Delay in Performing Primary Angioplasty: Is it Due to a Reason Related to the Patient or to the Healthcare System?

FEDERICO BLANCO†, MIGUEL A. RICCITELLI[MTSAC], ALEJANDRO GARCÍA ESCUDERO†, SUSANA AFATTATO, ROBERTO NEME, GERARDO GIGENA, PATRICIA ARCE, RICARDO A. SARMIENTO[MTSAC], LUIS VIDAL, JORGE SZARFER

Received: 09/19/2008
Accepted: 12/10/2008

Address for reprints:
Dr. Federico Blanco
División Cardiología.
Hospital General
de Agudos "Dr. Cosme Argerich"
Av. Almirante Brown 240
(C1155ADP) Buenos Aires,
Argentina
e-mail:
federicoblanco@ymail.com

SUMMARY

Introduction
One of the inconveniences in the general utilization of primary angioplasty (PTCA) would seem to be the delay in its application. Most of present data come from clinical trials from other countries, whereas little is known about its application in the regular practice in our country.

Objectives
To analize the periods of time needed for each stage of a PCTA in a center where the treatment of choice is used as a first step for a time-optimization program, and to determine if the delay is due to a situation related to the patient or to the healthcare system.

Material and Methods
This is a prospective observational study in patients with AMI lasting less than 12 hours. The "patient time" was counted from the onset of the symptoms to arrival at hospital, and the "medical care time" was determined from hospital arrival to balloon inflation.

Results
PCTA was performed in 224 patients admitted with diagnosis of AMI. The median values (25th to 75th percentile) were "patient time": 60 minutes (40-150), "medical care time": 93 minutes (72-128). "Medical care time" includes: time 1 (hospital arrival-EICT activation): 20 minutes (10-45), time 2 (EICT activation-admission to cath lab): 38 minutes (23-52), time 3 (admission to cath lab- first balloon inflation): 31 minutes (21-45).

Conclusions
"Patient time" represents less than half the total time consumed. "Medical care time" determines the higher delay for the procedure; therefore, more emphasis should be placed in improving this time, within which EICT activation-first balloon inflation time constitutes a key factor.

Rev Argent Cardiol 2009;77:14-20.

Key words > Myocardial infarction - Time - Angioplasty

Abbreviations >

S	Stroke	**EICT**	Emergency Interventional Cardiology Team
PTCA	Percutaneous transluminal coronary angioplasty	**AMI**	Acute myocardial infarction
LBBB	Left bundle branch block	**MCT**	Medical care time
ECG	Electrocardiogram		

BACKGROUND

Thrombotic occlusion of a coronary artery in the early phase of an acute myocardial infarction (AMI) can be reverted with percutaneous transluminal coronary angioplasty (PTCA). Several randomized clinical trials and meta analyses including these trials have demonstrated that coronary reperfusion achieved with primary PTCA improves short-term and long-term prognosis of patients with AMI compared to thrombolytic therapy. (1-8) The main limiting factors to perform coronary angioplasty include availability of PTCA facilities, material and well-trained staff to carry out the procedure; once AMI has been diagnosed, reperfusion of the culprit vessel should be achieved rapidly. Although time to treatment has not proved to be such a determinant for success of PTCA as with thrombolytic therapy (the gold hour), the benefit of

Department of Cardiology. Hospital General de Agudos "Dr. Cosme Argerich", Autonomous City of Buenos Aires, Argentina
[MTSAC] Full Member of the Argentine Society of Cardiology
†To apply as full member of the Argentine Society of Cardiology

primary angioplasty, over thrombolysis, depends on the former's additional time delay. (8, 9) Once we have understood the different time delays from symptoms onset until the end of PTCA, we shall be able to develop the necessary measures to reduce them and thus optimize the outcomes of the procedure. (10) The present study was carried out in a public hospital of the Autonomous City of Buenos Aires where PTCA is the treatment of choice of AMI, in order to recognize the time intervals of each phase from the onset of symptoms of AMI until first balloon inflation of the culprit vessel.

MATERIAL AND METHODS

We conducted a prospective observational study in a cohort of consecutive patients undergoing PTCA between January 1, 2004 and December 31, 2007. We considered only AMI patients undergoing primary PTCA according to ACC/AHA (American College of Cardiology/American Heart Association), (11) class I recommendations: angina-like chest pain or other symptoms suggestive of myocardial ischemia lasting more than 30 minutes,

ST-segment elevation ≥ 0.1 mV in at least two subsequent leads or new (or presumably new) left branch bundle block (LBBB) within 12 hours after symptoms onset. All patients presenting to the Emergency Department of our hospital with a probable diagnosis of AMI are evaluated by the cardiologist on duty who orders reperfusion treatment and immediately activates the Emergency Interventional Cardiology Team (EICT), constituted by an interventional cardiologist, a radiology technician and a nurse. Patients referred to our center from other hospitals with indication of PTCA were excluded from the study.

Variables

Demographic and basal data were obtained from each patient as well as the characteristics of the infarction at presentation and the type of procedure performed. Time intervals were defined as follows for further analyses:

- Patient time: from the onset of symptoms to hospital arrival.
- Medical care time (MCT): from arrival at the Emergency Department until first balloon inflation. In turn, this time interval was divided in three: time 1 (hospital arrival- EICT activation), time 2 (EICT activation-admission to the cardiac catheterization laboratory) and time 3 (admission to the cath lab-first balloon inflation).

Time from activation of the EICT to first balloon inflation was also analyzed (activation-balloon time) (includes time 2 and 3).

Time intervals were calculated as follows:

- Time intervals of symptoms onset and hospital arrival were determined based on patients' or relatives' interview.
- Activation time refers to the moment of the telephone call between the cardiologist on duty and the EICT.
- Time of patient admission to the cardiac catheterization laboratory refers to the moment of the first contact between any member of the EICT and the patient.
- The moment of first balloon inflation of the culprit vessel is the time recorded by the cardiac catheterization technician.

In addition, we also analyzed if the procedure was performed during regular working hours or off-duty hours. Time to medical consultation in patients living in the Autonomous City of Buenos Aires was compared to that of patients living in the outskirts of the city.

Statistical Analysis

Patients' basal characteristics are expressed as absolute values and percentages for qualitative variables and means with their corresponding standard deviation for quantitative variables. Time interval variables and their dispersion were expressed as medians and 25th and 75th percentiles. Analyses were performed using chi square test, Student's *t* test for normal distributions and Kruskall-Wallis test for non parametric distributions.

RESULTS

Between January 1st, 2004 and December 31st, 2007, 233 patients were examined in our hospital due to

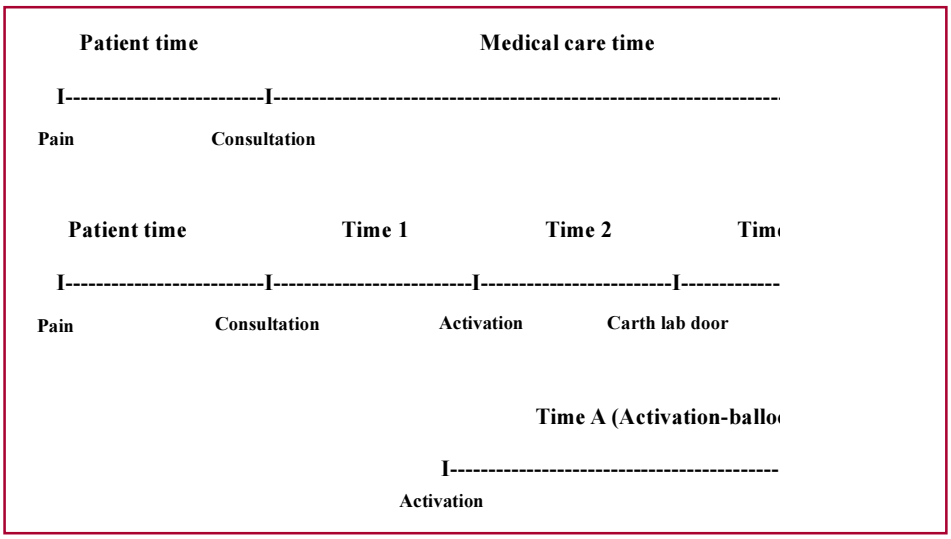

Fig. 1. Definition of the time intervals analyzed.

prolonged angina within the previous 12 hours associated with ST-segment elevation e" 0.1 mV in at least two contiguous leads or LBBB; all patients were candidates for reperfusion therapy. Percutaneous transluminal coronary angioplasty was performed in 224 patients (96.2%). In the remaining 9 patients (3.8%) coronary angiography showed non-significant coronary lesions. Basal characteristics are displayed in Table 1. Mean age was 59.5 ± 12.2 years and 81.5% were men. Seventy six percent lived a sedentary life, 66.5% were current smokers and half of them had hypertension or dyslipemia. Almost half of the infarctions (45.9%) were located in the anterior wall (107 patients). Only one third of this population (35.2%) had one-vessel coronary artery disease and 23.6% had a history of previous myocardial infarction. Congestive heart failure and cardiogenic shock were present in 24% and 16.7% of patients at admission, respectively.

Table 2 shows the different time intervals. Median "patient time" - from the onset of symptoms to hospital arrival- was 60 minutes (range, 40 - 150). Median medical care time (MCT) from patient's first contact with the hospital environment, was 93 minutes (range, 72-128). The procedure was ordered rapidly, with a median time of 20 minutes. Median time interval until the patient was admitted to the cardiac catheterization laboratory was 38 minutes. This delay includes the necessary time until all the members of the EICT arrive and patient is transported from the Emergency Department to the cath lab. Finally, median time from admission to the cath lab and first balloon inflation of the culprit vessel was 31 minutes and included different procedures, such as placing the patient on the catheterization table, preparing the patient and performing a diagnostic coronary angiography.

There were no significant differences in the time intervals of patients undergoing PTCA during regular working hours compared to patients intervened during off-duty hours or in week ends. In addition, there were no significant differences in time to medical consultation in patients living in the Autonomous City of Buenos Aires compared to patients living in the outskirts of the city [60 minutes (range 40-150) versus 63 minutes (range 30-150), respectively; p = ns]. This absence of differences might be attributed to a type 1 error.

DISCUSSION

As rapid initiation of reperfusion therapy in patients with AMI is associated with favorable outcomes, pa-

Table 1. Basal characteristics of the population (n = 233)

Age	59.5 ± 12.2
Male gender	190 (81.5%)
Age > 75 years	34 (14.6%)
Anterior wall	107 (45.9%)
Hypertension	127 (54.5%)
Diabetes	39 (16.7%)
Current smoking	155 (66.5%)
Dyslipemia	124 (53.2%)
Family history	64 (27.5%)
Overweight	105 (45.1%)
Sedentary life	177 (76%)
Previous AMI	55 (23.6%)
Shock	39 (16.7%)
Heart failure	56 (24%)
Procedure performed during regular working hours	119 (51%)
Procedure performed during off-regular working hours	86 (36.9%)
Procedure performed during weekend	28 (12%)
Patients from the Autonomous City of Buenos Aires	149 (63.9%)
Patients from the outskirts of the city	84 (36.1%)
Patients with social security coverage	123 (52.8%)
Patients without medical coverage	110 (47.2%)
One-vessel coronary artery disease	82 (35.2%)
Two-vessel coronary artery disease	89 (38.2%)
Three-vessel coronary artery disease	62 (26.6%)

Table 2. Time intervals observed in 233 patients admitted

Time interval	Time day in minutes [median (25-75)]
Patient time (pain onset-hospital)	60 (40-150)
Medical care time	93 (72-128)
Hospital arrival-indication of PTCA	20 (10-45)
Indication of PTCA-admission to Cardiac Catheterization Laboratory	38 (23-52)
Cath Lab door-balloon	31 (21-45)
Activation-balloon	68 (54-89)

tients with this condition should present to hospitals as soon as possible. This study, performed in the Autonomous City of Buenos Aires, demonstrated that patients arrived at hospitals relatively early (median patient time: 60 minutes) compared to other studies or registries (4, 5, 12-20) (Table 3). Data of the most important trials showed a lesser benefit in terms of mortality and preservation of ventricular function related to late reperfusion therapy. (8, 9, 21-24) Different studies demonstrate that approximately 1 in 5 patients with AMI present to the hospital within 1 hour of the onset of symptoms, a time interval associated with the greatest benefit of reperfusion therapy. (25) This figure differs from the patient time found in the present study where 50% of patients presented to hospital in the first 60 minutes. There is a remarkable variation in time interval from the onset of symptoms to arrival at hospital in different published studies. (12-20) The GRACE register (12) reported a median time of 139 minutes from symptoms onset which was slightly lower than the findings of the French register. (13) According to AMI registries, about 25% of patients in Argentina seek medical care within 2 hours from symptoms onset, with a median time of 4 hours until admission reported by the registry corresponding to the year 2005. (14, 15) These data are similar to those reported by the CONAREC II registry that included only patients hospitalized in centers with residencies in cardiology. (26) Patient's decision to seek medical care after the onset of symptoms of AMI depends on several interrelated variables. (27) These variables affect the time from symptoms onset to medical consultation, and include patient's psychological factors, personal history, clinical status, age, gender, and socioeconomic and educational level, among others. (25, 28, 29)

The second time interval (time 1) from hospital arrival to EICT activation, includes patient's first contact with hospital environment, the process of diagnosis of myocardial infarction and treatment decision-making. A reduction in the median time of 20 minutes reported in the present study is not likely to occur (as in most cases it includes taking a medical history and an ECG); however, more than 25% of our patients presented a window of 45 minutes from admission to the first contact with the EICT. In the present study, time 2 was the longest time interval (from EICT activation to patient's arrival at the cath lab) with a median of 38 minutes. Part of this delay was due to the arrival of the EICT. This aspect plays an important role that is related to transportation issues in our city. Other aspects regarding this time delay are associated with non-medical staff issues, hospital facilities and patient's admission to the Coronary Care Unit.

Median door-to-balloon time was 93 minutes, slightly greater than the time interval recommended by the ACC/AHA (American College of Cardiology/ American Heart Association) guidelines for the management of patients with acute myocardial infarction. (11) In fact, this ideal time interval is difficult to ac-

Table 3. Patient time in different studies and registries

Studies-Registries	Patient time (minutes)
Hospital Argerich (ACBA, Argentina)	60 (40-150)
DANAMI-2[a] (4)	105 (61-185)
PRAGUE[b] (5)	110
	112
	120
GRACE Registry[a] (12)	139 (73-313)
French Registry[a] (13)	180 (116-332)
SAC Registry, 1987[a] (14)	270 (144-480)
SAC Registry, 1991[a] (14)	360 (174-780)
SAC Registry, 1996[a] (14)	300 (120-720)
SAC Registry, 2000[a] (14)	192 (120-480)
SAC Registry, 2003[a] (14)	180 (60-360)
SAC Registry, 2005[a] (14)	240 (120-660)
Quebec Study[c] (16)	100 (60-200)
	90 (56-165)
	95 (59-166)
Minnesota Registry[a] (17)	100 (58-226)
NMRI 2 Registry[a] (18)	89 (54-150)
Spanish Registry[a] (19)	122 (70-240)
Viennese Registry[d] (20)	180 ± 156

[a]: Medians (percentiles 25-75). [b]: Medians of the three study arms. [c]: Medians (percentiles 25-75) of the three study arms. [d]: Mean ± SD.

complish in daily practice with numerous evidence showing that it is longer. (7, 8, 10, 13, 19, 30-32) The National Registry of Myocardial Infarction in USA reported that between 1999 and 2002 only 35% of all patients were intervened within 90 minutes from arrival at hospital and less than 15% of hospitals reported smaller median door-to balloon time. (33) More recent registries show that less than 5% of patients are treated within the 90 minutes recommended in the guidelines. (34) According to the French registry of AMI, time from medical consultation to initiation of angioplasty was 110 minutes (13), and a Spanish registry reported a time interval of 122 minutes from medical consultation to the introduction of the guide wire in the culprit vessel. (19)This delay was also observed in a study that selected those centers who reported great volume of primary angioplasties in the United States: median door-to-balloon time was > 90 minutes in 65% of the centers analyzed. (10) Some randomized studies have also reported time delays greater than 90 minutes. (4) In order to assess the relationship between time delays and outcomes after reperfusion therapy, a retrospective meta analysis of randomized trials comparing fibrinolytic therapy and PTCA was performed. The mortality benefit associated with PTCA may be lost when the difference between door-to-balloon time and door-to-needle time is greater than 60 minutes; the benefit of the procedure on the combined endpoint of death, reinfarction and stroke disappears when the difference is greater than 90minutes. (35) This limit might only be applied with fibrin-specific thrombolytic agents. (36) It should be noted that once the decision to use thrombolytic therapy is made, there is a minimal delay of 20 minutes until it is initiated. (4, 7, 30, 31, 33) A meta analysis of 21 randomized trials showed an equivalence time (time interval in which mortality rate for angioplasty remained the same to that for fibrinolysis) of 110 minutes (33); in other study that included 192509 patients mean equivalence time was 114 minutes. (38)

One strategy that should be modified is the moment of taking an ECG; according to data from the NRMI-3, hospitals with the lowest door-to-balloon times used pre-hospital electrocardiograms. (39) Another key factor is to allow emergency physicians to activate the EICT (39), even at the patient's home before transportation to the emergency room. Hospitals with an explicit goal of reducing door-to-balloon time also use other measures, such as periodical publication of these time intervals for motivating improvement efforts, standardized protocols, interdisciplinary collaborative teams, clinician leaders willing to monitor performance, data feedback to monitor progress and identify problems, and a persistent organizational culture. (10, 40) In this sense, these measures should be carried out by medical an non-medical staff involved in patients' reception, treatment and transport. Currently, we are not completely aware of the negative aspect of time delays and thus it will be difficult to achieve a reduction in time to treatment. This study allows us to recognize some of the factors that generate time delays in order to implement a program to modify current behaviors that are responsible for them.

CONCLUSIONS

"Patient time" represents less than half the total time consumed. "Medical care time" determines the higher delay for the procedure; therefore, more emphasis should be placed in improving this time interval, within which EICT activation-first balloon inflation time constitutes a key factor.

RESUMEN

La demora en la realización de la angioplastia primaria, ¿una causa relacionada con el paciente o con el sistema médico-asistencial?

Introducción
Uno de los inconvenientes en la utilización generalizada de la angioplastia primaria (ATCP) es el retraso en su aplicación. La mayoría de los datos actuales proceden de ensayos clínicos de otros países, en tanto que en nuestro medio existe poco conocimiento respecto de su aplicación en la práctica habitual.

Objetivos
Analizar los tiempos involucrados en cada etapa de la realización de una ATCP en un centro donde constituye el tratamiento de elección, como primer paso para un programa de optimización de los tiempos y determinar si la demora obedece a una situación vinculada al paciente o al sistema médico-asistencial.

Material y métodos
El presente es un estudio prospectivo observacional en pacientes con IAM de menos de 12 horas. Se consideró "tiempo paciente" desde el inicio de los síntomas hasta el arribo al hospital y "tiempo médico-asistencial" desde la llegada al hospital hasta la insuflación del balón.

Resultados
Se realizó ATCP en 224 pacientes ingresados con diagnóstico de IAM. Las medianas (percentiles 25-75) fueron "tiempo paciente": 60 minutos (40-150), "tiempo médico-asistencial": 93 minutos (72-128). Este último comprende: tiempo 1 (llegada al hospital-llamada al equipo de hemodinamia): 20 minutos (10-45), tiempo 2 (llamada al equipo de hemodinamia-ingreso en sala de hemodinamia): 38 minutos (23-52), tiempo 3 (ingreso en sala de hemodinamia-primer balón insuflado): 31 minutos (21-45).

Conclusiones
El "tiempo paciente" constituye menos de la mitad del tiempo total empleado. El "tiempo médico-asistencial" determina el mayor retraso al procedimiento; por lo tanto, inicialmente, el mayor énfasis debe dirigirse a corregir este último, dentro del cual el tiempo llamada-primer balón constituye un factor fundamental.

Palabras clave > Infarto de miocardio - Tiempo - Angioplastia

BIBLIOGRAPHY

1. Zijlstra F, de Boer MJ, Hoorntje JC, Reiffers S, Reiber JH, Suryapranata H. A comparison of immediate coronary angioplasty with intravenous streptokinase in acute myocardial infarction. N Engl J Med 1993;328:680-4.

2. Weaver WD, Simes RJ, Betriu A, Grines CL, Zijlstra F, Garcia E, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. JAMA 1997;278:2093-8.

3. Zijlstra F, Hoorntje JC, de Boer MJ, Reiffers S, Miedema K, Ottervanger JP, van 't Hof AW, et al. Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction. N Engl J Med 1999;341:1413-9.

4. Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P, et al; DANAMI-2 Investigators. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med 2003;349:733-42.

5. Widimský P, Groch L, Zelízko M, Aschermann M, Bednár F, Suryapranata H. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur Heart J 2000;21:823-31.

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

7. Boersma E; The Primary Coronary Angioplasty vs. Thrombolysis Group. 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;27:779-88.

8. Stenestrand U, Lindbäck J, Wallentin L; RIKS-HIA Registry. Long-term outcome of primary percutaneous coronary intervention vs prehospital and in-hospital thrombolysis for patients with ST-elevation myocardial infarction. JAMA 2006;296:1749-56.

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;100:14-20.

10. Bradley EH, Herrin J, Wang Y, Barton BA, Webster TR, Mattera JA, et al. Strategies for reducing the door-to-balloon time in acute myocardial infarction. N Engl J Med 2006;355:2308-20.

11. Antman EM, Hand M, Armstrong PW, Bates ER, Green LA, Halasyamani LK, et al; 2004 Writing Committee Members, Anbe DT, Kushner FG, Ornato JP, Jacobs AK, Adams CD, Anderson JL, et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: developed in collaboration With the Canadian Cardiovascular Society endorsed by the American Academy of Family Physicians: 2007 Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction, Writing on Behalf of the 2004 Writing Committee. Circulation 2008;117:296-329.

12. Goldberg RJ, Steg PG, Sadiq I, Granger CB, Jackson EA, Budaj A, et al. Extent of, and factors associated with, delay to hospital presentation in patients with acute coronary disease (the GRACE registry). Am J Cardiol 2002;89:791-6.

13. Danchin N, Coste P, Ferrières J, Steg PG, Cottin Y, Blanchard D, et al; FAST-MI Investigators. Comparison of thrombolysis followed by broad use of percutaneous coronary intervention with primary percutaneous coronary intervention for ST-segment-elevation acute myocardial infarction: data from the french registry on acute ST-elevation myocardial infarction (FAST-MI). Circulation 2008;118:268-76.

14. Gagliardi J, Charask A, Higa C, Blanco P, Dini A, Tajer C y col. Infarto agudo de miocardio en la República Argentina. Análisis comparativo en los últimos 18 años. Resultados de las Encuestas SAC. Rev Argent Cardiol 2007;75:171-8.

15. Blanco P, Gagliardi J, Higa C, Dini A, Guetta J, Di Toro D y col. Infarto agudo de miocardio. Resultados de la Encuesta SAC 2005 en la República Argentina. Rev Argent Cardiol 2007;75:163-70.

16. Huynh T, O'Loughlin J, Joseph L, Schampaert E, Rinfret S, Afilalo M, et al; AMI-QUEBEC Study Investigators. Delays to reperfusion therapy in acute ST-segment elevation myocardial infarction: results from the AMI-QUEBEC Study. CMAJ 2006;175:1527-32.

17. Henry TD, Sharkey SW, Burke MN, Chavez IJ, Graham KJ, Henry CR, et al. A regional system to provide timely access to percutaneous coronary intervention for ST-elevation myocardial infarction. Circulation 2007;116:721-8.

18. Barron HV, Bowlby LJ, Breen T, Rogers WJ, Canto JG, Zhang Y, et al. Use of Reperfusion Therapy for Acute Myocardial Infarction in the United States Data From the National Registry of Myocardial Infarction 2. Circulation 1998;97:1150-6.

19. Cequier A, Bueno H, Augé JM, Bardají A, Fernández-Ortiz A, Heras M. Características y mortalidad del infarto agudo de miocardio tratado con intervencionismo coronario percutáneo primario en España. Resultados del Registro TRIANA 1. Rev Esp Cardiol 2005; 58:341-50.

20. 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;113:2398-405.

21. Cannon CP, Gibson CM, Lambrew CT, Shoultz DA, Levy D, French WJ, et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. JAMA 2000;283:2941-7.

22. Brodie BR, Stuckey TD, Wall TC, Kissling G, Hansen CJ, Muncy DB, et al. Importance of time to reperfusion for 30-day and late survival and recovery of left ventricular function after primary angioplasty for acute myocardial infarction. J Am Coll Cardiol 1998;32:1312-9.

23. De Luca G, van 't Hof AW, de Boer MJ, Ottervanger JP, Hoorntje JC, Gosselink AT, et al. Time-to-treatment significantly affects the extent of ST-segment resolution and myocardial blush in patients with acute myocardial infarction treated by primary angioplasty. Eur Heart J 2004;25:1009-13.

24. 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;109:1223-5.

25. 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;159:2141-7.

26. Izaguirre A, Belziti C, Aranda G y col. Proyecto CONAREC II: Relevamiento de Infarto y Angina Inestable. Análisis de las demoras preunidad coronaria en pacientes cursando infarto agudo de miocardio en la Republica Argentina. Rev Argent Cardiol 1994;62:55-64.

27. Alonzo AA, Reynolds NR. The structure of emotions during acute myocardial infarction: a model of coping. Soc Sci Med 1998;46: 1099-110.

28. Schmidt SB, Borsch MA. The prehospital phase of acute myocardial infarction in the era of thrombolysis. Am J Cardiol 1990;65: 1411-5.

29. Gibler WB, Armstrong PW, Ohman EM, Weaver WD, Stebbins AL, Gore JM, et al; Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) Investigators. Persistence of delays in presentation and treatment for patients with acute myocardial infarction: The GUSTO-I and GUSTO-III experience. Ann Emerg Med 2002;39:123-30.

30. Jneid H, Fonarow GC, Cannon CP, Palacios IF, Kilic T, Moukarbel

GV, et al; Get With the Guidelines Steering Committee and Investigators. Impact of time of presentation on the care and outcomes of acute myocardial infarction. Circulation 2008;117:2502-9.
31. Rogers WJ, Canto JG, Barron HV, Boscarino JA, Shoultz DA, Every NR. Treatment and outcome of myocardial infarction in hospitals with and without invasive capability. Investigators in the National Registry of Myocardial Infarction. J Am Coll Cardiol 2000;35:371-9.
32. Angeja BG, Gibson CM, Chin R, Frederick PD, Every NR, Ross AM, et al; Participants in the National Registry of Myocardial Infarction 2-3. Predictors of door-to-balloon delay in primary angioplasty. Am J Cardiol 2002;89:1156-61.
33. McNamara RL, Herrin J, Bradley EH, Portnay EL, Curtis JP, Wang Y, et al; NRMI Investigators. Hospital improvement in time to reperfusion in patients with acute myocardial infarction, 1999 to 2002. J Am Coll Cardiol 2006;47:45-51.
34. Nallamothu BK, Bates ER, Herrin J, Wang Y, Bradley EH, Krumholz HM; NRMI Investigators. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 analysis. Circulation 2005;111:761-7.
35. Nallamothu BK, Bates ER. Percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: is timing (almost) everything? Am J Cardiol 2003;92:824-6.
36. Nallamothu BK, Antman EM, Bates ER. Primary percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: does the choice of fibrinolytic agent impact on the importance of time-to-treatment? Am J Cardiol 2004;94:772-4.
37. Betriu A, Masotti M. Comparison of mortality rates in acute myocardial infarction treated by percutaneous coronary intervention versus fibrinolysis. Am J Cardiol 2005;95:100-1.
38. 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;114:2019-25.
39. Bradley EH, Roumanis SA, Radford MJ, Webster TR, McNamara RL, Mattera JA, et al. Achieving door-to-balloon times that meet quality guidelines: how do successful hospitals do it? J Am Coll Cardiol 2005;46:1236-41.
40. Bradley EH, Curry LA, Webster TR, Mattera JA, Roumanis SA, Radford MJ, et al. Achieving rapid door-to-balloon times: how top hospitals improve complex clinical systems. Circulation 2006;113:1079-85.