



Factors associated with longer delays in reperfusion in ST-segment elevation myocardial infarction



Daisy Abreu ^{a,*}, M. Salomé Cabral ^{b,1}, Fernando Ribeiro ^{a,1}

^a Department of Cardiology, Hospital de Santa Maria, Universidade de Lisboa, Lisbon, Portugal

^b Centro de Estatística e Aplicações, Departamento de Estatística e Investigação Operacional, Faculdade de Ciências, Universidade de Lisboa, Portugal

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ABSTRACT

Background/objectives: The goal of this paper is to identify the predictors of delay in total ischemia time that would be the focus of improvement efforts in patients with ST-segment elevation myocardial infarction.

Methods: Data was collected retrospectively through the patient's clinical records and by direct telephone interview.

Total ischemic time was categorized in two classes according to the elapsed time since symptom presentation until restored flow, less than 6 h and 6 h or less. Logistic regression analysis was applied to evaluate the relationship between total ischemic time and a set of variables. Discrimination ability of the model was also assessed, as well as sensitivity and specificity, through ROC curves.

Results: Data from 128 patients, 74.22% males and 25.78% females, were analyzed. The average age was approximately 62 years (± 13.6).

Six variables associated with total ischemia were selected in the final model: the patient age, the level of pain intensity, the region of origin, the socioeconomic status, the activity that the patient was performing at the time of symptoms onset, and the fact that the patient has been transferred from another hospital.

Conclusion: The identification of variables associated with the total ischemia time allows the recognition of patients with possibility of worse prognosis, for which should be directed educational efforts and also the identification of variables that can be modified to optimize the therapy.

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1. Introduction

CHD by itself is the single most common cause of death in Europe: accounting for 1.8 million deaths in Europe each year. CHD is also the single most common cause of death in the EU, accounting for over 681,000 deaths in the EU each year [1].

The sense of urgency to attain early reperfusion flows to avoid the inexorable 'wavefront' of ischemic cell death that follows acute myocardial infarction (AMI) is essential, modern reperfusion techniques with thrombolysis and angioplasty have made the attainment of early coronary patency practical. This early restoration of flow aborts the infarct process, salvages threatened myocardium, reduces infarct size, and lowers morbidity and mortality in the months and years to follow [2].

Some studies have clearly demonstrate improved clinical outcomes for patients who present with early primary percutaneous coronary

intervention (PPCI) in AMI with ST elevation patients [3], since the benefits that can be obtained are still "time dependent". PPCI should be performed in character emergence in the early hours of infarction [4]. Unfortunately, a significant proportion of patients are unable to receive medical care within the first 2 h [3].

Currently accepted standards for gauging quality of care in the treatment of ST-segment elevation myocardial infarction (STEMI) mainly focus on shortening the time to treatment after the patient arrives at the hospital. But this narrow focus fails to consider the substantial duration of myocardial ischemia that exists prior to hospital arrival, and the large number of deaths that occur during the pre-hospital period. The time from symptom onset until reperfusion occurs is one estimate of total ischemic time. The shorter the delay in total ischemic, the better the clinical outcomes, including decreased rates of cardiogenic shock, left ventricular dysfunction, congestive heart failure, and death [5].

Clearly, any benefit of reperfusion is time-dependent from the first moment of occlusion. In a recent study, was demonstrated that time from symptom onset to balloon inflation, but not door-to-balloon time, is strongly related to 1-year mortality in patients treated by primary angioplasty [6,7].

* Corresponding author at : Cardiology Department, Hospital de Santa Maria Avenida Professor Egas Moniz, 1649-035 Lisbon, Portugal. Tel.: +351 21 780 5000.

E-mail address: Daideabreu@gmail.com (D. Abreu).

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The identification of the variables associated with longer total ischemia time is important since it is essential to understand how different patients react, to symptoms and to identify high-risk groups needing educational and clinical interventions [8].

The current American and European guidelines have mainly focused on the door-to-balloon or door-to-needle time as indicators of the quality of care and predictors of mortality. These intervals, however, are short compared to the cumulated time from symptom onset to the initiation of reperfusion therapy (i.e., treatment delay) and do not reflect the entire interval that can be modified by the healthcare system.

When the time from symptom onset to restoration of flow is less than 6 h the AMI can be defined as “developing”, studies have shown that the survival rate drops dramatically after 6 h, however up to 25% of the patients spent more than 6 h before they even presented to the hospital [2,3,9].

The goal of this analysis was to identify predictors of delay in total ischemia time that shall be the focus of improvement efforts.

2. Material and methods

Data from this study were collected in the Cardiology Department of Hospital Santa Maria (HSM) in Lisbon, Portugal, and had a target population of patients with confirmed AMI with ST elevation. The study protocol was submitted to the Ethics Committee of the HSM, on June 30, 2011 and received approval on 25 October 2011.

Inclusion criteria included patients who resorted to the Emergency Department (ED) of the HSM with confirmed AMI with ST elevation in which coronary flow was restored by PPCI between January 1, 2010 and December 31, 2010.

Data were retrospectively collected through two questionnaires, after obtaining oral consent for each patient. The first questionnaire contained demographic data, collected through patients' clinical records and also data such as presence of risk factors, history of ACS, region of the patient location's at the symptoms onset, rural or urban, being transferred from another hospital or not, the day of the occurrence of the AMI and the compute total ischemia time.

All the variables were then transformed in categorical variables. Dichotomous variables were simply categorized as 0 and 1. For variables like age, 3 categories were established, less than 55 years between 55 and 75 years and older than 75 years, also day of the week was categorized in working day (from Monday to Friday) and weekends and/or holiday (Table 1).

Table 1
Demographic description.

	n(number of individuals with total time \geq 6 h)
<i>Age (years)</i>	
Age < 55	42(10)
Age 55–75	64(30)
Age > 75	22(14)
<i>Sex</i>	
Female	33(14)
Male	95(40)
<i>Race</i>	
Caucasian	123(51)
Others	5(3)
<i>Socioeconomic level</i>	
High	13(3)
Medium–high	28(7)
Medium	33(12)
Low	54(32)
<i>Scholarship level</i>	
Primary school/no scholarship	73(39)
High school level	27(9)
College education	28(6)

A second questionnaire was also administered by direct telephone interview with the patient and consisted in a socioeconomic scale (Graffar scale) which attributes points, 1 to 5, to each factor of the scale (profession, scholarship level, source of income, housing quality and type of residential area).

The scale classifies a population in five-economic strata: (1) high; (2) medium-high; (3) medium; (4) medium-low and (5) low. In the present study, as the two last categories had few subjects, they were joined in one only category (low).

In the second questionnaire the level of pain experienced by each individual through the application of the numerical scale of pain intensity was also recorded divided in eleven equal parts successively numbered from 0 to 10. It is intended that the patient make the equivalence between the intensity of their pain and a numerical rating, where 0 corresponds to “no pain” and 10 correspond to “maximum pain” [10]. Variables such as level of education, categorized in primary school/no education, high school and college education were also recorded. Being with a companion at the onset of symptoms or not was also addressed. Companion could be a family member, friend or coworker. At last patient's performed activities at symptom onset were recorded and categorized in: leisure, work and physical exercise (Table 1).

3. Statistical analysis

Total ischemic time was categorized in two classes: less than 6 h and more or equal to 6 h from symptom presentation to restored flow. A logistic regression analysis was performed to evaluate the relationship between the categorized total ischemic time and the variables obtained from the questionnaires. The variable race could not be introduced in the model since it had very few subjects in the non-Caucasian category.

A stepwise both-selection technique was used to generate a multiple logistic regression model to determine the predictors of delay. All the variables included in the model were categorical (Tables 1 and 2).

To assess discrimination utility of the model the receiver operating characteristic (ROC) curve was applied and assessed the area under the curve. Sensitivity and specificity was also addressed through the ROC curve.

In order to assess prediction errors a classification table was constructed crossing the observed values for the dependent variable with adjusted values above and below a cut point of 0.5 [11].

Values of $p \leq 0.05$ were considered statistically significant. Variables considered clinically relevant were also kept in the model. All statistical analyses were performed in R software (version 2.13).

4. Results

Total ischemic time according to patients' demographic and clinical characteristics is reported in the Table 1.

The sample consisted of 128 patients, 74.22% male and mostly Caucasians, 123 individuals. The average age was approximately 62 years (± 13.6). More than half of the subjects, 57.03%, had only primary education or were illiterate, and most of the subjects were from lower middle class, 35.16%.

The percentage of individuals in the sample that had a total ischemic time exceeding the 6 h was 42.19% (54) with mean age of 65 (± 12.9). For those who arrived within the 6 h the mean age was 59 (± 13.6).

For the pain scale there were no records of pain levels corresponding to 0, 1 or 2 the lower pain intensity found in the sample was level 3.

Variables significantly related to total ischemic time were: age (p-value: 0.048), pain level (p-value: 0.003), transfer from another hospital (p-value: 0.1052), region (p-value: 0.026), socioeconomic level (p-value: 0.009), activities performed at the onset of symptoms (p-value: 0.026) (Table 2).

Although a non significant p-value was found for the variable transfer (p-value: 0.105) we decided to keep it in the model once it reflected the hospital structure.

Table 2
Frequency of individuals per category.

	n(number of individuals with total time ≥ 6 h)
Disease knowledge	67(21)
Yes	
Previous history of ACS	22(10)
Yes	
Risk factors	126(53)
Yes	
<i>Pain scale</i>	
Pain scale level: 3	8(6)
Pain scale level: 4	20(14)
Pain scale level: 5	8(3)
Pain scale level: 6	28(15)
Pain scale level: 7	14(4)
Pain scale level: 8	22(7)
Pain scale level: 9	14(7)
Pain scale level: 10	12(3)
<i>Being with a companion</i>	
Family members	67(37)
Friends	18(3)
Coworker	9(1)
Alone	34(13)
Activities performed at the time of the symptoms	18(4)
Leisure	20(7)
Work	
Physical exercise	20(6)
Sleep	70(37)
Region	115(45)
Rural	13(9)
Transfer from another hospital	109(43)
Yes	19(11)
<i>Day of the week</i>	
Working day	87(39)
Weekend/holyday	41(15)

The interpretation of the several variables was done taking in account that the subjects shared the same values of all the variables except the one to be compared

4.1. Sociodemographic factors

4.1.1. Age

The odds of having a total time of ischemia longer than 6 h was 3.62 times higher in subjects aged between 55 and 75 years and 4.96 times higher for individuals aged over 75 years, as compared to subjects under age 55.

4.1.2. Socioeconomic status

As socioeconomic level decreases, there was an increase in the odds of a total time ischemia ≥ 6 h. This increase was 1.09 times higher in subjects with medium-high socioeconomic level, 1.27 times higher in subjects of medium-low socioeconomic level and 5.47 times higher in low socioeconomic level.

4.2. Social factors

4.2.1. Region

The odds of having a total ischemia time ≥ 6 h was 10 times higher in subjects from a rural region compared to those from an urban region.

4.2.2. Activities performed

As compared to subjects who were in leisure, subjects who were asleep at the moment of symptom onset are 3.71 times more likely to have a total ischemic time ≥ 6 h, for subjects that were at work the

odds were slightly lower, 1.87. Among subjects who were performing some physical exercise, there is a reduction of 34.8% in the occurrence of a total time of ischemia.

4.3. Clinical factors

4.3.1. Pain scale

As the level of pain intensity scale increases, the odds of having a total ischemic time ≥ 6 h decrease (Table 3).

4.4. Healthcare system contributions to delay

4.4.1. Transfer patients

Surprisingly there was a decrease of 76.8% in the odds of total ischemia time ≥ 6 h in subjects who were transferred from another hospital.

Based on the classification table 78.12% of cases were correctly predicted by the model.

The value obtained for the area under the ROC curve was 0.856, which according to the values proposed [11] indicates that the model had an excellent ability to discriminate. The model had a sensitivity value of 81.5%, which was higher than the specificity, 77.0%.

5. Discussion

Few studies have been done in Portugal to establish which variables are associated with longer total ischemic time in AMI patients [12,13]. Once HSM is one of the biggest hospitals in the country and a referral hospital for PPCI, it seems essential to analyze which variables are related to longer delays for this sample.

Since mortality depends on the extent of the infarction as well as loss of ventricular function which on the other hand depends on the time between the occlusion of the vessel and the restoration of coronary flow, the decrease of this time becomes imperative.

The use of logistic regression allowed to obtain a model, which identified factors involved in the occurrence of a total ischemia time ≥ 6 h as: advanced age, low pain intensity, rural region, low socioeconomic status, and being working or being asleep. Variables associated with a decrease in the odds of total ischemic time ≥ 6 were: being

Table 3
Values obtained for the OR and CI.

	OR	95% CI	p-Value
<i>Age (years):</i>			
Age 55–75	3.627	1.121–11.735	0.032
Age > 75	4.965	1.053–23.420	0.043
<i>Pain scale</i>			
Pain scale level: 4	0.173	0.018–1.640	0.126
Pain scale level: 5	0.078	0.006–0.981	0.048
Pain scale level: 6	0.106	0.013–0.846	0.034
Pain scale level: 7	0.048	0.005–0.503	0.011
Pain scale level: 8	0.028	0.003–0.302	0.003
Pain scale level: 9	0.019	0.001–0.308	0.005
Pain scale level: 10	0.014	0.001–0.184	0.001
Rural region	10.333	1.233–86.565	0.031
<i>Socioeconomic level</i>			
Socioeconomic level: medium-high	1.096	0.166–7.236	0.924
Socioeconomic level: medium	1.278	0.209–7.841	0.790
Socioeconomic level: low	5.472	1.019–29.390	0.048
<i>Activities performed at the moment of the symptoms onset:</i>			
Working	1.877	0.307–11.467	0.495
Physical exercise	0.651	0.107–3.958	0.642
Sleeping	3.716	0.803–17.202	0.093
Transfer from another hospital	0.231	0.038–1.419	0.114

OR—Odds ratio; CI—confidence interval.

transferred from another hospital and performing some kind of physical exercise at symptom onset.

Sociodemographics factors have been identified in other studies as being associated with increased delays in seeking treatment and also less prompt delivery of care [14,15].

Social, cognitive, and emotional factors although not that extensively studied as sociodemographic factor there are also studies showing the great importance of these factors in pre-hospital delay [8,16–18].

It is found consistently in the literature that there is an increase in the total ischemia time as age increases [19]. This association results from the inaccuracy of symptoms, due to the uncertainty caused by the presentation of less common symptoms such as less pronounced chest pain and the presence of symptoms from other conditions which may mask symptoms inherent to the AMI. One explanation proposed is based on the fact that older people tend to accept the presence of new symptoms as part of life, coupled with the fact that identifying the precise origin of the symptoms and acting quickly to seek medical help in time may become more difficult with increasing age [8].

Less pain intensity led to a greater delay, this may be due to the mismatch between patients' expectations related symptoms and actual experience, as has been seen in other studies [8]. Many patients have reported that they feel disillusioned with the intensity of symptoms, including pain, because it does not resemble a typical "Hollywood heart attack" as seen on TV. A slow and cumulative symptom's development and less pain intensity, produce even greater delay [8].

Studies in developed countries suggest that low socioeconomic status is associated with a higher incidence of AMI and associated mortality. These facts are due to the higher prevalence of risk factors for heart disease (high blood pressure, smoking and diabetes) and less use of medications, as well as the reduction in adherence and quick access to treatment prevailing in this socioeconomic class [8]. The World Health Organization states that the pathways by which socioeconomic status may affect cardiovascular disease include: lifestyle and behavior patterns, ease of access to health care and chronic stress [20].

The need to travel long distances to get to the hospital, including the fact of living in a rural region are associated with longer delays [8].

Studies show that subjects who were resting or sleeping at onset of symptoms take longer than those who were exercising some sort of physical activity. Social commitments can prevail over the impulse to seek immediate care, even for acute symptoms. The situations and circumstances may restrict the individual's behavior [8,21].

Unlike most of the studies where there is an increase in total ischemia time in transferred patients, in this study we found a decrease in the odds of increased time in these patients. This may be due to the fact that patients who were transferred did not pass by ED and follow directly to the catheterization laboratory where primary PPCI was performed, which may be associated with a decrease in the total ischemia time [22], another possible explanation may be the fact that this patients were transfer, from the first hospital (hospitals with no cath lab) to the hospital under study by the ambulance or helicopter (depends on the basis of locations and availability) which could contribute to shorter total ischemia time, we hypothesized that most of the patients that came to the hospital came by their own means, did not call an ambulance thus taking more time than patients transferred from another hospital however transferred by an ambulance.

5.1. Study limitations

This study is retrospective and details a one-center experience, with all the limitations of this type of data analysis as a less precise measure of onset time once it depends on patient recall.

It is also important to acknowledge that there is a certain period that elapses between the occlusion of the infarct-related artery and the development of chest pain or similar symptoms of myocardial infarction [7,23].

Other limitation of the study is the reduced frequency of participants from other races other than Caucasians, namely blacks, a group which frequently only seeks acute care after some delay [24]. This leads that these results should not be generalized to all patients with AMI; further studies are needed to fill this gap.

6. Conclusion

This work allowed to identify the variables associated with the total ischemia time and enabled the selection of those that are likely to be modified for optimization of therapy in these patients. It also allowed identifying patients who are considered a high risk group for which should be directed educational efforts.

To the authors' knowledge, this is the first study conducted in Portugal to identify predictors of delay in total ischemic time in AMI patients. These findings add to the body of literature in this field.

Given the important relationship between delay to treatment and mortality in an evolving AMI it is critical that healthcare providers in all countries identify impediments to early reperfusion [25].

In particular, patients should be educated about the warning signs, including the severity of symptoms that should prompt them to seek health care early after the onset of symptoms and the form of switching on the network for specific medical emergency ACS.

Author's contributions

DA made most of the statistical analyses and wrote most of the articles; MSC, made part of the statistical analysis and revised the article for important intellectual content; FR revised the article for important intellectual content. DA had full access to the data and is the guarantor of the study.

Conflict of interest

The authors report no conflict of interest.

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