrics staff at the Politecnico of Milan for inclusion in the MOMI² database.

The data collected were: demographic features (age, gender), presenting signs (blood pressure, heart rate, Killip class at arrival), and symptoms (chest pain, abdominal pain, dyspnoea, syncope, other), history of coronary artery disease, site of infarction, mode of arrival (spontaneous; ambulance with basic life support, i.e. only rescuers on board, BLS; or with advanced life support, i.e. physician/

specialized nurse on board±ECG teletransmission, ALS), time of arrival, symptom onset time, total ischaemic time calculated as the interval between symptom onset and balloon time, in-hospital door-to-ECG time, door-to-balloon time, hospital organization (fast track to CathLab or ICCU), thrombolysis, and outcome (in-hospital survival status; reperfusion efficiency, i.e. ST resolution defined as 70% reduction in ST-segment elevation 1 hour after PCI). Killip class was assigned according to the severity of signs of heart failure: class I, no rales in lung fields and no S3 heart sound; class 2, rales in <50% of the lung fields, presence of S3 or jugular venous distention; class 3, rales in >50% of lung fields; class 4, pulmonary oedema with hypotension.

The data of STEMI patients who underwent primary PCI at the same hospital where they have been admitted were used to assess the relationship between patient characteristics and patient outcomes.

Statistical analysis

Two statistical techniques that are suitable for binary responses were used to analyse the two outcome parameters as a function of the other variables of the dataset: a generalized linear model (GLM) and a generalized additive model (GAM). GLM involved calculations of the probability related to the outcome variables using a logistic regression model. A backward stepwise model selection procedure based on Akaike information criterion and clinical best practice has been performed in order to choose the covariates to include in the model. GAM was adopted in addition to GLM because it was believed that a nonparametric model that did not force the data into a rigidly defined class would provide more information. The dependency of the probability of the outcome variable was estimated in terms of suitable smoothers of the predictors, i.e. natural cubic splines of order three.⁹

An in-depth explorative analysis of the database was conducted with three objectives: (1) to assess dependence patterns between covariates; (2) to study the relationships suggested by clinical know-how from a statistical perspective; and (3) to detect potential variables that can be acted upon in order to improve hospital performance indicators that have proved to be prognostic factors of the two principal outcomes, such as door-to-balloon time. A classification and regression tree (CART) analysis using Gini's impurity index split groups satisfying the 90-min limit for door-to-balloon time or not in terms of mode of arrival and time to first ECG within 10 minutes or not, the limit suggested by AHA/ACC guidelines.¹⁰ Statistical evidence of differences according to the split was evaluated applying the Mann–Whitney nonparametric test and the Fisher Exact test. A random forest analysis¹¹ applied to CART models¹² was performed to assess the discriminatory power of covariates.

Results

Patient characteristics

A total of 708 STEMI patients were observed during the five MOMI² periods. They were mostly middle-aged males (72.6%, mean age 64.4 years) in Killip class I, reporting chest pain. Two-thirds of them arrived in hospital by ambulance (62.5%), mainly in BLS ambulances (22.8%); 18.6% arrived in an ambulance that was able to record and transmit ECG en route. Arrival during off hours was slightly more common than during on hours (54.6%). Most patients were taken to the emergency room first and then to the CathLab (61.5%). Most of them underwent primary PCI (73.2%) and were not given a thrombolytic agent (90.5%; Table 1). There were no important differences among the five MOMI² periods.

Patient outcomes

Predictors of mortality. The in-hospital mortality rate in the total population was 6.3% and in the PCI population it was 5.3%. It diminished over time from 12.8% in MOMI^{2.1} to 3.4% in MOMI^{2.5}.

Backward stepwise model selection procedure and clinical best practice established that the main patient characteristics that explained survival by means of a GLM were Killip class, age, and total ischaemic time. The in-hospital survival probability was inversely related to age and total ischaemic time; the relationship was stronger when the patient was in Killip class 2 or more. According to GAM analysis, the inverse relationship with age continues until the ninth decade, whereas the relationship with total ischaemic time holds true until approximately 400 minutes (Figure 1).

Predictors of ST resolution. ST resolution was achieved in 76.4% of patients. An improvement over time was recorded from MOMI^{2.2} (70.9%) to MOMI^{2.4} (84.3%), but in MOMI^{2.5} it was down to 71.7% (this variable was not recorded in MOMI^{2.1}).

GLM established that door-to-balloon time and symptom onset-to-door time accounted for ST resolution (Figure 2). GAM analysis showed that door-to-balloon time had a continuous inverse relationship with ST resolution, whereas symptom onset time was closely related up to about 480 minutes and then levelled off (Figure 3).

Predictors of door-to-balloon time. On average, door-to-balloon time was 95.4 minutes. In 64% of cases, it was below the 90-min benchmark. Door-to-balloon time improved during the five MOMI² periods: the proportion of patients in whom door-to-balloon time was lower than 90 minutes increased from 54% in MOMI^{2.1} to 75% in MOMI^{2.5}.

The CART analysis (a statistical method exploring the discriminating power of each variable in affecting the binary

Table 1. Patient characteristics and outcomes

	Population (n=708)
Gender	
Males	514 (72.6)
Females	194 (27.4)
Age (years)	64.4±12.7
Killip class	
1	465 (78.9)
2	72 (12.2)
3	31 (5.3)
4	21 (3.6)
NA	119
Symptoms	
Chest pain	603 (86.0)
Abdominal pain	18 (2.6)
Dyspnoea	29 (4.1)
Syncope	11 (1.6)
Other	19 (2.7)
ACC	21 (3.0)
NA	7
ECG lesion site	
Anterolateral	307 (52.7)
Other	276 (47.3)
NA	125
Mode of arrival	
Spontaneous	262 (37.5)
BLS	159 (22.8)
ALS	60 (8.6)
ALS+teleECG	130 (18.6)
Transferred	87 (12.6)
NA	10
Hour of arrival	
On hours	316 (45.4)
Off hours	380 (54.6)
NA	12
Total ischaemic time (mins)	180 (126.5-290)
Door-to-emergency room ECG time (mins)	6 (3-15)
Door-to-balloon time (mins)	73 (45-112)
Percutaneous coronary intervention	
Primary	499 (73.2)
Rescue	15 (2.2)
Other	38 (5.6)
No	130 (19.0)
NA	26
Thrombolysis	
Yes	54 (8.7)
No	561 (90.5)
Prehospital	5 (0.8)
NA	88
Survival status at discharge	
Death	42 (6.3)
Alive	625 (93.7)
NA	41
ST resolution	
Yes	402 (76.4)
No	124 (23.6)
NA	182

Values are n (%), mean±SD, or median (interquartile range). ACC, American College of Cardiology; ALS, advanced life support; BLS, basic life support; NA, not applicable.

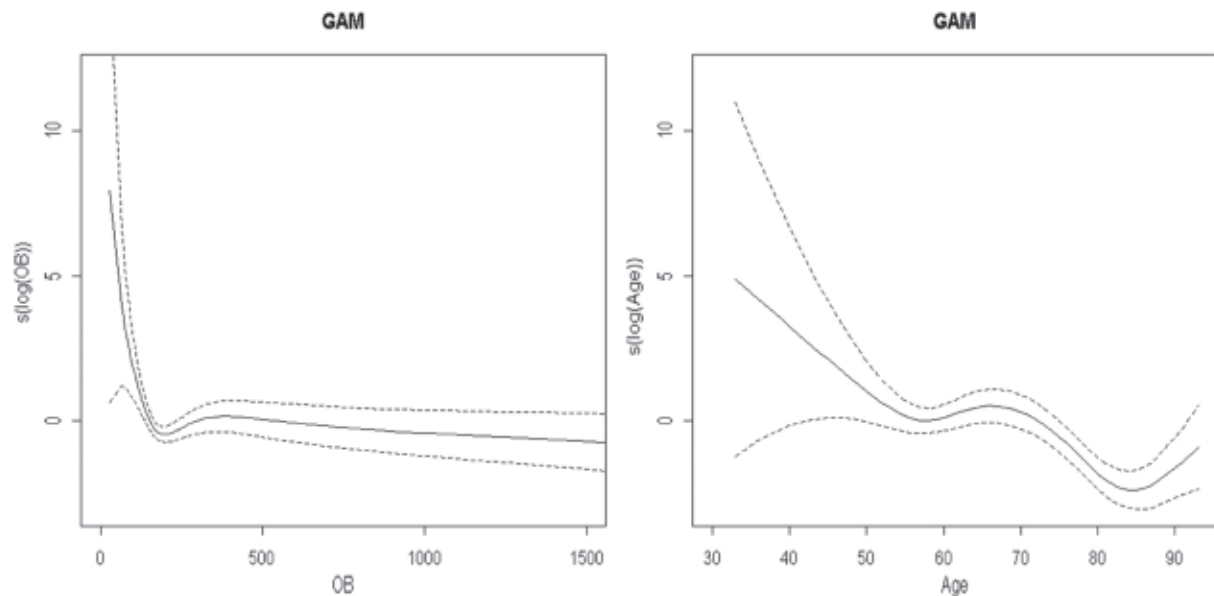


Figure 1. Estimated smoother for total ischaemic time (left) and age (right) in a generalized additive model (GAM) for in-hospital survival
OB, onset-to-balloon time. Pointwise standard errors are included.

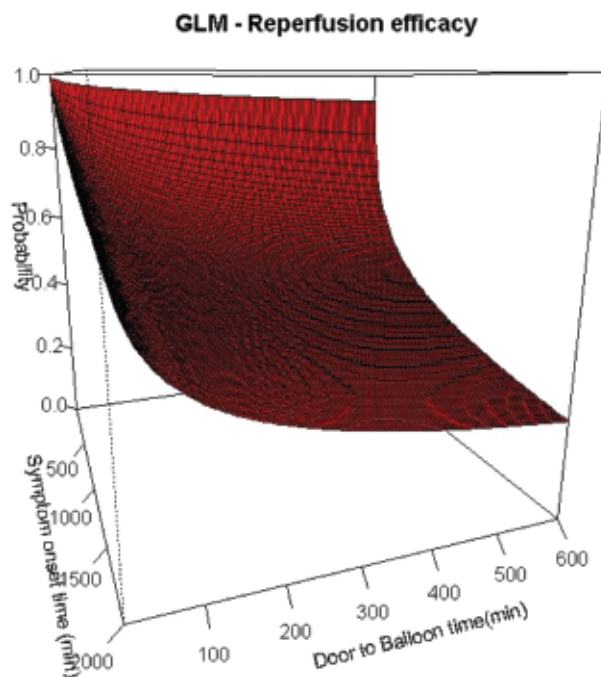


Figure 2. Reperfusion efficacy surface estimated by generalized linear model (GLM)

outcome) identified four predictors of door-to-balloon time: two major predictors, i.e. mode of arrival and time to first ECG; and two minor predictors, i.e. in-hospital fast track organization and time of arrival. Door-to-balloon time was significantly lower in the subgroup of patients who arrived in an ALS ambulance equipped with ECG transmission

device as compared to all other subgroups (Kruskal–Wallis test $p < 0.00001$; Figure 4).

Analogously, door-to-balloon time was significantly lower in the subgroup of patients in whom the first ECG was performed within 10 minutes from arrival in emergency room as compared to the subgroup with ECG after more than 10 minutes (Wilcoxon test $p < 0.00001$; Figure 5).

There was a masking effect between two covariates detected by the classification analysis: the mode of arrival and the time to first ECG. The Fisher Exact test, performed on the contingency table of the way of hospital arrival and a variable indicating whether the time of first ECG was within the first 10 minutes or not, showed that there was a strong dependence between these two covariates ($p < 0.00001$).

Discussion

The experience of the Milan network for cardiac emergency shows how a network coordinating the community, rescue units and hospitals in a complex urban area and making use of medical technology contributes to the health care of patients with STEMI.

Most patients received reperfusion therapy (82%), mainly PCI (73%). In-hospital mortality was low (6.3%) and door-to-balloon time was less than 90 min in nearly 64% of cases. These rates are not quite as good as in other countries, although in other places the networks consist of a smaller numbers of hub-and-spoke centres. In the Austrian acute PCI registry 2005–2007,¹³ the in-hospital mortality rate after primary PCI was 5.1%, the PCI rate

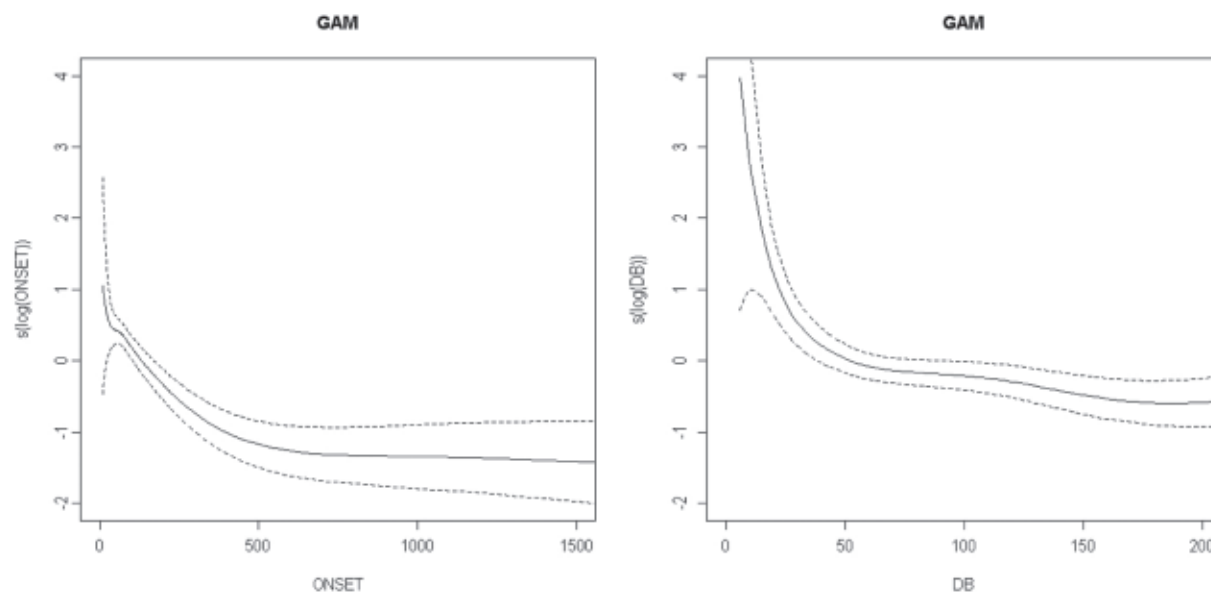


Figure 3. Estimated smoother for symptom onset-to-door time (left) and door-to-balloon time (right) in a generalized additive model (GAM) for reperfusion efficacy
DB, door-to-balloon time. Pointwise standard errors are included.

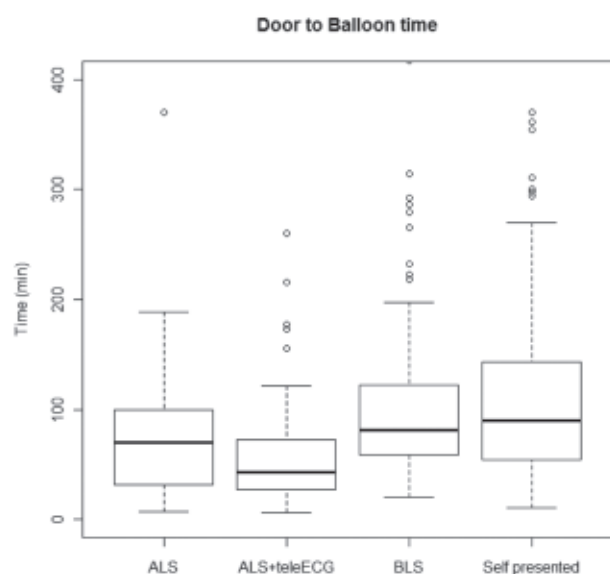


Figure 4. Flanked boxplots of distributions of the door-to-balloon time in patients stratified by mode of admission
ALS, advanced life support; BLS, basic life support.

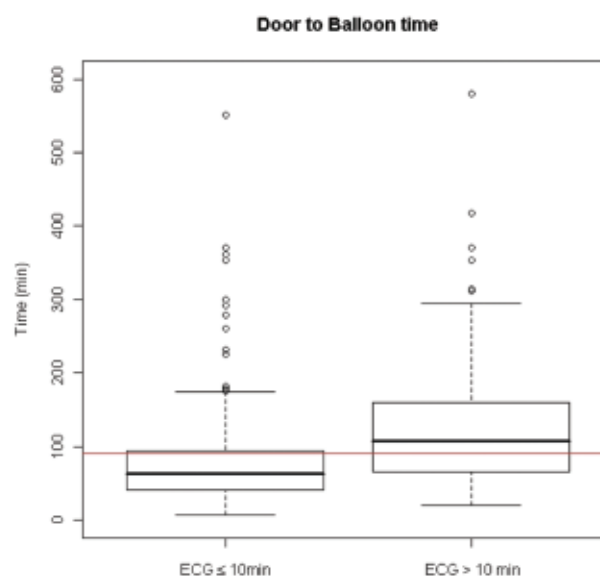


Figure 5. Flanked box plots of distributions of the door-to-balloon time in patients with the first ECG before or after 10 minutes

improved from 83.5 to 92.4% over the observation period, and median duration of door-to-balloon time was 60 min and diminished down to 53 min; in Belgium between 2007 and 2009,¹⁴ 86.4% of patients with STEMI underwent primary PCI and in-hospital mortality was 5.9%; in another Italian region, Umbria, the STEMI registry 2006–2008¹⁵ reported in-hospital mortality of 5.9%, a primary PCI rate of 45.9%, and mean door-to-balloon time 156 min.

We identified a number of non-modifiable and modifiable variables related to the outcome parameters. The non-modifiable factors were age and the severity of myocardial infarction expressed as Killip class, which were related to in-hospital mortality. The modifiable factors were total ischaemic time, which was inversely related to in-hospital mortality; door-to-balloon time and symptom onset time, which were inversely related to ST resolution. These findings are consistent with the literature,¹⁶ except for

door-to-balloon time, which should have been related also to in-hospital mortality;^{5,17} a possible explanation is that the relatively small sample size and low mortality rate did not allow us to detect this relationship.

Total ischaemic time depends on the time to first medical contact, time from medical contact to in-hospital admittance, and door-to-balloon time. Time to first medical contact depends on the time taken by the patient and/or other people to call the emergency service, which can be shortened by awareness campaigns.¹⁸ Door-to-balloon depends on prehospital and hospital logistics. In this study, four modifiable variables were found to have an impact on door-to-balloon time: major predictors were mode of arrival and time to first ECG; minor predictors were fast track organization in hospital and time of arrival. The mode of arrival had a major influence on door-to-balloon time, because the receptivity and hospital response were different in terms of triage and direct transport to the CathLab (fast-track) for patients whose arrival was expected or was managed by an advanced rescue unit. Worthy of note is that the significant difference was found only when the advanced rescue unit was equipped with 12-lead ECG recorder and transmitter. The difference between basic and advanced life support did not offer any additional advantage. Thus, the crucial factor was ECG transmission to hospital staff, who, after having made the diagnosis of STEMI while the patient was still en route, could alert the cardiology team and CathLab, which could then be prepared to receive the patient by fast track and perform PCI immediately. This is consistent with the literature, which has shown that prehospital 12-lead ECG reduces door-to-balloon time by 10–55 minutes^{19–24} and mortality by 7%;²⁴ it also suggests that prehospital ECG may either be transmitted for interpretation by hospital staff or can be interpreted locally by paramedics who then communicate their diagnosis to the hospital, with an acceptable false-positive diagnosis rate.^{22,23,25,26} We speculate that the beneficial effects of recording and transmitting a 12-lead ECG in the prehospital phase of STEMI may not be restricted to patients managed with PCI; they may extend also to patients treated with thrombolysis by allowing prehospital administration and by reducing the in-hospital delay.

The most important factor influencing the door-to-balloon time, however, was time to first ECG, independently of whether it was carried out in the field or in hospital. Recording the 12-lead ECG caused a small delay in transport time, but enabled activation of the hospital prealerting system, an appropriate diagnosis of STEMI, and initiation of treatment, including drugs such as aspirin, heparin, beta-blockers, nitrates, thrombolytics, and antiplatelet agents.

Next in order of importance for door-to-balloon time was fast track transport directly to the CathLab, without any emergency room delay due to patient re-evaluation, ECG recording, consultation of a cardiologist, and/or internal transfer time. This was possible only when a validated

interaction among an advanced rescue unit, the emergency hub, and the alerted hospital occurred as a result of 12-lead ECG teletransmission. This is consistent with experience elsewhere.^{27–29}

Finally, the fourth, albeit less important, factor was time of arrival, which reflects everyday experience that those who arrive at a hospital at night have a longer door-to-balloon time unless an alerting programme is active. Indeed, presentation during regular hours has been found to be associated with shorter door-to-balloon time,²⁴ but presentation during off hours in the presence of an alerting system did not affect outcome in the REAL registry in Bologna (Italy) covering more than 3000 STEMI patients.³⁰

These findings were made within the context of an emergency service, in which a hub is connected to rescue units and receiving hospitals in real time. Such a network ensures that an ambulance is directed to the nearest appropriate hospital, which, in the case of a STEMI patient, is a hospital with a 24-hour CathLab able to perform PCI. The efficiency of the organization is reflected by the very low transfer rate (only 6%) and by the fact that most patients underwent primary PCI (thrombolysis was performed in only 8% of cases). It should be borne in mind that all rescue units, i.e. not only ALS units but also those with BLS, were supplied with automatic external defibrillators and ambulance staff was trained to perform cardiopulmonary resuscitation manoeuvres. They were therefore in a position to immediately treat cardiac arrest out of hospital. This rarely occurred (3% of cases) and all cardiopulmonary resuscitations were successful. The importance of such networks involving a large number of hospital has already been acknowledged and this kind of organization is recommended by international guidelines.^{6,8}

As to the use of different survey periods to validate the advantages and limits of the Milan network, it is worth pointing out that the analysis of data collected for short periods of time by different observers has already proved to be a reliable and easily implemented method.³¹ In our case, the data collected were in accordance with STEMI epidemiology³² and were consistent among periods. Moreover, repeated data collections enabled continual updates that fuelled debates on logistics designed to optimize the system.

A limitation of the study was its observational design that did not allow any intervention to ensure appropriate management of the patient. Another limitation was its sample size and short observation periods, which did not enable an adequate estimate of the mortality rate and prognosis of the patients.

In conclusion, our study indicates that, in the presence of suspected acute myocardial infarction, the immediate performance of an ECG is essential to document STEMI and alert the CathLab at the nearest available hospital. In order to achieve this, it is essential to equip rescue units with devices able to record and transmit ECG to experienced

staff. This significantly shortens door-to-balloon time, which not only was found to contribute to effective reperfusion with ST resolution, but also to be an important component of total ischaemic time associated with mortality. These findings were made within the context of an emergency service that efficiently connects a hub to rescue units and receiving hospitals.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

None.

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