

Door-to-needle time for administration of fibrinolytics in acute myocardial infarction in Cape Town

Roshen C Maharaj, Heike Geduld, Lee A Wallis

Objectives. To determine the current door-to-needle time for the administration of fibrinolytics for acute myocardial infarction (AMI) in emergency centres (ECs) at three hospitals in Cape Town, and to compare it with the American Heart Association/American College of Cardiology (AHA/ACC) recommendation of 30 minutes as a marker of quality of care.

Methods. A retrospective review of case notes from January 2008 to July 2010 of all patients receiving thrombolytics for AMI in the ECs of three Cape Town hospitals. The total door-to-needle time was calculated and patient demographics and presentation, physician qualification, clinical symptomology and reasons for delays in thrombolytic administration were analysed.

Results. A total of 372 patients with acute ST elevation myocardial infarction (STEMI) were identified; 161 patients were eligible

for the study. The median door-to-needle time achieved was 54 minutes (range 13 - 553 mins). A door-to-needle time of 30 minutes or less was achieved in 33 (20.5%) patients; 51.3% of the patients arrived by ambulance; 34% of patients had a pre-hospital 12-lead ECG; and 88.8% had typical symptoms of myocardial infarction. Medical officers administered thrombolytics to 44.7% of the patients. The predominant infarct location on ECG was inferior (55.9%).

Conclusion. A significant number of patients were not thrombolysed within 30 minutes of presentation. The lack of senior doctors, difficulty interpreting ECGs, atypical presentations and EC system delays prolonged the door-to-needle time in this study.

S Afr Med J 2012;102:241-244.

Ischaemic heart disease (IHD) is a major cause of mortality and morbidity worldwide, especially in industrialised countries.¹ In the Western Cape, IHD was the leading cause of mortality in the cardiovascular category in 2000 and has consistently appeared in the top five causes of mortality since.² In keeping with international studies, mortality from IHD was higher in males than females.³

While primary prevention of IHD is considered the ideal, mortality and morbidity in patients presenting with acute myocardial infarction (AMI) can be reduced with early interventions such as fibrinolysis or percutaneous coronary intervention (PCI).⁴ Many studies have shown that early PCI is more advantageous in reducing mortality from re-infarction and the need for a coronary artery bypass graft (CABG) than fibrinolytic drug therapy.⁵⁻⁷ In the Western Cape, PCI is limited to two tertiary hospitals, making fibrinolytic drug therapy the more accessible form of treatment for ST elevation myocardial infarction (STEMI) patients.

Early administration of fibrinolytic therapy improves patient outcomes in terms of limiting infarct size, so preserving left ventricular function.^{8,9} This is achieved by re-establishing the patency of the occluded coronary vessel.⁸⁻¹⁰ Maximal benefit from fibrinolysis is seen when the fibrinolytic is given within the first hour of symptom onset.^{11,12}

Delaying fibrinolytic therapy by one hour increases the hazard ratio of death by 20%, (95% confidence interval (CI) 7 - 88), and a delay of 30 minutes or more can reduce the average life expectancy by one year.¹³ Minimising the time delay between onset of symptoms to definitive treatment improves mortality and morbidity.

Division of Emergency Medicine, Faculty of Health Sciences, University of Cape Town
Roshen C Maharaj, MB BCh, FCEM (SA), Dip PEC (SA), DA (SA)
Heike Geduld, MB ChB, FCEM (SA), MMed EM, Dip PEC (SA)
Lee A Wallis, MB ChB, MD, DIMRCSEd, Dip Sport Med, FRCSEd (A&E), FCEM (UK), FCEM (SA), FIFEM

Corresponding author: R Maharaj (roshenmaharaj@gmail.com)

The period between the onset of symptoms to administration of fibrinolytic therapy can be divided as follows:

- interval between onset of symptoms to seeking medical attention
- period taken to transport patient to definitive care
- interval between arrival at hospital to initiation of fibrinolytics (door-to-needle time).

The first two components can be improved by public education and developing efficient pre-hospital systems. The door-to-needle time is the one in-hospital factor that can be addressed by medical practitioners.

The American Heart Association/American College of Cardiology (AHA/ACC) guidelines recommend a door-to-needle time of 30 minutes or less for administration of fibrinolytics for STEMI patients.¹⁴ Compliance with this time period is considered a marker of quality of care.¹⁵

No data on the door-to-needle time in the emergency centres (ECs) of public hospitals in Cape Town were found. We aimed to determine the current door-to-needle time for fibrinolytic administration in patients with STEMI, determine patient demographics, and assess factors that could influence the door-to-needle time.

Methods

A retrospective audit was conducted of all patients who received thrombolytics for AMI in the ECs of 3 hospitals in Cape Town from January 2008 to July 2010.

Inclusion criteria

All adult patients with acute ST segment elevation, new onset left bundle branch block (LBBB), or posterior infarct on electrocardiogram (ECG) meeting AHA/ACC criteria for thrombolysis, who received thrombolytics in the above ECs.

Patients excluded

Patients who received pre-hospital thrombolysis or those thrombolysed at other centres before referral; patients receiving thrombolysis for conditions other than myocardial infarction; cases where patient files were missing from central records; and cases with incomplete data such that door-to-needle time could not be calculated.

Data collection

Eligible patients were identified from the EC registry. Case notes were reviewed by a single observer. The required data were extracted onto a standardised data collection form. The quality of data collected was dependent on the availability and accuracy of the case notes. Incomplete documentation, and illegible and ambiguous notes were identified.

The following data were collated and analysed: patient demographics; transport mode to hospital; pre-hospital ECG acquisition, either by emergency medical services (EMS) or the primary care facility staff; and time of day (working hours v. after hours) when patient arrived. Working hours was defined as 08h00 to 17h00, and after hours between 17h00 and 08h00 the next day. No distinction was made between weekdays or weekends as the ECs had similar staffing and dynamics on both weekdays and weekends.

The following time intervals were calculated:

- earliest time of presentation to hospital (taken from EMS records or admission chart) to time of triage
- time from triage to ECG acquisition
- time from ECG acquisition to actually commencing thrombolytics.

The sum of the above time intervals constitutes the total door-to-needle time.

All data were collected and transferred onto an Excel spreadsheet program. Simple descriptive statistics were used to describe the median time to triage, triage to ECG, ECG to fibrinolytic, and total door-to-needle times. Subgroup analysis was performed for determining prevalence of STEMI fibrinolysed based on gender and age group; anatomical localisation of myocardial infarction; transport times; and level of experience of treating physician. The symptoms on presentation were also assessed. Typical symptoms were defined as an acute onset of chest pain with radiation to the left arm, neck or jaw with associated autonomic symptoms (sweating, nausea or vomiting). Statistical analysis was undertaken using Microsoft Excel (Microsoft, Richmond, USA), EpiCalc 2000 (Brixton Books, London, UK) and STATA (Stata Corp, College St, USA).

Ethics

Ethics approval was granted by the University of Cape Town, Faculty of Health Sciences Ethics Committee (REC REF 539/2009).

Results

From the EC registries of the 3 hospitals under study, a total of 372 patients with STEMI were identified. The final number included in the study was 161. The consort diagram is shown as Fig. 1. Table 1 lists the demographic variables.

The largest category (39.8%; 95% CI 32.1 - 47.4) of patients thrombolysed were in the 45 - 54-year-old age group, with the next largest in the 55 - 64-year-old age group. A door-to-needle time ≤30 minutes was achieved in 33 (20.5%) patients. Table 2 shows the door-to-needle time of the entire study. The median door-to-needle time was 54 minutes (range 13 - 553). Table 3 depicts the median time achieved for each of the intervals studied.

Of the patients, 44.7% (CI 36.9 - 52.7) were seen and given fibrinolysis by medical officers, with 34.8 % (CI 27.5 - 42.7) treated by emergency medicine registrars. The remaining patients were seen and treated by interns (4.4%; CI 1.9 - 9.1), junior community service doctors (14.9%; CI 9.8 - 21.6), and emergency physicians (1.2%; CI 6.2- 14.9).

The predominant infarct location on ECG was inferior (55.9%; CI 47.9 - 63.6), followed by anterior (38.5%; CI 31.0 - 46.5). A door-to-ECG time <10 minutes was achieved in 41.2% of patients. Table 4 lists the influence of mode of arrival, time of arrival, symptoms,

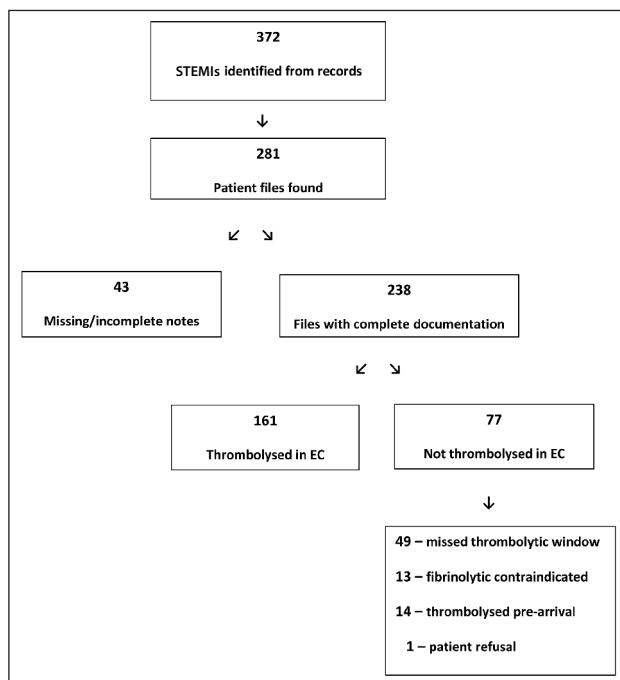


Fig. 1. Patient profile.

Table 1. Demographic variables

Demographic variable	Median (range)	N% (95% CI)
Median age (yrs)	54 (31 - 84)	
Sex		
Male		66.5 (58.5 - 73.6)
Female		33.5 (26.4 - 41.4)
Mode of arrival		
Ambulance		51.2 (43.2 - 59.2)
Walk-in		48.8 (40.8 - 56.7)
Time of arrival		
Working hours		52.2 (39.9 - 55.8)
After hours		47.8 (44.2 - 60.1)
Pre-hospital ECG		33.9 (26.8 - 41.9)
Median pain-to-arrival time (mins)	192.5 (10 - 765)	
Symptomatology		
Typical		88.8 (82.7 - 93.1)
Atypical		11.2 (6.9 - 17.3)

pre-hospital ECG and level of experience of treating doctor on the door-to-needle time.

The reasons for delays in initiating fibrinolytic therapy were documented by the attending doctor in 70 of the 161 cases (43.5%). Delays resulted from:

- The attending doctor seeking advice from the senior doctor in the EC or the Internal Medicine registrar before commencing fibrinolysis. The reason for consulting the senior was not documented. (28.6%).
- Difficulty in interpreting the ECG (18.6%).
- Patients presenting with atypical symptoms, hence delaying the diagnosis of AMI (12.9%).

Table 2. Door-to-needle time in minutes

Door-to-needle time (mins)	% (n); N=161
Within 30 mins	20.5 (33)
31 - 60 mins	37.9 (61)
61 - 90 mins	26.7 (43)
>90 mins	14.9 (24)

Table 3. Median time achieved for each interval in minutes

Time interval	Median time (range) (mins)
Door to triage	6 (0 - 157)
Triage to ECG	2 (0 - 245)
Door to ECG	13 (1 - 402)
ECG to fibrinolytic	38 (4 - 262)
Door-to-needle time	54 (13 - 553)

Table 4. Comparison of median door-to-needle times

Variable	Median door-to-needle time (range) (mins)
Mode of arrival	
Ambulance	53 (10 - 553)
Walk in	50 (10 - 270)
Time of arrival	
Working hours	53 (15 - 553)
After hours	54.5 (13 - 457)
Symptomatology	
Typical	53 (13 - 245)
Atypical	65 (17 - 553)
Prehospital ECG	
Yes	50 (15 - 553)
No	55 (13 - 270)
Level of experience of doctor	
Medical officer	50 (17 - 553)
Emergency medicine registrar	55 (15 - 195)

- Patients going into cardiac arrest and requiring cardiopulmonary resuscitation (CPR) before thrombolytic therapy could be commenced (11.4%).
- Patients presenting with hypertension (systolic blood pressure >180 mmHg), which is a relative contra-indication to fibrinolysis, hence blood pressure control was needed before administration of fibrinolytics (7.1%).
- Patients presenting during change of shifts for nurses or doctors were not attended to timously (7.1%).
- Delays in obtaining a chest X-ray (4.3%).
- Fibrinolytic agent not available in the EC, and a nurse had to fetch it from the pharmacy (4.3%).
- Waiting for results of cardiac enzymes, non-availability of intensive care beds, and equipment (infusion pump) failure accounted for the remainder of the delays (5.7%).

Discussion

Minimising the time between the onset of an AMI to initiation of a reperfusion strategy is important to improve prognosis and survival.^{11,12} In this study, less than a third of patients with STEMI received thrombolytics within the prescribed time interval of 30 minutes. The median door-to-needle time of 54 minutes was higher than the 45 minutes recorded by North American and European hospitals;¹⁶⁻¹⁹ it was comparable with studies done in the Middle East, Pakistan and India, and a study in Vancouver.²⁰⁻²³ However, in some of these studies, thrombolysis was given in the intensive care unit (ICU) and not in the EC, thereby prolonging door-to-needle times. The number of patients thrombolysed within 30 minutes was lower than other contemporary studies, although some of them had smaller sample sizes.^{16,17,20-23}

A key modifiable factor contributing to prolonged door-to-needle times was the need for senior review or advice on ECG interpretation that contributed to almost half of the documented delays in thrombolysis. Other studies also identified delay in diagnosis or ECG interpretation as a contributory factor to prolonged door-to-needle times.^{20,21} In our setting, physician experience may also be a contributory factor. Medical officers working in Cape Town public sector hospitals have variable levels of experience and training. Emergency medicine is also a new speciality in South Africa, with emergency medicine registrars at different points in their training. Although medical officers had shorter median door-to-needle times than emergency medicine (EM) registrars, they had a wider range than EM registrars. ECG interpretation and the decision to thrombolysed are more reliable in more experienced doctors than junior doctors.²⁴ Other reasons for seeking senior advice could not be reliably identified from the case notes.

Patients presenting with atypical symptoms or with undifferentiated chest pain require an ECG to diagnose a STEMI. A door-to-ECG time <10 minutes has been recommended by the AHA/ACC for all patients with chest pain or symptoms suggestive of ACS.¹⁴ Prolonged door-to-ECG time leads to an increased risk of adverse clinical outcomes in patients with a STEMI.²⁵ Our study gave a median door-to-ECG time of 13 minutes (range 1 - 402 mins), with <50% of patients having an ECG within 10 minutes.

The three hospitals studied have busy ECs often burdened with overcrowding that can prolong the door-to-triage sub-interval of the door-to-needle time. The Western Cape uses the South African Triage Scale consisting of two parts which has been validated in community health centres and hospitals:²⁶ (i) a triage early-warning score which involves taking the patients' vitals, and assessing the patients' level of consciousness, mobility and evidence of trauma; and (ii) a discriminator list which allows the 'triager' to upgrade a patient to a higher colour category. Chest pain is part of this discriminator list and upgrades all chest-pain patients to at least an orange category. All orange/red patients should be attended to immediately or within 10 minutes of presentation.²⁶ The median door-to-triage time was 6 minutes. We did not measure the time from triage to first physician contact owing to the poor record-keeping of this time in the patient records.

The organisational ability and patient flow characteristics of a hospital also influence door-to-needle times. We identified many factors that hindered patient flow. Delays in obtaining X-rays, patients arriving during nurse and doctor handovers not being attended to timously, and prolonged door-to-ECG times, all suggest shortcomings in patient flow pathways.

The ECG to commencement of fibrinolytic time interval constituted the longest delay in the door-to-needle time and is attributed to patient and physician factors. Some patients went into

cardiac arrest and required cardiopulmonary resuscitation. Others presented with hypertension, which required blood pressure lowering before commencing lysis.

Pre-hospital factors prolonging door-to-needle times included patient demographics, pre-hospital transport delays and time of presentation to hospital. The AMI Quebec Study investigated some of these factors and found that older patients had a decreased likelihood of getting timely reperfusion therapy;¹⁶ possible reasons were that elderly patients had more atypical symptoms and an increased risk of complications from fibrinolysis.^{27,28} Patients presenting after hours had longer door-to-needle times, probably owing to fewer staff being available after hours.¹⁶ In another study, the time to fibrinolysis did not differ much by patient arrival time.²⁹ Patient factors such as denial of symptoms and delays in activating EMS also contribute to delayed fibrinolysis.³⁰ Pre-hospital transport delays secondary to resource limitations, distance to hospital with reperfusion capability, and traffic delays are other factors contributing to prolonged times to fibrinolysis.^{30,31}

Although the present study suggested that shorter median door-to-needle times were achieved in patients who arrived with their own transport, presented during working hours, had typical symptoms of AMI and had a pre-hospital ECG, the sample size was too small to draw definite conclusions.

Most quality improvement studies suggest a team-based approach to improving the time-to-reperfusion therapy for MI patients.^{16,17,31} In our setting, quality improvement audits must focus on in-hospital and pre-hospital factors. Most of the in-hospital reasons that we identified for delays in door-to-needle times could be improved by efficient triaging, early ECG acquisition for at-risk patients, ECG physician training, the presence of a senior doctor/physician on the floor or being readily available telephonically, knowing the population profile, and having a low threshold for investigating those with atypical symptoms. Other in-hospital organisational strategies include close co-operation between hospital administration, emergency centre staff and auxiliary services to enhance patient flow, and interpretation of the ECG by the most competent physician in the EC. The ready availability of fibrinolytic stock in the EC, and rapid nurse-driven administration of fibrinolytics once diagnosis has been made, should be encouraged. Keeping a provincial registry of all AMI presentations will aid data analysis and protocol development.

Pre-hospital quality improvement in our setting should include education of the public to recognise signs and symptoms of AMI, and early activation of emergency services or accessing the nearest health facility. An integrated local EMS chest pain protocol supporting rapid diagnosis and pre-hospital ECG acquisition should be developed.

As international quality improvement audits have shown significant decreases in door-to-needle times, similar audits need to be done in Cape Town hospitals to improve door-to-needle time and hence reduce mortality and morbidity from STEMI.¹⁷ Developing a standardised protocol and checklist for thrombolysis would be beneficial.

Limitations

This was a retrospective chart review that relied on the accuracy of data recorded; 24.5% of patient files could not be located from the central records of the hospitals, and 15% of the files located had incomplete documentation or missing notes and could not be included. Times recorded are dependent on the attending doctor or nurse, which could have influenced the accuracy of our findings.

Conclusion

Only 20.5% (95% CI 14.71 - 27.72) of patients with STEMI met the AHA/ACC guideline of receiving fibrinolytics within a 30-minute

door-to-needle time. This is below international standards of greater than 40%.^{22,23} There are several factors contributing to a prolonged door-to-needle time that need to be addressed by creating an efficient, team-based approach to managing these patients. A repeat audit is needed once hospital systems are changed to determine if there is an improvement in the door-to-needle time.

References

1. Yusuf S, Reddy S, Ounpuu S, et al. Global burden of cardiovascular diseases: Part 1: General considerations, the epidemiological transition, risk factors and impact of urbanization. *Circulation* 2001;104:2746-2753.
2. Bradshaw D, Nannan N, Laubscher R, et al. South African National Burden of Disease Study, Western Cape Province: Estimates of Provincial Mortality 2000. <http://www.mrc.ac.za> (accessed 15 February 2011).
3. Statistics South Africa. Mortality and Causes of Death in South Africa, 2008. Findings from Death Notifications. <http://www.statssa.gov.za> (accessed 15 February 2011).
4. Armstrong PW, Bogaty P, Buller CE, et al. The 2004 ACC/AHA guidelines: a perspective adaptation for Canada by the Canadian Cardiovascular Society Working Group. *Can J Cardiol* 2004;20:1075-1079.
5. de Boer MJ, Hoornje JC, Ottervanger JP, et al. Immediate coronary angioplasty versus intravenous streptokinase in acute myocardial infarction: left ventricular ejection fraction, hospital mortality and reinfarction. *J Am Coll Cardiol* 1994;23:1004-1008.
6. Stone GW, Grines CL, Browne KE, et al. Implications of recurrent ischemia after reperfusion therapy in acute myocardial infarction: a comparison of thrombolytic therapy and primary angioplasty. *J Am Coll Cardiol* 1995;26:66-72.
7. Weaver WD, Simes RJ, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. *JAMA* 1997;278:2093-2098.
8. Wilcox RG, von der Lippe G, Olsson CG, et al. Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. Anglo-Scandinavian Study of Early Thrombolysis (ASSET). *Lancet* 1988;8610:525-530.
9. Second International Study of Infarct Survival (ISIS-2) Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988;8607:349-360.
10. Linderer T, Schroder R, Arntz R, et al. Prehospital thrombolysis: beneficial effects of very early treatment on infarct size and left ventricular function. *J Am Coll Cardiol* 1993;22:1304-1310.
11. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet* 1994;343:311.
12. Boersma E, Maas AC, Deckers JW, et al. Early thrombolytic treatment in acute myocardial infarction: Reappraisal of the golden hour. *Lancet* 1996;9030:771-775.
13. Rawles JM (GREAT Group). Quantification of the benefit of earlier thrombolytic therapy: Five-year results of the Grampian Region Early Anistreplase Trial (GREAT). *J Am Coll Cardiol* 1997;30:1181-1186.
14. O'Connor RE, Brady W, Brooks CS, et al. Acute coronary syndromes: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2010;122:S787-S817.
15. Kuppussawmy VC, Webb D, Gupta S, et al. Meeting the NSF targets for door-to-needle time in acute myocardial infarction – the role of a bolus thrombolytic. *Br J Cardiol* 2006;13:36-41.
16. Huynh T, O'Loughlin J, Joseph L, et al. for the AMI-QUEBEC Study Investigators. Delays to reperfusion therapy in acute ST-segment elevation myocardial infarction: results from the AMI-QUEBEC Study. *CMAJ* 2006; 175(12):1527-32. doi: 10.1503/cmaj.060359.
17. Tsai CL, David J, Magid MD, et al. Quality of Care for acute myocardial infarction in 58 US emergency departments. *Acad Emerg Med* 2010;17:940-950.
18. Schiele F, Hochadel M, Tubaro M, et al. Reperfusion strategy in Europe: temporal trends in performance measures for reperfusion therapy in ST-elevation myocardial infarction. *Eur Heart J* 2010;31(21):2614-2624. doi: 10.1093/eurheartj/ehq305.
19. Glickman SW, Cairns CB, Chen AY, et al. Delays in fibrinolysis as primary reperfusion therapy for acute ST-segment elevation myocardial infarction. *Am Heart J* 2010;159:998-1004.
20. Jehangir W, Daoud MS, Khan M, et al. Evaluation of the door-to-needle time in patients undergoing fibrinolytic therapy after acute myocardial infarction. *Pak J Physiol* 2009;5(2):38-39.
21. Masurkar VA, Kapadia FN, Shirwadkar G, et al. Evaluation of the door-to-needle time for fibrinolytic administration for acute myocardial infarction. *Indian Journal of Critical Care Medicine* 2005;9(3):137-140.
22. Abba AA, Wann BA, Rahmatullah RA, et al. Door-to-needle time in administering thrombolytic therapy for acute myocardial infarction. *Saudi Med J* 2003;24(4):361-364.
23. Zed PJ, Abu-Laban RB, Cadieu TM, et al. Fibrinolytic administration for acute myocardial infarction in a tertiary ED: Factors associated with an increased door-to-needle time. *Am J Emerg Med* 2004;22:192-196.
24. Massel D. Observer variability in ECG interpretation for thrombolysis eligibility: Experience and context matter. *J Thromb Thrombolysis* 2000;15(3):131-140.
25. Diercks DB, Peacock WF, Hiestand BC, et al. Frequency and consequences of recording an electrocardiogram >10 minutes after arrival in an emergency room in non-ST-segment elevation acute coronary syndromes (from the CRUSADE Initiative). *Am J Cardiol* 2006;97:437-442.
26. Gottschalk S, Wood D, De Vries, et al, on behalf of the Cape Triage Group. The Cape triage score: a new triage system South Africa. Proposal from the Cape triage group. *Emerg Med J* 2006;23:149-153.
27. Boucher JM, Racine N, Huynh T, et al. Quebec Acute Coronary Care Working Group. Age-related differences in in-hospital mortality and the use of thrombolytic therapy for acute myocardial infarction. *CMAJ* 2001;164(9):1285-1290.
28. Berger AK, Radford MJ, Krumholz HM. Factors associated with delay in reperfusion therapy in elderly patients with acute myocardial infarction: analysis of the Cooperative Cardiovascular Project. *Am Heart J* 2000;139:985-992.
29. Magid DJ, Wang Y, Herrin J, et al. Relationship between time of day, day of week, timeliness of reperfusion, and in-hospital mortality for patients with acute ST-segment elevation myocardial infarction. *JAMA* 2005;294(7):803-812.
30. GISSI – Avoidable Delay Study Group. Epidemiology of avoidable delay in the care of patients with acute myocardial infarction in Italy. GISSI generated study. *Arch Intern Med* 1995;155:1481-1488.
31. Ho MT, Eisenberg MS, Litvin PE, et al. Delay between onset of chest pain and seeking medical care. The effects of public education. *Ann Emerg Med* 1989;18:727-731.

Accepted 16 August 2011.