

In-hospital Mortality with Relation to Time of Presentation in Patients with Acute ST Elevation Myocardial Infarction

ABDUL SATTAR, ABDUL BARI, MOAZAM ALI NAQVI, AHMAD NOEMAN

ABSTRACT

Aim: To determine the frequency of in-hospital mortality in different groups with relation to time of presentation in patients of acute ST Elevation Myocardial Infarction (STEMI).

Methods: This Descriptive Case Series conducted in the Department of Cardiology, Punjab Institute of Cardiology, Lahore from December 2011 to June 2012. Two hundred patients of acute ST elevation myocardial infarction fulfilling the inclusion criteria from emergency department of PIC Lahore were enrolled after informed consent. This study population was divided into four groups. Group I was consisted of patients presenting in <3 hours of onset of symptoms, Group II, patients presenting in 3-6 hours after symptom onset, Group III, patients presenting in 6-12 hours and Group IV was comprise of patients presenting after 12 hours of onset of symptoms of acute myocardial infarction. Routine protocol was offered to each patient and all patients will be followed for mortality for four days.

Results: Mean age of the patients was 55.5 ±13.2 years. Out of 200 patients 148 (74%) were male and 52 (26%) were female. Out of 200 patients, 108 (54%) were smokers. Hypertension was found in 94 (47%) of the patients. 80 (40%) were having diabetes. Out of 200 patients 37(18.5%) died during hospital admission.

Conclusion: Delayed presentation is associated with older age and female gender. Patients presenting late are in more advanced Killip class and are less frequently thrombolysed and are predisposed to increased in-hospital mortality.

Keywords: Acute ST Elevation Myocardial Infarction; Acute coronary syndromes; In-hospital mortality; Reperfusion therapy; Killip class.

INTRODUCTION

The burden of cardiovascular disease is growing worldwide. Ischemic heart disease is the leading cause of death in the United States and other developed countries and is projected to emerge as the No. 1 cause of death worldwide by the year 2020^{1,2}.

More than 50% of the 1.2 million people who suffer an acute myocardial infarction (AMI) or coronary death each year in the United States die in an emergency department (ED) or before reaching a hospital within an hour of symptom onset¹.

Delay to treatment for acute coronary syndromes (ACS) and stroke is a major contributor to the morbidity burden of cardiovascular disease because a significant number of individuals who delay seeking care develop potentially preventable complications^{3,4}.

Delay has been an important predictor of patient morbidity and mortality outcomes in numerous clinical trials of reperfusion therapy³⁻⁶. Survival rates are improved by up to 50% if reperfusion is achieved

within 1 hour of symptom onset and by 23% if it is achieved within 3 hours of symptom onset⁷. In one trial, delaying treatment by 30 minutes reduced average life expectancy by 1 year.⁸ In another recent study of 565 patients undergoing angioplasty for AMI, those who received the first balloon inflation within 60 minutes of arrival at the hospital had a 30-day mortality rate of 1%, but for every 15 minutes longer than 1 hour the odds of death increased 1.6 times.⁵ Delay also affects morbidity. A shorter interval between symptom onset and treatment is associated with better cardiac function⁷. The level of cardiac function is the best predictor of morbidity, as well as of mortality^{8,9}. Thus, early treatment with reperfusion, as well as with other agents such as angiotensin-converting enzyme inhibitors, β -blockers, and aspirin, can reduce mortality and morbidity.

In the United States, median delay time from symptom onset to hospital arrival ranges from 1.5 to 6.0 hours^{4,10}. Data from the Atherosclerosis Risk in Communities Study indicate no improvement in delay from 1987 through 2000: 49.5% of patients delayed >4 hours.¹¹ This study is designed to evaluate the impact of delayed presentation on in-hospital outcome of acute myocardial infarction. This study will be helpful to find out the frequency of late presentation of myocardial infarction patients and to

Department of Cardiology, Punjab Institute of Cardiology, Lahore

Correspondence to Dr. Abdul Sattar, Assistant Professor of Cardiology, Email: drabdulsattar66@yahoo.com

help the general public by educating them regarding the symptoms and importance of early treatment.

MATERIAL AND METHODS

This study was conducted in the Department of Cardiology, Punjab Institute of Cardiology, Lahore, over a period of six months from December 2011 to June 2012. It was a descriptive case series. Sample size of 200 cases was taken by non probability purposive sampling calculated with 95% confidence level, 4% margin of error and taking expected percentage of in hospital mortality in group -1 (within or upto 3 hours) i.e., 9.03% (least among all groups) after onset of symptoms till arrival in patients of STEMI presenting in a tertiary care hospital.

Adult patients with acute STEMI between 30-70 years of age and of both genders were included. We excluded patients who were already hospitalized at the time of occurrence of symptoms.

Two hundred patients of Acute ST Elevation Myocardial Infarction fulfilling the inclusion criteria from emergency department of PIC Lahore were enrolled after informed consent. This study population were divided into four groups. Group I was consisted of patients presenting in <3 hours of onset of symptoms, Group II, patients presenting in 3-6 hours after symptom onset, Group III, patients presenting in 6-12 hours and Group IV was comprised of patients presenting after 12 hours of onset of symptoms of acute myocardial infarction. Routine protocol was offered to each patient and all patients were followed for mortality for four days.

Data Analysis Procedure: All the collected information was entered and analyzed using SPSS version 10.0. Quantitative variables like age was presented by calculating mean and standard deviation. Qualitative variables like gender, groups of presenting time and in-hospital mortality in each group were presented by calculating frequency and percentage. Data was stratified for DM, HTN, Smoking, family history to address effect modifiers.

RESULTS

Mean age of the study population was 55.5 ± 13.2 years. Mean age was similar in all the groups. Table 1. There were 148(74%) males and 52(26%) females. Lesser number of female patients 9(18%) presented early as compared to 20(40%) patients

presenting late $p < 0.097$. There were 80(40%) diabetics with similar number of patients in all the groups $p < 0.359$. Overall 108(54%) were smokers and 94(47%) patients were hypertensive with similar percentages in all the four groups (Table 2).

Mean heart rate at the time of presentation was 81.1 ± 13.2 per minute. Mean heart rate was similar in all the four groups. Mean systolic blood pressure was 121.5 ± 27.6 mm Hg and mean diastolic BP was 75.2 ± 16.8 mm Hg. Mean blood pressure, systolic and diastolic at the time of presentation was similar in all groups. Table 3: Overall 126(63%) patients presented in Killip class I, 32(61%) in class II, 24(12%) in class III and 18(9%) in class IV. There was tendency of presenting in advanced killip class with delayed presentation. In Group I, 36(72%) patients presented in Killip class I, 7(14%) in class II, 4(8%) in class III, 3(6%) in class IV. In patients presenting late i.e. Group IV 25(50%) patients presented in Killip class I, 9(18%) in class II, 12(24%) in class III and 4(8%) in class IV $p < 0.018$. Table 4. Site of myocardial infarction was similar in all the four groups as 103(51.5%) patients had anterior wall myocardial infarction, 69(34.5%) had inferior wall MI, 20(10%) had lateral wall MI and 8(4%) had LBBB. Table 5: Overall 144(74%) patients received streptokinase therapy. In Group I, 48(98%) patients received streptokinase with a gradual decline with delayed presentation as 49(98%) patients in Group II received Streptokinase, 41(82%) in Group III and 6(12%) in Group IV received streptokinase $p < 0.0001$. Table 6: Door to needle time of <30 minutes was observed in 94(47%) patients, 37(74%) in Group I, 31(62%) in Group II, 21(42%) in Group III and 5(10%) in Group IV $p < 0.0001$. Door to needle time of 30 minutes to 1 hour was observed in 42(21%), 10(20%) in Group I, 15(30%) in Group II, 16(32%) in Group III and 1(2%) in Group IV. Door to needle time was prolonged to >1 hour in 8(4%) patients, 1(2%) in Group I, 3(6%) in Group II, 4(8%) in Group III and 0(0%) in Group IV. Table 7; there was an increasing trend in complications like VSD, MR, Cardiogenic Shock, Reinfarction, CVA, VT/VF, asystole and CHB with delayed presentation.

Table 8: In-hospital mortality was 37(18.5%). There was an increasing, trend in in-hospital mortality with delayed presentation. As mortality was 5(10%) in Group I, 6(12%) in Group II, 8(16%) in Group III and 18(36%) in Group IV $p < 0.001$

Table 1. Epidemiological characteristics.

Characteristics	Group I (n=50)	Group II (n=50)	Group III (n=50)	Group IV (n=50)	Total (n=200)
Age mean years	51.6±11.03	53.5±12.3	58.9±13.6	58.04±14.5	55.5±13.2
Male	41(82%)	40(80%)	37(74%)	30(60%)	148(74%)
Female	9(18%)	10(20%)	13(26%)	20(40%)	52(26%)
Diabetes	17(34%)	20(40%)	20(40%)	23(46%)	80(40%)
Hypertension	24(48%)	23(46%)	21(42%)	26(52%)	94(47%)
Smoking	34(68%)	28(56%)	26(52%)	20(40%)	108(54%)
Family history	16(32%)	13(26%)	10(20%)	17(34%)	56(28%)

Table 2. Presentation characteristics.

Characteristics	Group I (n=50)	Group II (n=50)	Group III (n=50)	Group IV (n=50)	Total (n=200)
Heart rate mean/ minute	82.5±20.8	80.9±19.4	82±21.1	79.2±20.6	81.1±13.2
Systolic BP mean mm Hg	128.6±26.6	121.4±26.8	122.4±26.4	113.8±29.2	121.5±27.6
Diastolic BP mean mm Hg	77.6±16.1	76.4±16.9	76.4±16.2	70.6±17.7	75.2±16.8

Table 3. Killip Class

Characteristics	Group I (n=50)	Group II (n=50)	Group III (n=50)	Group IV (n=50)	Total(n=200)
CLASS I	36(72%)	35(70%)	30(60%)	25(50%)	126(63%)
CLASS II	7(14%)	7(14%)	9(18%)	9(18%)	32(16%)
CLASS III	4(8%)	4(8%)	4(8%)	12(24%)	24(12%)
CLASS IV	3(6%)	4(8%)	7(14%)	4(8%)	18(9%)

Table 4. Site of MI.

Site of MI	Group I(n=50)	Group II (n=50)	Group III(n=50)	Group IV(n=50)	Total (n=200)
AWMI	27(54%)	30(60%)	25(50%)	21(42%)	103(51.5%)
IWMI	19(38%)	15(30%)	16(32%)	19(38%)	69(34.5%)
Lateral wall MI	2(4%)	4(8%)	7(14%)	7(14%)	20(10%)
LBBB	2(4%)	1(2%)	2(4%)	3(6%)	8(4%)

AWMI=Anterior wall myocardial infarction; IWMI=Inferior wall myocardial infarction; Lateral wall MI=Lateral wall myocardial infarction; LBBB=Left bundle branch block

Table 5. SK given

Characteristics	Group I (n=50)	Group II (n=50)	Group III (n=50)	Group IV (n=50)	Total (n=200)
SK Given	48(98%)	49(98%)	41(82%)	6(12%)	144(72%)

SK=Streptokinase

Table 6. Door To Needle Time

Characteristics	Group I (n=50)	Group II (n=50)	Group III (n=50)	Group IV (n=50)	Total (n=200)
<30 MIN	37(74%)	31(62%)	21(42%)	5(10%)	94(47%)
30-60 MIN	10(20%)	15(30%)	16(32%)	1(2.0%)	42(21%)
>60 MIN	1(2.0%)	3(6%)	4(8%)	0(0%)	8(4%)

Table 7. Details of complications

Complications	Group I(n=50)	Group II (n=50)	Group III (n=50)	Group IV(n=50)	Total (n=200)
VSD	2(4%)	2(4%)	2(4%)	1(2%)	7(3.5%)
MR	4(8%)	7(14%)	2(4%)	5(10%)	18(9%)
Cadiogenic shock	7(14%)	12(24%)	8(16%)	17(34%)	44(22%)
Reinfarction	3(6%)	2(4%)	6(12%)	5(10%)	16(8%)
CVA	1(2%)	0(0%)	0(0%)	4(8%)	5(2.5%)
VT	5(10%)	4(8%)	7(14%)	14(28%)	30(15%)
VF	5(10%)	5(10%)	5(10%)	11(22%)	26(13%)
Asystole	5(10%)	6(12%)	7(14%)	19(38%)	37(18.5%)
CHB	2(4%)	5(10%)	5(10%)	9(18%)	21(10.5%)

VSD=Ventricular septal defect, MR=Mitral regurgitation, CVA=Cerebrovascular accidents, VT=Ventricular tachycardia, VF= Ventricular fibrillation, CHB=Complete heart block

Table 8. Outcome of study population.

Characteristics	Group I (n=50)	Group II (n=50)	Group III (n=50)	Group IV (n=50)	Total (n=200)
In-hospital mortality	5(10%)	6(12%)	8(16%)	18(36%)	37(18.5%)

P value <0.003

DISCUSSION

In the current study we observed significantly increased mortality in patients with delayed presentation. Our results are consistent with previous studies.^{13,15,16-17} Multiple studies evaluating fibrinolytic therapy in patients with STEMI have found improved survival for shorter time from symptom onset to hospital presentation^{13,15,16-17} and from symptom onset to treatment (including both symptom onset-to-door time and door-to-needle time.^{12,18} In a meta-analysis¹⁹, the absolute reduction in mortality with the use of fibrinolytic therapy compared with placebo was greatest among patients who presented within 1 hour after symptom onset.¹⁹ The evidence concerning the specific association between door to-needle time and mortality is less well established. In our study we also observed longer door to needle time even in patients presenting early. The Global Utilization of Streptokinase and tPA for Occluded Coronary Arteries (GUSTO) trial¹³ did find in-hospital mortality to increase with increasing door-to-needle times. However, these patients were highly selected, and the analysis was not adjusted for time to presentation or patient characteristics. In the GUSTO trial, which enrolled patients from 1990–1993, only 7% were treated within 30 minutes of arrival. The Cooperative Cardiovascular Project (CCP)²¹ 30-day mortality significantly increased from 12.5% for those treated within 30 minutes, to 14.1% for those treated 31–90 minutes, and 19.9% for those treated after 90 minutes.²¹

Our study has demonstrated the independent effect of longer time intervals from symptom onset to hospital presentation among patients with ST-elevation myocardial infarction. We demonstrated that longer times to hospital presentation were associated with significantly lower use of any reperfusion therapy, longer door-to-needle times. The novel finding from our study is that longer times to hospital presentation is a risk factor for additional downstream hospital delays in treatment with and timeliness of any reperfusion therapy.

Possible explanations for the relationship between delay in hospital presentation and use of any reperfusion and timeliness of reperfusion therapy include: (a) patients who present early after onset of symptoms may elicit more urgency from providers to initiate reperfusion therapy; and (b) patients who present late may exhibit more atypical or no symptoms which subsequently lead to missed or late diagnosis as well as confusion or reluctance to administer reperfusion therapy. Among patients with ST-elevation myocardial infarction eligible to receive reperfusion, an optimal system of care should not exclude patients from reperfusion therapy or incur

incremental delays in door-to-balloon or door-to-drug times simply because of longer times to hospital presentation.

In the Fibrinolytic therapy Trialists' (FTT) overview,²⁰ among the 45,000 patients presenting with STEMI or BBB, the relation between benefit and delay from symptom onset indicated highly significant absolute mortality reductions of about 30 deaths prevented per 1,000 patients (by 35 days) treated within 6 h of symptom onset. For those presenting at 7 to 12 h, there were approximately 20 deaths prevented per 1,000 patients treated; beyond 12 h, there was a statistically uncertain benefit of about 10 per 1,000. While the FTT overview²⁰ reported an apparent linear relationship between absolute mortality benefit and time from symptom onset to treatment (1.6 deaths per hour of delay per 1,000 patients treated). The FTT overview¹³⁶ indicates that patients with BBB are at high risk when presenting with a presumed MI and had an evident mortality benefit of fibrinolysis.²⁰

The hospital mortality of 13.6% appears high compared to recently published randomized acute myocardial infarction trials (ISIS-3 10.4%, GUSTO 7.3/ 6.3%, GISSI-2 9.4%, FTT 10.5%)^{13,15,18,20} lower mortality in the randomized trials is due to the exclusion of high risk patients, and to the fact that all patients in these trials received thrombolysis. Also, patients presenting after 12 h have a higher mortality. The National Registry of Myocardial Infarction (NRM) registry had a mortality of 10-6%, but also included non Q-wave infarctions with a better prognosis (18% of the patients).²³

In the GISSI-Avoidable Delay (GISSI-AD) study,²⁴ conducted in 1990 on 5301 patients in 118 CCUs, the median pre-hospital delay was 230 min. This overall reduction is to be attributed to a shorter decision time and an increasing percentage of patients arriving within 2 h from symptom onset (34%), whereas the proportions of patients arriving between 2 and 6 h (29%) and between 6 and 12 h (14%) were similar. Part of the merit for this important progress in care delivery was ascribed to the nationwide application of the Emergency Medical Service 118 number which, however, was used as first aid only by 30% of the patients. The reductions in delay observed in the National Registry of Myocardial Infarction in about 10 years (1990 to 1999, median delay from 132 to 120 min²⁵ and in the Worcester Study (1986 to 1997, median delay from 132 to 120 min)²⁶ are less impressive.

Timely administration of reperfusion therapy by primary angioplasty or thrombolysis is the recommended treatment for most patients with myocardial infarction and ST segment elevation²⁷. Reperfusion treatment was administered in hospital

to 53.3% of patients with STE-MI, with a ratio of 3.4:1 in favour of thrombolysis.

The present data also favourably compare with those of the GISSI-AD study²⁴ which, in 1990, reported a very low rate of reperfusion therapy (40%) irrespective of time delays. In the GISSI-AD study, 40% of the patients admitted within 2 h did not receive reperfusion therapy, corresponding proportions for the 2–6 h delay were 51%, for 6–12 h 79% and for patients admitted later than 12 h from symptom onset 92% respectively.

The reperfusion rates observed in the present study are very close to those reported in the most recent surveys. In European Network for Acute Coronary Treatment. (ENACT)²⁸ 51% of the patients received thrombolysis, and only 8% had primary PCI, with wide variations among different European countries. In Euro Heart Survey ACS.²⁹ 55% of patients received some form of reperfusion therapy, A late admission was the cause of exclusion in only 22% and age in only 3% of the patients; most exclusions (35%) were motivated by the lack of a clear indication. The different enrolling sites could explain these differences. In the Global Registry of Acute Coronary Events (GRACE) survey,³⁰ 47% of STE-MI received thrombolytic treatment, and 18% primary PCI with an overall ratio similar to The Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS).²⁹

CONCLUSION

Delayed presentation is associated with older age and female gender. Patients presenting late are in more advanced Killip class and are less frequently thrombolysed and thus are predisposed to increased in-hospital mortality.

REFERENCES

1. American Heart Association. Heart Disease and Stroke Statistics—2005 Update. Dallas, Tex: American Heart Association; 2005.
2. Ad Hoc Committee on Health Research Relating to Future Intervention Options. Investing in Health Research and Development. Geneva, Switzerland: World Health Organization; 2006.
3. Goldberg RJ, Mooradd M, Gurwitz JH, Rogers WJ, French WJ, Barron HV, Gore JM. Impact of time to treatment with tissue plasminogen activator on morbidity and mortality following acute myocardial infarction (the second National Registry of Myocardial Infarction). *Am J Cardiol.* 2008;82:259–264.
4. Newby LK, Rutsch WR, Califf RM, Simoons ML, Aylward PE, Armstrong PW, Woodlief LH, Lee KL, Topol EJ, Van de Werf F. Time from symptom onset to treatment and outcomes after thrombolytic therapy. *GUSTO-1 Investigators. J Am Coll Cardiol.* 2006;27:1646–1655.
5. Berger PB, Ellis SG, Holmes DR Jr, Granger CB, Criger DA, Betriu A, Topol EJ, Califf RM. 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.* 2007;116:14–20.
6. 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. Fibrinolytic therapy Trialists' (FTT) Collaborative Group [published correction appears in *Lancet.* 2006;343:742]. *Lancet.* 2007;343: 311–322.
7. Simoons ML, Serruys PW, van den Brand M, Res J, Verheugt FW, Krauss XH, Remme WJ, Bar F, de Zwaan C, van der Laarse A, et al. Early thrombolysis in acute myocardial infarction: limitation of infarct size and improved survival. *J Am Coll Cardiol.* 2006;7:717–728.
8. Rawles JM, Metcalfe MJ, Shirreffs C, Jennings K, Kenmure AC. Association of patient delay with symptoms, cardiac enzymes, and outcome in acute myocardial infarction. *Eur Heart J.* 2006;11:643–648.
9. Six-month survival in 20,891 patients with acute myocardial infarction randomized between alteplase and streptokinase with or without heparin. GISSI-2 and International Study Group. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto. *Eur Heart J.* 2007;13:1692–1697.
10. Dracup K, Moser DK, McKinley S, Ball C, Yamasaki K, Kim CJ, Doering LV, Caldwell MA. An international perspective on the time to treatment for acute myocardial infarction. *J Nurs Scholarsh.* 2008;35: 317–323.
11. McGinn AP, Rosamond WD, Goff DC Jr, Taylor HA, Miles JS, Chambless L. Trends in prehospital delay time and use of emergency medical services for acute myocardial infarction: experience in 4 US communities from 1987–2000. *Am Heart J.* 2005;150:392–400.
12. Goldberg RJ, Mooradd M, Gurwitz JH, Rogers WJ, French WJ, Barron HV, Gore JM. Impact of time to treatment with tissue plasminogen activator on morbidity and mortality following acute myocardial infarction (the second National Registry of Myocardial Infarction). *Am J Cardiol.* 1998;82:259–264.
13. Newby LK, Rutsch WR, Califf RM, Simoons ML, Aylward PE, Armstrong PW, Woodlief LH, Lee KL, Topol EJ, Van de Werf F. Time from symptom onset to treatment and outcomes after thrombolytic therapy. *GUSTO-1 Investigators. J Am Coll Cardiol.* 1996;27: 1646–1655.
14. Simoons ML, Serruys PW, van den Brand M, Res J, Verheugt FW, Krauss XH, Remme WJ, Bar F, de Zwaan C, van der Laarse A, et al. Early thrombolysis in acute myocardial infarction: limitation of infarct size and improved survival. *J Am Coll Cardiol.* 1986;7:717–728.

15. Six-month survival in 20,891 patients with acute myocardial infarction randomized between alteplase and streptokinase with or without heparin. GISSI-2 and International Study Group. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto. *Eur Heart J* 1992;13:1692–1697.
16. Italian Group for the Study of Streptokinase in Myocardial Infarction (Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. *Lancet* 1986;1:397–402.
17. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. *J Am Coll Cardiol* 1988;12:3A–13A.
18. The GUSTO Investigators. An International randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med* 1993;329:673–682.
19. Boersma E, Mass ACP. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet* 1996;348:771–775.
20. 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. Fibrinolytic therapy Trialists' (FTT) Collaborative Group [published correction appears in *Lancet*. 2006;343:742]. *Lancet*. 2007;343: 311–322.
21. 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.
22. ISIS-3 (Third International Study of Infarct Survival) Collaborative Group: ISIS-3: a randomised comparison of streptokinase vs. tissue plasminogen activator vs. anistreplase and or aspirin plus heparin vs. aspirin alone among 41 299 cases of suspected myocardial infarction. *Lancet* 1992; 339: 753-70.
23. Rogers WJ, Bowlby LJ, Chandra NC, et al. Treatment of myocardial infarction in the United States (1990-1993). Observations from the National Registry of Myocardial Infarction. *Circulation* 1994; 90: 2103-14.
24. [Epidemiology of avoidable delay in the treatment of acute myocardial infarct: study conducted by 'GISSI' (Italian Group for the Study of Survival after Myocardial Infarct)]. *G Ital Cardiol* 1996;26:807–820.
25. Rogers WJ, Canto JG, Lambrew CT et al. Temporal trends in the treatment of over 1.5 million patients with myocardial infarction in the US from 1990 through 1999: the National Registry of Myocardial Infarction 1, 2 and 3. *J Am Coll Cardiol* 2000;36:2056–63.
26. Goldberg RJ, Yarzebski J, Lessard D, et al. Decade-long trends and factors associated with time to hospital presentation in patients with acute myocardial infarction: the Worcester Heart Attack study. *Arch Intern Med* 2000;160:3217–23.
27. Ryan TJ, Antman EM, Brooks NH, et al. Update 1999: ACC/AHA guidelines for the management of patients with acute myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1999; 34:890–911.
28. Fox KA, Cokkinos DV, Deckers J, et al. The ENACT study: a pan- European survey of acute coronary syndromes. European Network for Acute Coronary Treatment. *Eur Heart J* 2000;21:1440–9.
29. Hasdai D, Behar S, Wallentin L, et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin. The Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). *Eur Heart J* 2002;23:1190–201.
30. Steg P, Goldberg R, Gore J, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). *Am J Cardiol* 2002;90:358.