

## ST-Elevation Myocardial Infarction Network: Systematization in 205 Cases Reduced Clinical Events in the Public Health Care System

Ana Christina Vellozo Caluza<sup>1</sup>, Adriano H. Barbosa<sup>1</sup>, Iran Gonçalves<sup>1</sup>, Carlos Alexandre L. de Oliveira<sup>1</sup>, Livia Nascimento de Matos<sup>1</sup>, Claus Zeefried<sup>2</sup>, Antonio Célio C. Moreno<sup>3</sup>, Elcio Tarkieltaub<sup>4</sup>, Cláudia Maria R. Alves<sup>1</sup>, Antonio Carlos Carvalho<sup>1</sup>

UNIFESP - Escola Paulista de Medicina - Disciplina de Cardiologia<sup>1</sup>; Serviço de Atendimento Móvel de Urgência – SAMU<sup>2</sup>; Coordenadoria Técnica de Cardiologia - Secretaria de Saúde da Prefeitura Municipal de São Paulo<sup>3</sup>; Hospital Municipal Prof. Dr. Alípio Correa Netto<sup>4</sup>, São Paulo, SP - Brazil

### Abstract

**Background:** The major cause of death in the city of São Paulo (SP) is cardiac events. At its periphery, in-hospital mortality in acute myocardial infarction is estimated to range between 15% and 20% due to difficulties inherent in large metropolises.

**Objective:** To describe in-hospital mortality in ST-segment elevation acute myocardial infarction (STEMI) of patients admitted via ambulance or peripheral hospitals, which are part of a structured training network (STEMI Network).

**Methods:** Health care teams of four emergency services (Ermelino Matarazzo, Campo Limpo, Tatuapé and Saboya) of the periphery of the city of São Paulo and advanced ambulances of the Emergency Mobile Health Care Service (abbreviation in Portuguese, SAMU) were trained to use tenecteplase or to refer for primary angioplasty. A central office for electrocardiogram reading was used. After thrombolysis, the patient was sent to a tertiary reference hospital to undergo cardiac catheterization immediately (in case of failed thrombolysis) or in 6 to 24 hours, if the patient was stable. Quantitative and qualitative variables were assessed by use of uni- and multivariate analysis.

**Results:** From January 2010 to June 2011, 205 consecutive patients used the STEMI Network, and the findings were as follows: 87 anterior wall infarctions; 11 left bundle-branch blocks; 14 complete atrioventricular blocks; and 14 resuscitations after initial cardiorespiratory arrest. In-hospital mortality was 6.8% (14 patients), most of which due to cardiogenic shock, one hemorrhagic cerebrovascular accident, and one bleeding.

**Conclusion:** The organization in the public health care system of a network for the treatment of STEMI, involving diagnosis, reperfusion, immediate transfer, and tertiary reference hospital, resulted in immediate improvement of STEMI outcomes. (*Arq Bras Cardiol* 2012;99(5):1040-1048)

**Keywords:** Myocardial infarction; guidelines; emergencies; quality of health care.

### Introduction

Acute myocardial infarction (AMI) is the major cause of death in the majority of developed countries, which is expected to occur in the next decades in developing countries<sup>1-2</sup>. In Brazil, data of the Unified Public Health Care System (abbreviation in Portuguese, SUS) have shown that cardiovascular causes account for 35% of the deaths, cerebrovascular accident (CVA) being the major cause in the North and Northeastern regions, and AMI in the cities of São Paulo, Rio de Janeiro, Curitiba, and Porto Alegre<sup>3-4</sup>.

In São Paulo, a city with more than 11 million inhabitants, the distribution of emergency services (ESs) and public hospitals is heterogeneous, with scarcity in peripheral zones. That heterogeneity of resources also involves the quality of the medical care provided.

Consequently, there is great difficulty in the clinical and electrocardiographic diagnosis of AMI, which delays the beginning of the treatment for cardiovascular emergencies. The ST-segment elevation AMI (STEMI) has immediate myocardial reperfusion as the basis of its treatment. The difficulties previously mentioned in the city of São Paulo contribute to maintain the mean mortality due to STEMI ranging from 15% to 20%<sup>5</sup>. Such figures are very different from the mortality found in centers that perform systematic reperfusion, where mortality ranges from 5% to 7%<sup>6-8</sup>.

This article aimed at describing the pilot operation of the STEMI network in the periphery of the city of São Paulo. In addition, this study also provides the results obtained at the hospital of the public health care system, which is part of the project, after systematization of STEMI management.

### Methods

This report, as a registry, comprises all cases diagnosed in the STEMI network and treated as STEMI according to a protocol, with no exclusion. The Hospital São Paulo of the Universidade Federal de São Paulo (Unifesp) was the tertiary

**Mailing Address:** Ana Christina Vellozo Caluza •

Rua Pedro de Toledo 544, Vila Clementino. Postal Code 04039-001, São Paulo, SP - Brazil

E-mail: acvcaluza@cardiol.br, acvcaluza@yahoo.com.br

Manuscript received November 30, 2011; manuscript revised December 8, 2011; accepted July 4, 2012.

reference hospital of the project. No patient was denied transfer to another institution. This project was discussed with and approved by the Emergency Mobile Health Care Service (abbreviation in Portuguese, SAMU) at the Brazilian Agency of Sanitary Surveillance (abbreviation in Portuguese, Anvisa) and the Ethics Committees of the São Paulo City Hall and Unifesp. The protocol uses recommendations of Brazilian and international guidelines<sup>9-11</sup>, and is the same adopted for the management of STEMI at Unifesp regarding the indications for thrombolytic agents, primary and rescue percutaneous transluminal coronary angioplasty (PTCA), and pharmacoinvasive therapy. The project of the STEMI network and the diagnostic and treatment protocol are briefly described.

### Organization of the STEMI network

Initially, a 24-hour central office for electrocardiogram (ECG) reading was installed at the Hospital São Paulo to receive exams sent from 126 SAMU ambulances (16 advanced and 110 basic ambulances), covering the entire São Paulo metropolitan region. The ECGs are transmitted to the central office via mobile phone, fixed phone or internet, and immediately interpreted by a team of cardiologists, by using guidelines for STEMI ECG diagnosis<sup>9,12</sup>. The ECG reports are sent to the mobile phone of the transmitting ambulance; a study on that topic has already been published<sup>13</sup>.

In addition to advanced ambulances, the São Paulo Municipal Health Secretariat has made the fibrinolytic agent tenecteplase (TNK) available at four municipal ESs with a history of a large number of infarcted patients:

Ermelino Matarazzo, Campo Limpo, Tatuapé, and Saboya. The medical and nursing teams of those ESs were trained and updated on the clinical diagnosis of acute coronary syndrome, ECG recognition of STEMI, and indications of thrombolytic agents and primary PTCA in STEMI. A direct and immediate contact via a dedicated and exclusive mobile phone line was established between the advanced ambulances or the four ESs assessed and the Coronary Unit (COU) of the Hospital São Paulo. Thus, a patient diagnosed with STEMI, who was at an ES or SAMU ambulance and could be in a catheterization laboratory in less than 90 minutes was referred for primary PTCA. If the advanced ambulance was very far away or if the estimated travel time for a patient at one of the ESs was longer than 90 minutes, he/she would receive TNK; after thrombolysis, the patient would be immediately transferred to the Hospital São Paulo, and would undergo either rescue PTCA, if necessary, or cardiac catheterization within 6 to 24 hours, if clinically stable (Figure 1). The thrombolytic agent was used for as much as three hours in the advanced ambulances or for as much as six hours in the municipal ESs. The dose of TNK ranged from 30 mg to 50 mg, meeting the known criteria for indication and contraindication of fibrinolytic drugs. In addition to TNK, the patients received as adjuvant therapy and according to the Brazilian and international guidelines the recommended doses of morphine, low-molecular weight heparin (properly corrected to weight and renal function), and oral medications, such as nitrate, aspirin, antiplatelet drugs, and beta-blockers (if Killip I)<sup>9-11</sup>. The patients of the ambulances underwent antiplatelet therapy after their arrival at the ES or tertiary reference hospital.

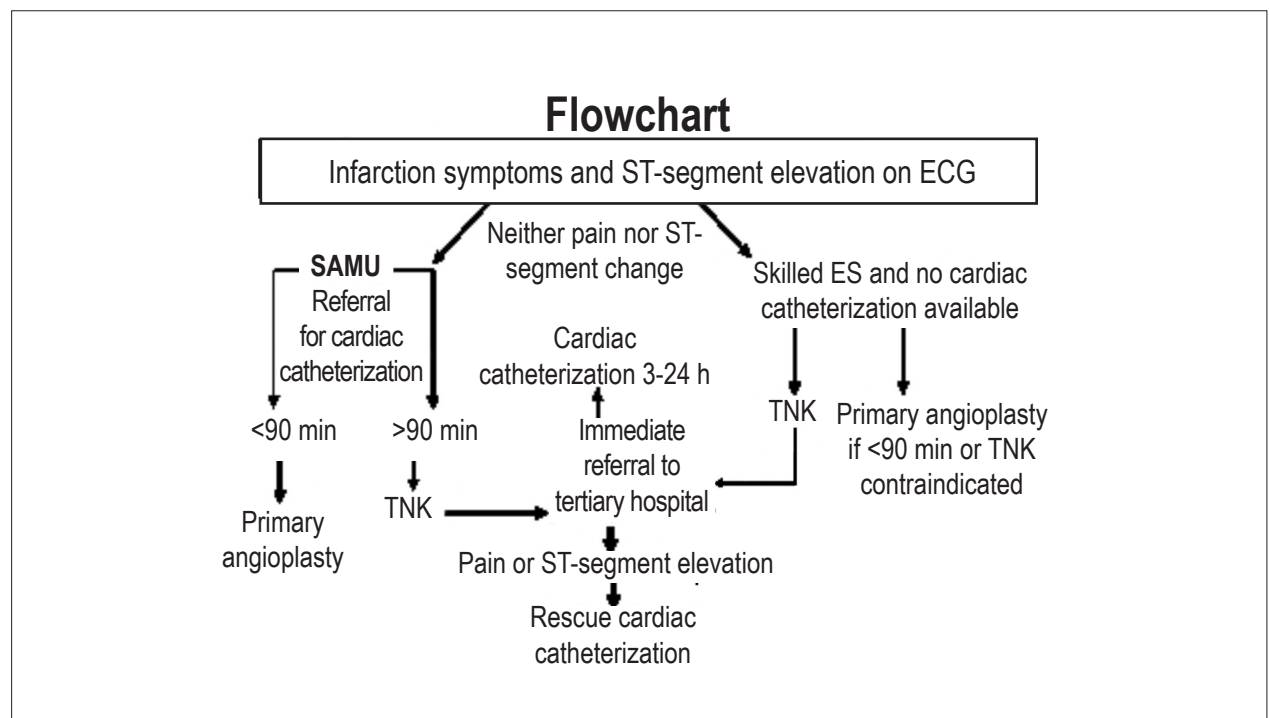


Figure 1 – STEMI network – Flowchart; SAMU: Emergency Mobile Health Care Service; TNK: tenecteplase; ES: emergency service; ECG: electrocardiogram

**Definitions**

This study adopted the definitions used in the already cited guidelines<sup>9-11</sup>. Primary PTCA was defined as initial mechanical reperfusion during cardiac catheterization for a STEMI with no previous use of fibrinolytic drugs or glycoprotein IIB/IIIa inhibitors. Rescue PTCA was defined as an emergency cardiac catheterization due to ineffective thrombolysis, characterized by persistence of pain at an intensity of at least 50% of that at onset or persistence of at least 50% of the ST-segment elevation on ECG in the leads initially involved. Pharmacoinvasive strategy was defined as the use of full-dose chemical thrombolysis, followed by routine cardiac catheterization within 6 to 24 hours, even in stable patients.

**Complications**

The complications were defined according to the already cited guidelines, and all data from the patients were entered to an Excel sheet developed for that purpose and comprising 91 pieces of information on each case<sup>12</sup>. The following complications are described in this article: initial cardiorespiratory arrest (CRA); Killip II-IV; complete atrioventricular block (CAVB); pain recurrence; and new ECG changes or changes in cardiac markers during disease progression. The diagnosis of ischemic or hemorrhagic CVA was confirmed by use of computed tomography or cerebral magnetic resonance imaging.

**Statistical analysis**

Regarding the data collected, quantitative variables were expressed as mean and standard deviation and compared by use of Wilcoxon test or Student *t* test. The chi-square test was used to compare the qualitative variables regarding in-

hospital mortality at the Ermelino Matarazzo ES before and after establishing the STEMI network. Uni- and multivariate analyses to identify factors possibly related to in-hospital death were performed.

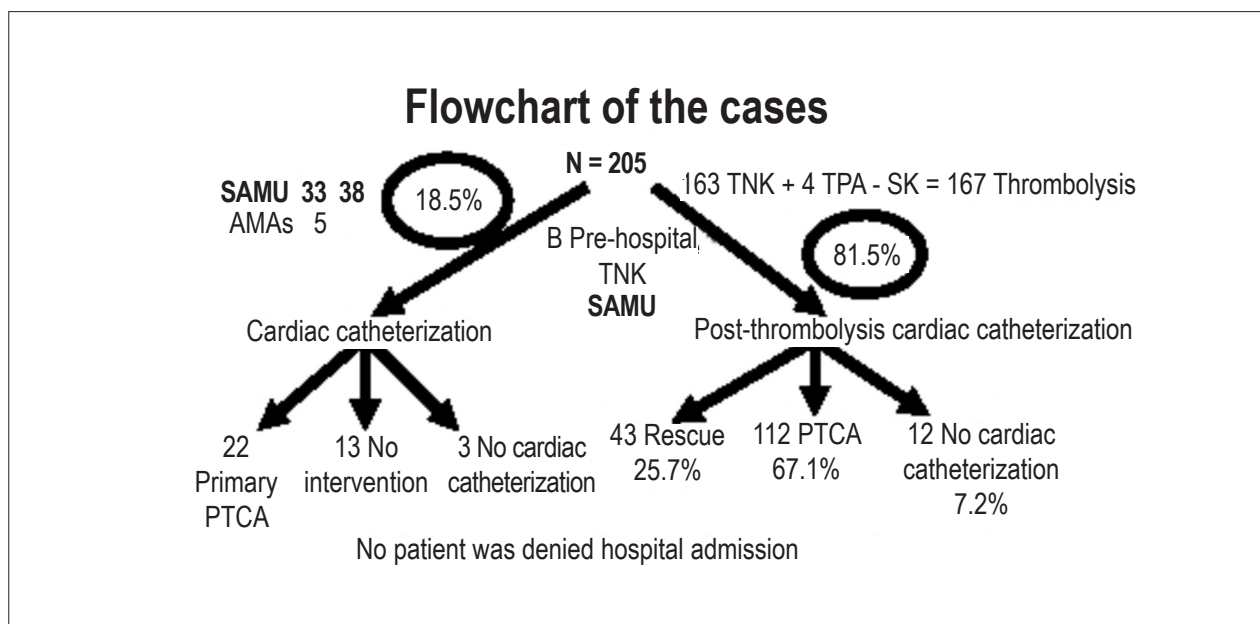
**Results**

This study assessed 205 consecutive patients cared for at the STEMI network, with no exclusions, and who underwent the complete sequence, that is, from diagnosis to transfer to the tertiary reference hospital, from January 2010 to June 2011. Of those 205 patients, 190 (92.7%) underwent cardiac catheterization. Figure 2 shows the flowchart of the case series, in which only 38 (18.5%) patients with STEMI were referred for initial cardiac catheterization without previous thrombolysis. The other 167 patients with STEMI (81.5%) underwent thrombolysis; 43 of them (25.7%) underwent rescue PTCA and the others underwent elective cardiac catheterization with stent implantation, when necessary.

The origins of the patients were as follows: SAMU ambulances, 46 patients; Ermelino Matarazzo ES, 59; Tatuapé ES, 41; Saboya ES, 31; and Campo Limpo ES, 24. Four other patients originated from other ESs, were diagnosed via the ECG central office, and were transferred in SAMU ambulances<sup>13</sup>.

**Demography**

The demographic data are shown in Table 1. Most patients (71.7%) were males. Their mean age was 58.8 years (range, 33 to 88), and 24 patients (11.7%) were over the age of 75 years. Their characteristics were as follows: 63.4% had hypertension; 31.7% had diabetes; 49.2% smoked; 15.1% had had a previous AMI; and 7.8% had had a previous CVA. Seventeen patients had an initial heart rate over 100 beats



**Figure 2** – STEMI network – Flowchart of the cases; SAMU: Emergency Mobile Health Care Service; TNK: tenecteplase; AMAs; TPA: Tissue plasminogen activator; SK: streptokinase; PTCA: percutaneous transluminal coronary angioplasty

**Table 1 – Patients' characteristics and risk factors**

Characteristics	n = 205	%
Mean age	58.8 (32 ± 88)	-
> 75 years	24	11.7
Male	147	71.7
Female	58	28.3
Heart rate > 100 bpm	17	8.3
Blood pressure < 100 mm Hg	16	7.8
Killip II - IV	53	25.8
Smoking habit	101	49.2
Diabetes mellitus	65	31.7
SAH	130	63.4
Family history for CVD	55	26.8
Dyslipidemia	113	55.1
Previous AMI	31	15.1
Peripheral vascular disease	22	10.7
Chronic renal failure	23	11.2
Previous CVA	16	7.8

*Killip II - IV: Killip and Kimball classification; CVD: cardiovascular disease; SAH: systemic arterial hypertension; AMI: acute myocardial infarction; CVA: cerebrovascular accident*

per minute, and 16 (7.8%) had blood pressure levels under 100 mm Hg.

Regarding initial ECG, an ST-segment elevation greater than 1 mm was observed in two or more leads in the following walls: anterior, 87; inferior, 56; and lateral, dorsal or combinations, 51. Involvement of the right ventricle (RV) was observed in 12 patients, and complete left bundle-branch block in 11 patients.

### Coronary reperfusion method

Thrombolytic agents were used in 167 patients, TNK in almost all of them. Only four patients did not receive TNK, because of lack of immediate availability at the time of the infarction, as follows: in one patient, the thrombolytic used was tissue plasminogen activator (t-PA); and, in the other three, streptokinase (SK). No death occurred during patients' transfer to the tertiary reference hospital, either inter-hospital or pre-hospital transfer. However, one patient had CRA on the street and was resuscitated by the SAMU team, arriving alive at the tertiary reference hospital. That patient underwent cardiac catheterization, which evidenced occlusion of the right coronary artery, being submitted to PTCA. The patient had neurological complications and died.

Primary PTCA was indicated as the procedure of choice to 38 patients, in accordance with the flowchart in Figure 1, but was effectively performed in 22 patients. In the remaining 16 patients, PTCA was not performed due to the following reasons: three patients showed a residual lesion of little importance and evidence of distal thrombus in the reperfused coronary artery; two patients had only coronary ectasia and

slow flow; six patients showed occlusion in small vessels, such as the diagonal artery, posterior descending artery, and second marginal branch of the circumflex artery, or diffuse lesions with poor distal coronary bed; two patients had severe lesion in the left main coronary artery not amenable to PTCA; and three patients did not undergo cardiac catheterization after assessment at arrival at the reference hospital (Figure 2).

Cardiac catheterization was routinely performed in patients undergoing previous chemical thrombolysis, and in almost all cases within 6 to 24 hours after receiving the fibrinolytic agent. Of the 167 thrombolysed patients, 12 did not undergo cardiac catheterization because of the presence of either other morbid conditions contraindicating the exam or a recent exam. Cardiac catheterization was performed on an emergency basis (rescue) in 43 patients (25.7%). In the remaining 112 thrombolysed patients, cardiac catheterization was performed under stable conditions. Of the 205 patients, 155 (75.6%) underwent a pharmacoinvasive strategy, either elective or rescue. Stents were placed in 152 patients (all bare-metal stents), and seven balloon dilations were performed, corresponding to 77.5% of the immediate percutaneous intervention in the entire sample.

### Complications of STEMI or of its invasive management

The following complications were observed (Table 2): recurrence of chest pain, 15 patients (7.3%); reinfarctions, three patients (1.5%); congestive heart failure, 20 patients (9.7%); CAVB, 14 patients (6.8%); Killip II-IV, 53 patients (25.8%); cardiogenic shock, 15 patients (7.3%); use of intraaortic balloon, 12 patients (5.8%); hemorrhagic CVA, one

Table 2 – Complications

Complications	n = 205	%
CRA - ventricular fibrillation	14	6.8
Recurrent angina	15	7.3
Reinfarction	3	1.5
Congestive heart failure	20	9.8
Cardiogenic shock	15	7.3
Intraaortic balloon	12	5.8
Right ventricular infarction	12	5.8
Complete atrioventricular block	14	6.8
Major bleeding	3	1.5
Minor bleeding	7	3.4
Blood transfusion	12	5.8
Hemorrhagic CVA	1	0.5
Ischemic CVA	1	0.5

CRA: cardiorespiratory arrest; CVA: cerebrovascular accident

patient (0.5%); and ischemic CVA, one patient (0.5%). The complications due to the hemodynamic study were as follows: three patients (1.5%) had severe bleeding at the vascular access site, two of whom required transfusion; and one patient had a femoral pseudoaneurysm, corrected with surgery. In addition, the following were observed: seven minor bleedings; one ventricular fibrillation on the catheterization table, which was promptly reverted; and partial displacement of one thrombus from an ostial lesion of the anterior descending artery to the circumflex artery, causing its occlusion and irreversible CRA.

### Mortality

In this consecutive case series of 205 patients with STEMI, diagnosed either in an ambulance or at ESs of the periphery of the São Paulo city and transferred to a public reference hospital, 14 in-hospital deaths (6.8%) occurred, as shown in Table 3. Almost all deaths involved either elderly patients or situations of low cardiac output. In addition, other deaths were as follows: one sudden death prior to hospital discharge; one death due to upper gastrointestinal hemorrhage; one due to neurological injury following CRA at home at the beginning of AMI; and one due to hemorrhagic CVA. Univariate analysis was used to identify elements related to in-hospital death, and, later, only the factors that remained significant ( $p < 0.01$ ) were used on multivariate analysis. The items identified, their respective odds ratios, and  $p$  values were as follows: previous CVA (OR 8.7;  $p = 0.002$ ); occluded infarct-related artery (OR 12.1;  $p = 0.002$ ); CAVB (OR 6.23;  $p = 0.01$ ); use of intraaortic balloon (OR 11.75;  $p = 0.001$ ); myocardial flow index (blush) of zero on the initial injection in the infarct-related artery (OR 13.7;  $p = 0.001$ ); and cardiogenic shock, the best predictor (OR 308.3;  $p < 0.001$ ). On the final adjustment of the multivariate analysis, all variables identified (except previous CVA) were associated with the presence of cardiogenic shock.

### Discussion

Mortality due to acute coronary syndrome, especially STEMI, is a severe public health problem, due to its high prevalence and the fact that it is a permanent challenge in great metropolises, requiring several levels of integration of the health care system. Unfortunately, the price paid in such situations, which lack organization of the general health care provided, is significantly higher morbidity and mortality<sup>5</sup>. To increase the reperfusion rate is extremely important to improve the results of STEMI therapy: although there is no doubt that primary PTCA provides better coronary patency, with better distal flow, smaller residual lesion, and lower mortality as compared with the use of fibrinolytic drugs<sup>14-15</sup>, the systematic use of primary PTCA for all STEMI patients involves considerable logistic difficulties, especially in great metropolises with chaotic traffic, large distances from the periphery to the area with higher hospital concentration, and heterogeneous 24/7 operation of catheterization laboratories. It is worth noting that this is not an exclusively Brazilian problem, it also occurs in developed countries. Consequently, several recent publications have shown that PTCA performed within 60 minutes is the reperfusion strategy in around 20% to 30% of all STEMI cases<sup>7,12,13,16-18</sup>.

The STEMI network project aimed at standardizing the steps usually accounting for the delay in the treatment of AMI or its complications: rapid clinical diagnosis; immediate ECG for the patient with chest pain, with reading support from an ECG central office if necessary; immediate definition of management (primary PTCA or TNK use); immediate use of therapeutic adjuvants; and immediate availability of a reference hospital, even for stable patients. In addition, the project systematically comprised rescue PTCA and cardiac catheterization within 6 to 24 hours for stable patients. This option was considered in the 2010 European Society of Cardiology guidelines on myocardial

**Table 3 – Specification of the patients who died and their major causes of death**

PATIENT	AGE	SEX	REPERFUSION	CAUSE OF DEATH
1-	87	F	Mechanical	Sudden death
2-	86	F	Not performed Left main coronary artery - IAB	Cardiogenic shock
3-	55	M	Chemical	Cardiogenic shock
4-	53	M	Chemical	Cardiogenic shock
5-	50	M	Chemical	Hemorrhagic CVA
6-	67	M	Chemical	Cardiogenic shock
7-	83	F	Chemical	Septic shock
8-	76	M	Chemical	Upper gastrointestinal hemorrhage
9-	56	M	Mechanical	Neurological injury after CRA on the street
10-	56	F	Chemical	Cardiogenic shock
11-	49	M	Chemical	Sudden death before hospital discharge
12-	82	F	Chemical	Cardiogenic shock
13-	77	F	Mechanical	Cardiogenic shock
14-	76	M	Chemical	Cardiogenic shock

F: female; M: male; CVA: cerebrovascular accident; IAB: Intraaortic balloon; CRA: cardiorespiratory arrest.

revascularization, in which pharmacoinvasive therapy was ranked class I and level of evidence A for STEMI, 3 to 24 hours after reperfusion<sup>13,19,20,21-25</sup>.

The STEMI network had extremely promising results for an initial project, operationally and effectively involving several links of a previously non-operating chain. The COU-dedicated mobile phone eliminated the problems of contact delay and there was neither difficulty nor refusal of admission at the tertiary reference hospital.

The 205 patients with STEMI in this sample represented the severity profile usually observed in that condition, as we found 31.7% of diabetic patients, 63.4% of hypertensives, and almost half of the sample (45,2%) of active smokers. In addition, 15.1% and 7.8% of the patients had already been diagnosed with AMI and CVA, respectively. The following were also observed: 12 patients with AMI of the RV; 14 patients with CAVB; 14 CRA; and 15 cardiogenic shocks.

As expected, due to the logistic difficulties of the city of São Paulo and the distances between the centers involved in the STEMI network, only 18.5% of the sample was directly referred for cardiac catheterization to undergo primary PTCA. The remaining patients (81.5%) received a thrombolytic agent, and the contact for their transfer was immediately performed, even when they were stable. On the other hand, of the 46 patients transferred in the SAMU ambulances, only eight (20%) underwent pre-hospital thrombolysis, a number that, although low, is frequently found in other countries<sup>26</sup>. It is worth noting that almost 25% of the thrombolysed patients required rescue PTCA, some still while in the ambulance (they left their origin stable and, on the way, their ST-segment elevation worsened, pain recurred, or hemodynamic instability occurred), emphasizing the need for immediate transfer to a reference hospital after thrombolysis. Only 12 patients were referred for

coronary artery bypass graft surgery during hospitalization (6.3% of the 205 patients).

The initial results of the STEMI network project were extremely encouraging because in-hospital mortality was only 6.8%. The sequence comprising clinical diagnosis, rapid ECG interpretation, decision about the use of either fibrinolytic drugs or primary PTCA, TNK use, and transfer with systematic cardiac catheterization, performed immediately or within 6 to 24 hours, seems to have improved the outcome of those patients.

A specific analysis of the ES of the Hospital Ermelino Matarazzo was performed, comparing the results of in-hospital mortality at the institution in 2009, before the STEMI network, and that in the 2010-2011 period, with the STEMI network installed. The Hospital Ermelino Matarazzo was chosen because it had the largest case series and the best records on hospital admission and discharge. In 2009, in 88 STEMI treated at the Hospital Ermelino Matarazzo, mortality was 26.1%, while in the 2010-2011 period, among all 65 patients who initiated treatment there and completed it at the Hospital São Paulo, the in-hospital mortality was 6.1% (Figure 3 - pre and post  $\chi^2$  : 8.94;  $p = 0.0028$ ).

It is worth emphasizing the importance of those results, because they were obtained in patients of the SUS, from the periphery of the city of São Paulo, involving the municipal and federal public health care systems. In addition, they confirm recent publications showing that organizing a myocardial infarction network determines an immediate improvement in outcomes, which motivated an on-going study (STREAM study), comparing directly pharmacoinvasive therapy versus primary PTCA<sup>27-35,36</sup>.

This study, however, shows that any project to treat STEMI should consider and interpret local needs and characteristics, and not only copy models of distinct realities.

### Limitations

This was not a randomized blind study. It does not suggest that the results obtained are definitive or that the strategy is better or equivalent to the systematic use of primary PTCA. This study involved municipal ESs and ambulances, which, after training, submitted the cases identified as STEMI to the tertiary reference hospital. We could not assess whether there were cases in which the tertiary reference hospital was not contacted. In addition, the project did not encompass the entire public health care system of the city. One of the positive aspects of this case series is that no patient was denied admission to the tertiary reference hospital, being, thus, a consecutive case series, similar to a registry, with no exclusion factors, such as age, sex, and renal function.

### Conclusion

Systematization of the treatment of STEMI with training of the teams involved in the initial care, use of thrombolytic and

antiplatelet agents according to protocols, and patient's transfer to the tertiary reference hospital showed in-hospital mortality lower than that observed for patients with STEMI treated conventionally in the municipal public health care system of the city of São Paulo.

### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

### Sources of Funding

There were no external funding sources for this study.

### Study Association

This article is part of the doctoral dissertation submitted by Ana Christina Vellozo Caluza, from Universidade Federal de São Paulo.

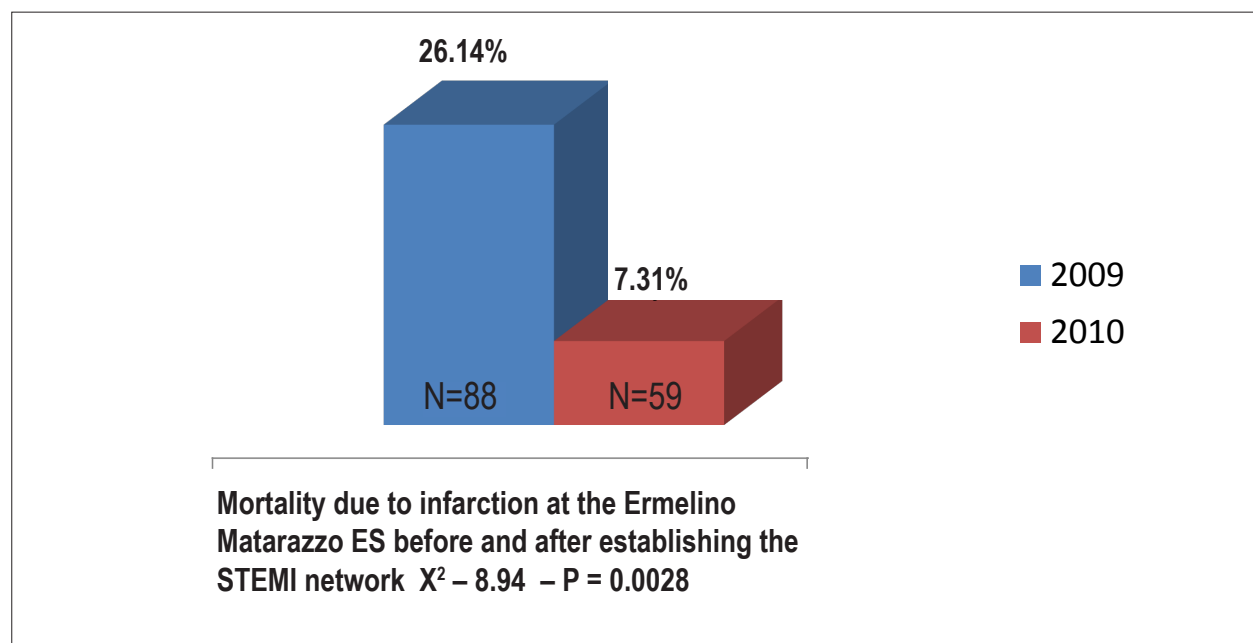


Figure 3 – Mortality at the Hospital Ermelino Matarazzo before and after the STEMI network; ES: emergency service.

### References

1. Mendis S, Abegunde D, Yusuf S, Ebrahim S, Shaper G, Ghannem H, et al. WHO PREMISE.WHO study on Prevention of REcurrences of Myocardial Infarction and Stroke.Bull. World Health Organ. 2005;83(11):820-9.
2. Leeder S, Raymond S, Greenberg H, Liu H, Esson K. A race against time: the challenge of cardiovascular disease in developing economies. New York, NY: Trustees of Columbia University;2004.
3. Lotufo PA, Bensenor IM. Mortalidade por doença coronária e cerebrovascular. 2011. [Citado em 2011 jan 10]. Disponível em <http://saude.hsw.uol.com.br/avc-epidemiologia.htm>
4. Souza MF, Alencar AP, Malta DC, Moura L, Mansur AP. Análise de séries temporais da mortalidade por doenças isquêmicas do coração e cerebrovasculares, nas cinco regiões do Brasil, no período de 1981 a 2001. Arq Bras Cardiol. 2006;87(6):735-40.
5. Ministério da Saúde. DATASUS.[Citado em 2011 maio 14]. Disponível em: <http://tabnet.datasus.gov.br/cgi/tabcgi.exe?db=2009/CO8.def>-CID 10 I20 a I24,CNES,2004 a 2009. DEF=C:\TabWin |RD2008.DEF Linha=Hospital SP(CNES).
6. Goldstein P, Wiel E. Management of prehospital thrombolytic therapy in ST segment elevation acute coronary syndrome (< 12 hours). Minerva Anestesiol. 2005;71(6):297-302.

7. Widimsky P, Wijns W, Fajadet J, de Belder M, Knot J, Aaberge L, et al. Reperfusion therapy for ST elevation acute myocardial infarction in Europe: description of the current situation in 30 countries. *Eur Heart J*. 2010;31(8):943–57.
8. Barreto R, Cantarelli MJC, Castello HJ, Gonçalves R, Gioppato S, Guimarães JBF, et al. Resultados da intervenção coronária percutânea primária em pacientes do sistema único de saúde e da saúde suplementar. *Rev Bras cardiol Invasiva*. 2011;19(3):2-7.
9. Piegas LS, Feitosa G, Mattos LA, Nicolau JC, Rossi Neto JM, Timerman A, et al. Sociedade Brasileira de Cardiologia. Diretriz da Sociedade Brasileira de Cardiologia sobre tratamento do infarto agudo do miocárdio com supradesnível do segmento ST. *Arq Bras Cardiol*. 2009;93(6 supl.2):e179-e264.
10. Matos LN, Gonçalves I, Moraes E, Rodrigues AE, Moreno ACC, Sales Filho et al. Are emergency cardiologic cases originating from ambulance calls different from light ER outposts? Analysis of 64002 pre-hospital ECG's[abstract]. ESC Congress 2011, Paris, August 29. *Eur Heart J*. 2011;32:348-9.
11. Guidelines on myocardial revascularization. The task force on myocardial revascularization of the European society of cardiology (ESC) and the European association for cardio-thoracic surgery (EACTS). The European Society of Cardiology. *Eur Heart J*. 2010;31:2501-5.
12. Pastore CA, Pinho C, Germiniani H, Samesima N, Mano R, et al. Sociedade Brasileira de Cardiologia. Diretrizes da Sociedade Brasileira de Cardiologia sobre análise e emissão de laudos eletrocardiográficos. *Arq Bras Cardiol*. 2009;93(3 supl.2):1-19.
13. Moraes ERFL, Rodrigues AAE, Araujo GA, Oliveira LH, Ribeiro WN, Amaral AZ, et al. Tele-eletrocardiografia e atendimento pré-hospitalar do serviço de atendimento móvel de urgência: atendimento SUS com qualidade mesmo em regiões periféricas da cidade de São Paulo. *Arq Bras Cardiol*. 2010;95(3 supl.1):1-92.
14. Keeley EC, Boura JA, Grines CL. Comparison of primary and facilitated percutaneous coronary interventions for ST elevation myocardial infarction: quantitative review of randomized trials. *Lancet*. 2006;367(9510):579–87.
15. Boersma E. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. *Eur Heart J*. 2006;27(7):779– 88.
16. Wijeyundera HC, You JJ, Nallamothu Bk, Krumhold Hm, Cantor WJ, Ko DT. An early invasive strategy versus ischemia guided management after fibrinolytic therapy for ST segment elevation myocardial infarction: A meta-analysis of contemporary randomized controlled trials. *Am Heart J*. 2008;156(3):564–72.e2.
17. Nallamothu B, Fox KA, Kennelly BM, Van De Werf F, Gore JM, Steg PG, et al. Relationship of treatment delays and mortality in patients undergoing fibrinolysis and primary percutaneous coronary intervention. The Global Registry of Acute Coronary Events. *Heart*. 2007;93(12):1552–5.
18. Scheller B, Hennen B, Hammer B, Walle J, Hofer C, Hipert V, et al., SIAM III Study Group. Beneficial effects of immediate stenting after thrombolysis in acute myocardial infarction. *J Am Coll Cardiol*. 2003;42(4):634–41.
19. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST – segment elevation acute myocardial infarction (ASSENT-4 PCI): randomized trial. *Lancet*. 2006;367(9510):569-76.
20. Ellis SG, Tendera M, Belder MA, Van Boven AJ, Widimsky P, Janssen L, et al. for the FINESSE Investigators. Facilitated PCI in patients with ST elevation myocardial infarction. *N Eng J Med*. 2008; 358(21):2205–17.
21. Bonnefoy E, Steg PG, Boutitie F, Dubien PY, Lapostolle F, Roncalli J, et al. Comparison of primary angioplasty and pre-hospital fibrinolysis in acute myocardial infarction (CAPTIM) trial: a 5-year follow-up. *Eur Heart J*. 2009;30(13):1598–606.
22. Afilalo J, Roy AM, Eisenberg MJ. Systematic review of fibrinolytic-facilitated percutaneous coronary intervention : potential benefits and future challenges. *Can J Cardiol*. 2009;25(3):141-8.
23. Bohmer E, Hoffmann P, Addehnoor M, Arnesen H, Halvorsen S. Efficacy and safety of immediate angioplasty versus ischemia guided management after thrombolysis in acute myocardial infarction in areas with very long transfer distances. Results of the NORDSTEMI (NORwegian study on District treatment of ST Elevation Myocardial Infarction). *J Am Coll Cardiol*. 2010;55(2):102–10.
24. Cantor JW, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, Cohen EA, et al. Routine early angioplasty after fibrinolysis for acute myocardial infarction. *N Engl J Med*. 2009;360(26):2705–18.
25. Di Mario C, Dudek D, Piscione F, Mielecki W, Savonitto S, Murena E, et al. Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. *Lancet*. 2008;371(9612):559–68.
26. Wainstein R, Furtado MV, Polanczyk CA. Trombólise pré-hospitalar no infarto agudo do miocárdio: uma alternativa factível para o Brasil? *Arq Bras Cardiol*. 2008;90(2):77-9.
27. Fernandez AF, Alonso JJ, Castro-Beiras A, Vazquez N, Blanco J, Alonso-Briales J, et al. Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. *Lancet*. 2004; 364(9439):1045–53.
28. Wong CK, Barra SL, Herbison P. Does ST resolution achieved via different reperfusion strategies (fibrinolysis vs percutaneous coronary intervention) have different prognostic meaning in ST elevation myocardial infarction: A systematic review. *Am Heart J*. 2010;160(5):81-2.
29. Van der Werf F. Reperfusion therapy for acute myocardial infarction: can the improvement in early survival be extended over time? *Eur Heart J*. 1999;20(11):785-6.
30. Kalla K, Christ G, Karnik R, Malzer R, Norman G, Prachar H, et al. Vienna STEMI Registry Group. Implementation of guidelines improves the standard of care: the Viennese registry on reperfusion strategies in ST-elevation myocardial infarction (Vienna STEMI registry). *Circulation*. 2006;113(20):2398-405.
31. Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al. ESC Committee for Practice Guidelines (CPG). Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. *Eur Heart J*. 2008;29(23):2909-45.
32. Eagle KA, Nallamothu BK, Mehta RH, Granger CB, Steg PG, Van de Werf F, et al. Global Registry of Acute Coronary Events (GRACE) Investigators. Trends in acute reperfusion therapy for ST-segment elevation myocardial infarction from 1999 to 2006: we are getting better but we have got a long way to go. *Eur Heart J*. 2008;29 (5):609-17.
33. Doonan AL, Newell MC, Larson DM, Henry TD. Pharmaco-invasive strategies expand access to percutaneous coronary intervention in ST-elevation myocardial infarction. *Prog Cardiovasc Dis*. 2010;53(3):188-94.
34. Tarantini G, Van de Werf F, Bilato C, Gersh B. Primary percutaneous coronary intervention for acute myocardial infarction: Is it worth the wait? The risk-time relationship and the need to quantify the impact of delay. *Am Heart J*. 2011;161(2):247-53.
35. Armstrong PW, Gershlick A, Goldstein P, Wilcox R, Danays T, Bluhmki E, et al., STREAM Study Group. The strategic reperfusion early after myocardial infarction (STREAM) study. *Am Heart J*. 2010;160(1):30–6.
36. Escosteguy CC, Teixeira AB, Portela MC, Guimarães AEC, Lima SML, Ferreira VMB, et al. Implementando diretrizes clínicas na atenção ao infarto agudo do miocárdio em uma emergência pública. *Arq Bras Cardiol*. 2011;96(1):18-25.



