ORIGINAL ARTICLE

Knock on the Right Door. How we are Treating the Patient with Acute Myocardial Infarction

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Abstract

Background: To reduce mortality of acute myocardial infarction, medical care must be provided within the first hours of the event.

Objective: To identify the "front door" to medical care of acute coronary patients and the time elapsed between patients' admission and performance of myocardial reperfusion in the public health system of the city of Joinville, Brazil.

Methods: The study was a retrospective analysis of the medical records of 112 consecutive patients diagnosed with acute myocardial infarction by coronary angiography. We identified the place of the first medical contact and calculated the time between admission to this place and admission to the referral hospital, as well as the time until coronary angiography, with or without percutaneous transluminal angioplasty. A descriptive analysis of data was made using mean and standard deviation, and a $p < 0.05$ was set as statistically significant.

Results: Only 16 (14.3%) patients were admitted through the cardiology referral unit. Door-to-angiography time was shorter than 90 minutes in 50 (44.2%) patients and longer than 270 minutes in 39 (34.5%) patients. No statistically significant difference was observed in door-to-angiography time between patients transported directly to the referral hospital and those transferred from other health units ($p < 0.240$). Considering the time between pain onset and angiography, only 3 (2.9%) patients may have benefited from myocardial reperfusion performed within less than 240 minutes.

Conclusion: Management of patients with acute myocardial infarction is not in conformity with current guidelines for the treatment of this condition. The structure of the healthcare system should be urgently modified so that users in need of emergency services receive adequate care in accordance with local conditions. (Int J Cardiovasc Sci. 2018;31(5)520-526)

Keywords: Guidelines Adherence; Failure to Rescue, Health Care; Unified Health, System; Myocardial Infarction; Emergency Medical Services.

Introduction

Acute myocardial infarction (AMI) is one of the major causes of death in Brazil.[1,2] Heart failure and sudden death, the most severe complications of AMI, are the most serious manifestations of atherosclerotic disease. The majority of deaths occur in the first 24 hours of disease onset, and nearly half of them in the first hour.[1-3] Similar to the in-hospital mortality, 30-day mortality decreased from 8.6% to 3.6% in some North American states between 1988 and 2000.[3] In Brazil, 30-day mortality is 15.4%[2] according to the Brazilian Unified Health System (SUS) Computing Department (DATASUS).

When AMI patients seek medical care, therapeutic interventions should be promptly performed to result in beneficial outcomes. Fibrinolytic therapy and coronary angioplasty have no or low efficiency when performed after four hours of AMI with ST-segment elevation.[1-19]

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For this reason, patients' diagnosis, transportation and treatment should be fast.

In 2011, the Ministry of Health implemented an integrated system for AMI management (the *Linha de Cuidado do Infarto Agudo do Miocárdio*) through healthcare units of the SUS, and a clinical protocol on acute coronary syndrome (ACS) (the *Protocolo Clínico sobre Síndrome Coronariana Aguda*).[2] These were created to propose an integrated action for ACS treatment, grounded on its high prevalence and important role in morbidity and mortality.

In the city of Joinville, SUS provides emergency care units, general hospitals and a referral hospital. Coronary angiography and angioplasty are available in the referral hospital only, and none offers cardiac care services available 24 hours a day. Joinville Secretary of Health promoted the publication of a booklet entitled "*Bata na porta certa*" ("Knock on the right door") to guide healthcare providers and users in directing themselves to the correct units for health assistance.[20] For example, the booklet suggests the best emergency care units for chest pain in the city. Our study aimed to identify where AMI patients sought medical care at first place (the "front door") and the time elapsed from initial care received by the patients (first medical contact) and myocardial reperfusion.

Methods

This was a retrospective analysis of medical records, including 112 patients with ST-segment elevation myocardial infarction (STEMI) who had undergone coronary angiography in the period between 09/28/2013 and 05/28/2014. Data were collected at the Catheterization Laboratory, at Santa Catarina State referral hospital, at Joinville Hospital and at three emergency care units of the city.

We registered: the place where patients received initial care, the time (min) between pain onset and the moment the patient was seen at the unit; the time (min) between admission to the first unit and admission to the referral hospital; the time (min) between admission to the referral hospital and coronary angiography test; and whether coronary thrombolysis was performed. Due to missing data, the door-to-balloon time was not recorded. When the "front door" to medical care was not found in patients' records, we attempted to contact patients by telephone. In addition, we also collected data on the occurrence of heart failure, myocardial revascularization and death.

The study was approved by the ethics committee of Joinville Regional University (UNIVILLE), by Joinville Secretary of Health, and by hospitals and catheterization laboratory involved in the study.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences for Windows version 17 (SPSS Inc. Chicago, Illinois). Continuous variables with normal distribution were expressed as mean ± standard deviation, and frequency analysis was used for categorical variables. Data normality was verified by the Kolmogorov-Smirnov test. Between-group comparisons were performed by the Student's t test for independent, continuous variables and by the chi-square test for nominal variables. The level of significance was set at 5% (95% confidence interval, 95%CI).

Results

We studied 87 men and 24 women, mean age of 58.3 (23-82) years. The "front door" to the emergency care was the emergency care unit for 44 patients, the referral hospital for 16 patients, the city hospital for 4, the emergency medical service transport system for 5, and primary health centers for 2 patients; in 29 patients this information was not available. The other patients were transfered from other cities. Event duration (time elapsed between pain onset and coronary angiography) was probably shorter than 12 hours in 71 patients (65.7%) and longer than 12 hours in 39. This was in fact an estimate, calculated as the sum of minutes during the period between the first medical assistance and coronary angiography test, since duration of pain was not recorded in the medical records. In addition, in emergency care units, most of the medical records could not be accessed, since they were usually registered behalf of patients and filled in other institution. The medical records of patients referred from other cities were also not available, and we rarely obtained useful information by phone contact in these cases. Percutaneous transluminal angioplasty (PTA) was performed in 92 (82.1%) patients and the door-to-angiography time (DAT) was shorter than 90 minutes in 50 (44.2%) patients (Table 1). No statistically significant difference was seen in DAT, sex or age between patients admitted to the referral hospital and the others. DAT was not available in 14 patients. No patients received thrombolytic drugs.

Table 1 - Comparison of door-to-angiography time (DAT) between patients seen at the referral hospital patients seen in other healthcare units

	Referral hospital *	Others**	Total
Initial care	16	96	112
DAT < 90 min	7 (43.7%)*	43 (44.3%)**	50 (44.2%)
DAT > 270 min	4 (25%)*	45 (46.3%)**	49 (43.3%)
DAT > 720 min	3 (18.7%)*	36 (37%)**	39 (34.8%)
Maximum DAT	15.695	48.439	48.439
Minimum DAT	19	10	10
Mean DAT	1,433	2,132	2,033 (+/-5,542)
Angioplasty	14 (87.5%)	78 (80.41%)	92 (82.1%)

**Pearson $X^2 = 2.124$; P = 0.145 /Fisher`s Exact Test 0.169; ** Pearson $X^2 = 0.436$/Fisher´s Exact Test 0.511.*

Discussion

In 2001, Gibson posed a question he was often asked: "what do we need to do to improve mortality by another 1% in the setting of acute myocardial infarction?" and then answered that this could not be achieved exclusively with new drugs and devices but also by reducing the time to treatment.[4] Our results suggest that we are far from achieving these objectives. When mentioning the Assessment of the Safety and Efficacy of a New Thrombolytic (ASSENT 2) report,[5] Gibson emphasized the importance of performing electrocardiography for the diagnosis and a time to treatment < 2 hours.

In the ASSENT-2 trial, the investigators assessed electrocardiographic changes and 1-year mortality in 13,100 patients undergoing primary thrombolysis. In-hospital mortality and late mortality were proportional to pain duration and inversely proportional to ST-T resolution (lower and upper limits of 3.8 and 13%) in one year.[5]

In our study, analysis of the medical records revealed that results of cardiac enzyme tests for diagnosis and treatment decisions are still lacking in many of them.

Acute coronary syndrome, notably AMI, is the major cause of cardiac deaths in Brazil.[1,2] A considerable percentage of deaths occur quickly and unexpectedly before patients get medical care.[1-3] Until 1980, there were insufficient medical resources to achieve significant reductions in in-hospital and late mortality. In 1979, Rentrop published the first results of intracoronary injection of streptokinase. Coronary angiography performed during and after STEMI showed spontaneous recanalization in nearly 40% of patients, increased to 70% with thrombolytic therapy. These findings were confirmed by Ganz in 1982. The potential of reperfusion therapy with thrombolytic drugs and angioplasty in reducing mortality has already been shown;[1-17] nevertheless, a significant reduction in mortality depends on how early reperfusion therapy is performed.[5-19,21] In Stemi, the therapy should be started within the first four hours of the event.[5,12,15,17-19] A mean reperfusion time < 180min has been reported in attempt to provide adequate assistance to patients before (by administration of thrombolytic drugs) and during hospitalization (primary angioplasty). Systematic reviews by Keeley et al.,[13] updated by Asseburg et al.,[14] including short term and six-month outcomes, showed that compared with thrombolytic agents, reduction in mortality and in non-fatal outcomes with primary angioplasty was only significant when time delay was shorter than 45 minutes and 90 minutes, respectively.[15,16] The use of thrombolytic therapy was even more efficient in reducing mortality according to six randomized studies by Morrison et al.[15] In-hospital thrombolysis and prehospital thrombolysis decreased the mean duration of pain until reperfusion by 162 and 104 minutes, respectively. Thrombolytic therapy followed by short-term angioplasty is efficient in reducing short-term and long-term events, regardless of the presence of multi-vessel or one-vessel injury.[16]

Many factors can influence the rescue of patients with STEMI – the patient, who should seek medical assistance as soon (and if) he perceives the symptoms; healthcare professionals who should diagnose the condition and provide the patient with adequate treatment as early as possible, and performance of reperfusion therapy. In Joinville, the SUS offers three emergency care units and three public hospitals (including one referral center for coronary angiography and angioplasty). The efficacy of this system was unknown, although there were reports of difficult accessibility of paramedics to the referral hospital and delayed arrival of patients to the catheterization laboratory. With the permission of the catheterization laboratory, we identified the patients with ACS seen at the unit, their "front door" to medical care, and the time from the first assistance to reperfusion with angioplasty. Patients' transportation depends on the experience of the

staff in dealing with ACS patients and symptoms, as well as possibility of transport to well-equipped facilities.[6,7,10,20-23] It is estimated that approximately 20% of patients arrive at the clinics within two hours of pain onset.[2]

In fact, public health systems can provide guidance for their users through several actions.[3,10,20] Healthcare providers are expected to be able to identify the disease, especially by recognizing suggestive symptoms and electrocardiographic changes.[1-4,21-23] Electrocardiography (ECG) is an old, cheap test, essential in diagnosing and guiding therapeutic approaches. In 2002, a European task force emphasized the importance for both patients and healthcare providers to identify high-risk chest pain.[24] When symptoms occurred at home, patients wait a mean of 60 minutes before seeking help, and up to 25% of them wait for four hours or more.[7,24] In emergency services, the unawareness of the low sensitivity (approximately 50%) of the ECG test in confirming AMI may affect the diagnosis. The authors reinforced the need for serial ECG at short intervals (minutes) to diagnose the disease, in accordance with Brazilian guidelines recommendations,[1] rather than performing ECG tests every three hours, as usually occurs.

Unfortunately, some paramedics do not receive adequate training in ECG and rely on cardiac enzyme tests. In STEMI, cardiac enzymes are useful for confirming the event and indicating the prognosis but are not essentially required for the diagnosis.[1-3,21] Delay in the results leads to a delayed and inefficient reperfusion therapy.

Boersma et al.,[12] in a review of 22 studies published between 1983 and 1993 including 50,246 patients undergoing coronary thrombolysis showed that the greatest benefit on 30-day mortality is achieved by the therapy performed within the first two hours. In case of STEMI, thrombolytic drugs are recommended when waiting time to angioplasty is longer than 90 minutes.[7-9,11,13-17]

The ACCEPT/SBC (Clinical Outcomes at 30 days in the Brazilian Registry of Acute Coronary Syndromes),[22] a multicenter study of 47 Brazilian hospitals carried out in 2010 and 2011 showed a use of thrombolytic drugs lower than 15%. In addition, reperfusion therapy was not performed in 22.3% of patients with STEMI; mortality in this group was higher than that in the group that received reperfusion therapy (8.1% vs. 2.0%). In the reperfusion group, mean door-to-angiography was 125 (± 90) minutes.

The Global Registry of Acute Coronary Events (GRACE), in a six-month follow-up, also showed greater mortality in patients that did not receive reperfusion therapy.[26] In our sample, no patient used thrombolytic drugs (which are not available in the emergency care units but are available in the hospitals). Transluminal angioplasty was performed in 86.1% of patients. Our results indicated that almost all STEMI patients were negatively affected by delayed or absent reperfusion. Approximately 40% of STEMI patients survive the event irrespectively of the medical therapy, and among these patients with less severe infarction, those with late presentation STEMI cause biases in analyzing the benefits of myocardial reperfusion.[10-13] Several reports[3,6,13,15,21-23] have demonstrated that extensive myocardial infarction depends on the best quality medical care to prevent complications and in-hospital and late mortality.

Due to incomplete or missing data in the medical records, we could not identify the complications of STEMI. In the study group, two in-hospital deaths were registered, suggesting the presence of less severe conditions in this group. One limitation of the study is the lack of documentation of pain duration before medical assistance in all medical reports. If we assume a 2-hour period for that,[1,4,5,24] few patients would have been undergone angioplasty within a four-hour period. Some patients had a very short DAT (10-20 minutes) because the front door, in these cases, was the catheterization laboratory. Only three patients went directly to the referral hospital and hence may have had a pain-door-angiography time shorter than 4 hours.

Wang et al.,[27] analyzed the data from 101 hospitals in the "Get With the Guidelines" program of the American Heart Association, started in 2000 and reinforced by the D2B Alliance campaign focused on reducing door-to-balloon time. Data of 43,678 AMI patients were compared between 2005 and 2007. After exclusion of patients with non-STEMI, patients transferred in from other hospitals, patients without angioplasty or with late angioplasty, 5,881 patients undergoing primary angioplasty were assessed. Although door-to-balloon time decreased from 101 to 87 minutes, there was no significant reductions (from 5.1% to 4.7%) in in-hospital mortality. Since 2005 data had already revealed satisfactory in-hospital mortality parameters, the authors highlighted the importance of prehospital measures.

Between 2002 and 2008 in Denmark, Terkelsen et al.,[10] included 13,439 consecutive patients with STEMI referred for reperfusion therapy. The Danish National Health Service provides ambulances equipped with electrocardiographic system and defibrillator. Users

of the health service can call the emergency medical service, and those deemed in need of an ambulance are transported to the catheterization laboratory. The study was designed to evaluate the effect of several variables on late mortality. Patients were allocated into two groups, one transported directly to the percutaneous coronary intervention center and the other group transported to local hospitals first and then transferred to the treatment center. The time from pain onset to initiation of reperfusion therapy was calculated and categorized in patient delay, transportation delay, door-to-balloon time, system delay and total delay in both groups, in addition to hospital delay and prehospital system delay (time between transportation and arrival at the percutaneous coronary intervention center in one of the groups. After exclusion of patients that did not receive reperfusion, patients with a treatment delay longer than 12 hours, and patients with missing data, a total of 6,209 patients were followed-up. Door to balloon time was 39 (24-70) minutes in the group directly transported to treatment center and 29 (21-72) minutes in the other group. The study showed that in the group transferred from other hospitals, treatment delay was significantly longer (240 minutes vs. 170 minutes) than in the group directly transported for treatment. Mean follow-up period was 3.4 (1.8-5.2) years, with mortality of 15.4% in patients with system delays < 60 minutes, 23.3% in those with delays of 61-120 minutes, 28.1% in those with delays of 121-180 minutes, and 30.8% in those with delays of 180-360 minutes. Multivariate analysis showed that both prehospital delay and door-to-balloon time were associated with mortality, and efforts should be made to reduce them. Barreto et al.,[28] also demonstrated that transportation delay from other centers to the catheterization laboratory was a predictor of adverse events.

Bagai et al.,[22,23] compared patients evaluated in the emergency department and those transported directly to the catheterization laboratory. The authors reported that a median time of 30 minutes was spent in the emergency department, with potential decrease. The authors confirmed the beneficial effects of ambulance services and direct transportation of patients to the catheterization laboratory on the door-to-balloon time. However, the authors highlighted that the service is used infrequently and no differences in in-hospital mortality was observed between the groups.

Jollis et al.,[21] published the first results of the STEMI Systems Accelerator project, a large national effort to adequate regional STEMI care to national guidelines in the USA. The program was developed in 2012 and included emergency medical services and hospitals, regional and central coordinators, training of leaders, physicians and paramedics, ambulance and emergency staff, development of protocols, establishment of common criteria for STEMI diagnosis and treatment, and data storage in a national registry and timely feedback. Analysis of the program during the first two years revealed that the call for medical emergency by the citizens causes a decrease in the pain-to-first medical contact time and in door-to-balloon time, incrementing the percentage of patients who receives primary percutaneous coronary intervention within 90 minutes of paramedic arrival. Shorter delays in emergency services resulted in a reduction in in-hospital mortality.

In our study, prehospital delay was estimated using partial data, and seemed to be greater than 240 minutes in almost all patients. Also, the DAT was elevated, suggesting many possibilities for improvement.

In view of the studies cited in this study, we can say that difficulties in the treatment of STEMI are present (and similar) in many countries, and the strongest difference is in the efforts for their improvement.

In Brazil, some interventions have been published.[29-32] Escosteguy et al.,[29] published the results of a multidisciplinary program for implementation of clinical guidelines on AMI in a public emergency unit in Rio de Janeiro. Caluza et al.,[30] described the implementation steps and the first results of an AMI treatment system in Sao Paulo. The program standardized the processes of clinical diagnosis of STEMI, immediate ECG using tele-ECG, therapy decision (PTA or thrombolysis) and availability of care in the referral hospital. Andrade et al.,[31] described an integrated system for cardiovascular emergency services in Marilia, Brazil, with direct transportation of patients to the catheterization laboratory. The authors reported high symptom-to-balloon time in patients transferred from other units (5.0 ± 2.2 hours) and in those directly admitted to the hospital (3.3 ± 2.2 hours). Marcolino et al.,[32] reported the results of an integrated system for AMI approach (*Linha de Cuidado do Infarto Agudo do Miocárdio*) implemented in the city of Belo Horizonte, Brazil, between 2010 and 2011, which included training and motivation programs of the emergency service staff, interaction between the units and accessibility to the catheterization laboratory.

Study limitations

Limitations of the study include its retrospective nature, the limited number of patients, the inclusion of patients undergoing catheterization only, the impossibility of determining the time interval from pain onset, patient admission and procedure, and the lack of data at the time of angioplasty.

Conclusions

We identified a flawed healthcare system for STEMI management, in which the first medical contact rarely occurs in the referral hospital, physicians have difficulties in diagnosing the disease and do not use validated therapeutic approaches, and much data are missing from the medical records (which are filed in inadequate locations). Difficulties are encountered in the transfer of patients to the referral hospital and the emergency medical services are infrequently called, causing a delay in mechanical reperfusion. The importance of the catheterization laboratory is highlighted, with more than half of patients treated within a DAT consistent with current guidelines, reinforcing the need for a direct transportation of patients to this facility. We recommend the implementation of an integrated system for AMI management compatible with local conditions and patients' needs, characterized by centralized coordination, continuing education of the medical staff, presence of paramedics trained in ECG and use of thrombolysis therapy. We believe that the situation here described is not exclusive of the city of Joinville, justifying and encouraging the development of further studies and improvements in the system. We suggest a prospective, continuing study to evaluate the development and adherence of the system to current guidelines.

Author contributions

Conception and design of the research: Hoepfner C. Acquisition of data: Roma E, Lana JV, Santin AL, Borga AL, Yamamoto AC, Techentin JV. Analysis and interpretation of the data: Hoepfner C, Roma E, Lana JV, Santin AL. Writing of the manuscript: Hoepfner C, Lana JV, Santin AL, Borga AL, Yamamoto AC, Techentin JV. Critical revision of the manuscript for intellectual content: Hoepfner C, Roma E, Lana JV, Santin AL.

Potential Conflict of Interest

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

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There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Fundação Educacional da Região de Joinville - UNIVILLE under the protocol number 33651114.6.0000.5366. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Piegas LS, Feitosa GS, Mattos LA, Nicolau JC, Rossi Neto JM, et al; Sociedade Brasileira de Cardiologia. IV 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):e179-264.
2. Brasil. Ministério da Saúde. Portaria nº 1600, 07/06/2011. Rede de atenção às urgências e emergências. Institui a linha de cuidado do infarto agudo do miocárdio no âmbito do Sistema Único de Saúde (SUS), bem como o protocolo clínico sobre síndrome coronariana aguda. Diário Oficial da União Brasília (DF). 08 de julho de 2011. Seção 1. p. 70.
3. Kushner FG, Hand M, Smith SC Jr, King SB 3rd, Anderson JL, Antman EM, et al. 2009 focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update) a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2009;54(23):2005-41. Erratum in: J Am Coll Cardiol. 2009;54(25):2464. J Am Coll Cardiol. 2010;55(6):612.
4. Gibson CM. Time is myocardium and time is outcomes. Circulation. 2001;104(22):2632-24.
5. Fu Y, Goodman S, Chang WC, Van de Werf F, Granger CB, Armstrong PW. Time to treatment influences the impact of ST-segment resolution on one-year prognosis: insights from the assessment of the safety and efficacy of a new thrombolytic (ASSENT-2) trial. Circulation. 2001;104(22):2653-9.
6. Goldberg RJ, Gurwitz JH, Gore JM. Duration of, and temporal trends (1994–1997) in, prehospital delay in patients with acute myocardial infarction: the Second National Registry of Myocardial Infarction. Arch Intern Med. 1999;159(18):2141-7.

7. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomized trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Lancet. 1994;343(8893):311-22. Erratum in: Lancet. 1994;343(8899):742.

8. GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Engl J Med. 1993;329(10):673-82.

9. Berger PB, Ellis SG, Holmes DR Jr, Granger CB, Criger DA, Betriu A, et al. Relationship between delay in performing direct coronary angioplasty and early clinical outcome in patients with acute myocardial infarction: results from the global use of strategies to open occluded arteries in Acute Coronary Syndromes (GUSTO-IIb) trial. Circulation. 1999;100(1):14-20.

10. Terkelsen CJ, Sorensen JT, Maeng M, Jensen LO, Tilsted HH, Trautner S, et al. System delay and mortality among patients with STEMI treated with primary percutaneous coronary intervention. JAMA. 2010;304(7):763-71.

11. Pinto DS, Kirtane AJ, Nallamothu BK, Murphy SA, Cohen DJ, Laham RJ, et al. Hospital delays in reperfusion for ST-elevation myocardial infarction implications when selecting a reperfusion strategy. Circulation. 2006;114(19):2019-25.

12. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Lancet. 1996;348(9030):771-5.

13. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomized trials. Lancet. 2003;361(9351):13-20.

14. Asseburg C, Vergel YB, Palmer S, Fenwick E, de Belder M, Abrams KR, et al. Assessing the effectiveness of primary angioplasty compared with thrombolysis and its relationship to time delay: a Bayesian evidence synthesis. Heart. 2007;93(10):1244-50.

15. Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: a meta-analysis. JAMA. 2000;283(20):2686-92.

16. Elbarouni B, Cantor WJ, Ducas J, Borgundvaag B, Džavík V, Heffernan M, et al; TRANSFER-AMI Trial Investigators. Efficacy of an early invasive strategy after fibrinolysis in ST-elevation myocardial infarction relative to the extent of coronary artery disease. Can J Cardiol. 2014;30(12):1555-61.

17. Newby LK, Rutsch WR, Califf RM, Simoons ML, Aylward PE, Armstrong PW, et al. Time from symptom onset to treatment and outcomes after thrombolytic therapy. J Am Coll Cardiol. 1996;27(7):1646-55.

18. De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction. Every minute of delay counts. Circulation. 2004;109(10):1223-5.

19. De Luca G, Suryapranata H, Zijlstra F, Hof JAW, Hoorntje JC, Marcel Gosselink AT, et al; ZWOLLE Myocardial Infarction Study Group. Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. J Am Coll Cardiol. 2003;42(6):991-7.

20. Santa Catarina, Estado. Secretaria da Saúde. Bata na porta certa: programa de conscientização. Joinville: Câmara de Vereadores; 2014.

21. Jollis JG, Al-Khalidi HR, Roettig ML, Berger PB, Corbett CC, Dauerman HL, et al; Mission: Lifeline STEMI Systems Accelerator Project. Regional systems of care demonstration project. American Heart Association Mission: Lifeline STEMI Systems Accelerator. Circulation. 2016;134(5):365-74.

22. Bagai A, Al-Khalidi HR, Muñoz D, Monk L, Roettig ML, Corbett CC, et al. Bypassing the emergency department and time to reperfusion in patients with prehospital ST-segment–elevation. Findings from the reperfusion in acute myocardial infarction in Carolina Emergency Departments Project. Circ Cardiovasc Interv. 2013;6(4):399-406.

23. Bagai A, Jollis JG, Dauerman HL, Peng SA, Rokos IC, Bates ER, et al. Emergency department bypass for ST-segment–elevation myocardial infarction patients identified with a prehospital electrocardiogram. A report from the American Heart Association Mission: Lifeline Program. Circulation. 2013;128:352-359.

24. Erhardt L, Herlitz J, Bossaert M, Halinen M, Keltai M, Koster R, et al. Task force on the management of chest pain. Eur Heart J. 2002;23(15):1153-76.

25. Mattos LA, Berwanger O, Santos ES, Reis HJ, Romano ER, Petriz JL, et al. Clinical outcomes at 30 days in the brazilian registry of acute coronary syndromes (ACCEPT). Arq Bras Cardiol. 2013;100(1):6-13.

26. Eagle KA, Lim MJ, Dabbous OH, Pieper KS, Goldberg RJ, Van de Werf E, et al; GRACE investigators. A validated prediction model for all forms of acute coronary syndrome estimating the risk of 6-month postdischarge death in an international registry. JAMA. 2004;291(22):2727-33.

27. Wang TY, Fonarow GC, Hernandez AF, Liang L, Ellrodt G, Nallamothu BK, et al. The dissociation between door-to-balloon time improvement and improvements in other acute myocardial infarction care processes and patient outcomes. Arch Intern Med. 2009;169(15):1411-9.

28. Canesin FP, Cantarelli MJ, Castello Jr HJ, Gonçalves R, Gioppato S, Guimarães JB, 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):279-85.

29. Escosteguy CC, Teixeira AB, Portela MC, Guimarães AE, Lima SM, Ferreira VM, et al. Implementing clinical guidelines on acute myocardial infarction care in an emergency service. Arq Bras Cardiol. 2011;96(1):18-25.

30. Caluza AC, Barbosa AH, Gonçalves I, Oliveira CA, Matos LN, Zeefried C, et al. ST-Elevation myocardial infarction network: systematization in 205 cases reduced clinical events in the public health care system. Arq Bras Cardiol. 2012;99(5):1040-8.

31. Andrade PB, Tebet MA, Nogueira EF, Rinaldi FS, Esteves VC, Andrade MVA et al. Impact of inter-hospital transfer on the outcomes of primary percutaneous coronary intervention. Rev Bras Cardiol Invasiva. 2012;20(4):361-6.

32. Marcolino MS, Brant LCC, Araújo JG, Nascimento BR, Castro LRA, Martins P, et al. Implementation of the myocardial infarction system of care in city of Belo Horizonte, Brazil. Arq Bras Cardiol. 2013;100(4):307-14.