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Acute Myocardial Infarction: Profile and Management at a Tertiary Care Hospital in Karachi

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Abstract

Objective: Acute Myocardial Infarction (AMI) is a rising epidemic in developing countries. While studies in the West have established the characteristics and management of AMI patients, comprehensive data reflecting these issues in the Pakistani subjects is scarce. This study examined the profile and management of AMI in patients hospitalized at a tertiary care hospital in Karachi, Pakistan.

Methods: Three hundred forty four patients admitted in 1998 with the diagnosis of AMI met our inclusion criteria. Data on presentation, investigations, monitoring and therapy was obtained. Chi-square and t tests were used to analyze the data.

Results: Out of 344 patients with AMI, 71% were males; 58% had a Q wave MI. Majority of the patients who presented within 2 hours of symptom onset (36%), had chest pain. Patients with dyspnea and no chest pain were more likely to present after 12 hours of the onset of symptoms. In-house mortality was found to be 10.8%. Low HDL and diabetes was associated with in-hospital complications. Twenty nine percent of patients were given thrombolytic therapy with a mean door-to-needle time of 1 hour 36 minutes; 33% of patients who were eligible of Streptokinase did not receive it. Cardiac catheterization was performed in 28% patients. Echocardiography and Exercise Tolerance Test, both under utilized, were performed in 67% and 16% of patients, respectively. Two hundred sixteen (70%) patients discharged from hospital were contacted via telephone and the 1-year mortality rate among them was 28%.

Conclusion: The profile and management of AMP was in coherence with earlier, Western studies. Chest pain units need to be established in the Emergency Room. Patients should be risk stratified prior to discharge. Public awareness regarding primary and secondary prevention and symptoms of AMI needs to be increased (JPMA 52:45, 2002).

Introduction

Atherosclerotic coronary artery disease (CAD) is among the leading cause of death throughout the world^{1,2}. In 1990 cardiovascular disease (CVD) claimed 14 million lives, two thirds of which were in the developing countries³. The prevalence of CAD in Pakistan is probably as high as in developed countries⁴. In developed countries, the acute myocardial infarction (AMI) in-hospital mortality has registered a decline from 30% three decades ago, to less than 8% in the 90's⁵. This decline in mortality has largely been attributed to dramatic changes in management strategies over the past few decades⁶. The management of AMI initially focused on treatment and/or prevention of complications. In the pre-thrombolytic era, the therapeutic regimens mainly comprised of the use of anti-anginal and anti-arrhythmic drugs⁷. The demonstration that the vast majority of AMI are

caused by an occlusive thrombus in the coronary artery, together with the concept that myocardium can be salvaged within a period of time after the onset of such occlusion, herald a new era of management of this disorder⁸. Data shows that coronary flow can be re established using intravenous thrombolytics, coronary angioplasty, or coronary artery-bypass grafting⁹⁻¹¹. Adjuvant therapy for AMI should also include Aspirin¹², beta-blocking agents¹³, Heparin¹⁴ and in most patients, Angiotensin-converting enzyme inhibitors¹⁵. Postinfarction, the use of Aspirin, beta-blockers¹⁶, ACEIs¹⁷ and lipid lowering agents¹⁸ has shown a survival benefit.

Although widely known, these technologies are not consistently applied^{19,20}. Recommended treatments are still under utilized in patients with AMI²⁰. Sufficient data regarding the utilization of therapies and in-hospital AMI mortality for Pakistan is lacking.

Clinical characteristics and simple bedside laboratory tests can now be used to identify subsets of patients with AMI at different levels of risks and to adjust treatment accordingly²². In various studies, risk indicators for death were related to age, gender, Killip class²³, history of smoking²⁴, diabetes, hypertension, previous CAD and a family history of CAD and hyperlipidemia²⁵. Perhaps as many as a third of all patients are at very low risk and therefore, can be safely discharged from the hospital within 72 hours²⁶. The substantial resources thus saved could then be directed towards applying the more expensive therapies to patients at a higher risk. Although considerable information is available regarding the prognosis after AMI in western population, little is known about the fate of Pakistani subjects after AMI. Thus the aim of the study is to see the profile, management and predictors of mortality in AMI patients presenting to a tertiary care hospital in Pakistan.

Materials and Methods

This was a retrospective descriptive study of patients with AMI admitted to the emergency room (ER) of The Aga Khan University Hospital (AKUH) from January 1, 1998 to December 31, 1998. Patients with the discharge diagnosis of AMI according to the ICD-9, were included using a list generated by the coding department of AKUH. Patients were excluded if there was an obvious coding error, transferred to or from another hospital (to avoid tertiary referral bias), if the MI developed following Coronary artery bypass grafting (CABG) or any other invasive procedure, if they developed AMI while in hospital for another reason.

Data Collection

Data was taken from the clinical history, coded at the time of hospital discharge. Information was obtained on patient's signs and symptoms, medical history, cardiac enzyme levels, hospital course, monitoring and therapy. Diagnosis of AMI in the charts was based on any two of the following three criterion: (1) Typical chest pain; (2) ST changes in one standard or two precordial leads and (3) Rise in CK concentration more than twice the normal. Variables were evaluated to determine their ability to predict cardiac deaths. In-hospital deaths were classified into categories of cardiac and non-cardiac causes after a review of hospital records. Follow up after discharge was obtained from charts and later telephone. Details of readmission and other procedures (CABG, angioplasty etc.) were also obtained.

Statistical Analysis

All data was transferred from pre coded data sheets to a computed database for analysis using SPSS 8.0. $P < 0.05$ was considered statistically significant. The association between mortality as the dependant variable and all other variables as independent variables was evaluated using Chi square. Student's t test was used to assess differences between continuous variables. All categorical characteristics are described as percent and continuous measures are summarized with medians and means.

Results

Among the 344 patients studied retrospectively, 71 percent were male and 29 percent were female. Age was normally distributed with a range of 25 to 92 years and a mean of 60 years.

Risk factors

The risk factors associated with AMI in our population are shown in Table 1.

Table 1. Risk factor profile (n=334).

Risk factors	%
Previously history of coronary artery disease	52
Hypertension	47
Diabetes	40
Family history of premature coronary artery disease	26
Current smoker	23
Ex-smoker	17
Prior cholesterol > 200 mg/dl	18
Cerebrovascular disease	5
Previous TIA/CVA	4
Peripheral vascular disease	2

Presenting symptoms

Presenting sign, symptoms and time to presentation are shown in Table 2a and 2b.

Table 2a. Presenting signs/symptoms (n=334).

Presenting sign/symptom	%
Chest pain	76
Dyspnea	32
Syncope/ cardiac arrest	4
Killip I	60
Killip II	29
Killip III/IV	9

Table 2b. Time to presentation

Time of presentation	%
<2 hours	37
2-6 hours	18
6-12 hours	4
>12 hours	36

The median duration of symptoms was four hours and the mode was two hours. The majority of patients presented before 2 hours (37%) or after twelve hours (36%).

Streptokinase

Streptokinase was given to 29% of patients and median door-to-needle time was 40 minutes. The mean time to Streptokinase administration was 1 hour and 36 minutes (SD \pm 4 hours, 26 minutes). One third of those eligible for Streptokinase therapy (neither late presentation nor contraindications for the treatment) did not receive it. There was no significant gender bias in the treatment provided.

Investigations and Procedures

Electrocardiogram (EKG) was performed on all patients in the ER. Serial lab investigations, echocardiogram, and exercise tolerance test were not done on the entire study population (Table 3).

Table 3. Investigation findings in percent.

	n	%
Electrocardiogram	344	100
ST elevation	-	54
ST depression	-	41
New bundle branch block	-	4
Echocardiogram	230	67
Wall motion abnormality	-	84
Exercise tolerance test	55	16
ST changes	-	46
Chest pain	-	13

Hospital procedures include cardiac catheterization in 28 percent, CABG in 9 percent and PTCA in 6 percent. Cardiac catheterization (OR: 4.4, 95% CI: 1.9-10.2, p

Medications

At the time of admission, medications already in use, included nitrates (27%), aspirin (24%), beta blockers (22%), ACEI (15%), and calcium channel blockers (CCB)(13%).

Only 5 percent patients were on lipid lowering drugs. In the emergency room, the most commonly administered medications were as follows: aspirin (65%), intravenous (IV) heparin (53%), IV nitrates (58%), sublingual nitrates (44%), and oxygen (44%).

Morphine was given to 30 percent while 24 percent required diuretics. It is important to note that only 22 percent of patients received either IV or oral beta-blockers. During hospital stay, the majority of patients received aspirin (90%), IV heparin (77%), oral nitrates (66%), ACEI (62%), or oral beta-blockers (60%). On discharge, patients were most frequently prescribed aspirin (78%), oral nitrates (62%), oral beta-blockers (61%), and ACEI (48%). Only 28% patients were sent with a In-Hospital Course and Mortality. The median hospital stay was 9 days (S.D. 7.4) with median CCU/CSDU stay of 4 days (S.D. 5.4). In-hospital complications occurred in 33% of patients. The most common being CHF requiring diuretics (37%), recurrent angina (34%) and cardiac shock requiring pressors (29%).

Thirty-seven deaths were recorded which constituted an overall mortality of 10.8 percent. In-hospital mortality was compared with patient variables. Gender had no significant association with in-hospital mortality. Age and peripheral vascular disease was associated with in-hospital mortality. Among the presenting symptoms (Table 4) syncope/cardiac arrest was a predictor of mortality, while the others had no significant association. EKG findings on presentation had no relation with mortality (Table 4).

Table 4. Comparison of ER findings and length of hospital stay with in-hospital mortality.

Variable	Death +	.	P-value
Presenting symptom			
Chest pain	25 (67.6)	238 (77.5)	N/S
Dyspnea		15 (40.5)	95 (30.9)
N/S			
Syncope/Cardiac arrest	5 (13.5)	8 (2.6)	0.01
ECG findings			
ST elevation	21 (56.8)	165 (21.2)	N/S
ST depression	12 (32.4)	127 (41.4)	N/S
Bundle branch block	4 (10.8)	9 (2.9)	N/S
Laboratory investigations			
CKpeak (IU/dl) ±SD	2651±28 27	1187±149 8	<0.01 320
CKMB peak (IU/dl) ±SD	208±373	58±74	<0.01 135
Length of stay in ward			
(mean days±SD)	23±6.9	40±3.9	<0.01

Overall, in-hospital complications were strongly associated with in-hospital mortality (OR: 18.2, 95% CI: 6.8-48.2,p

The population was divided into those with ST elevation and those with ST depression. A comparison of all risk factors and in-hospital mortality was done for the individual subsets. The significant associations are summarized in Tables 5a and 5b.

Table 5a. ST elevation comparison of in-hospital mortality with risk factors: Mean and standard deviation.

Variable	Death		P-value
Age (years)	65.4±11.1	57.2±11.6	<0.01
Length of stay in ward (days)	1.8±5.0	4.4±4.2	0.01
CK peak (IU/dL)	3101±3210	1595±1754	<0.01
Estimated LVEF on echocardiography (%)	34.1±10.8	48.9±12.1	<0.01

Table 5b. ST depression: comparison of in-hospital mortality with risk factors (Mean±SD).

Variable	Death		P-value
CK peak (IU/dL) (mean+SD)	1743±1611	687±924	0.01
ckmb PEAK (IU/dL) (mean+SD)	614±450	47.5±58.5	<0.01

Risk factors associated with severe MI

Investigations were found to predict in-hospital mortality. Survivors had higher LVEF ($p=0.02$), lower peak CKMB values ($p<0.01$), and lower peak CK values ($p<0.01$). Severity of myocardial infarction was studied using the following parameters: CCU stay, Killip class, in-type of myocardial infarction, compared with risk factors. The with a longer CCU stay was Risk factors associated with II were: age > 60 ($p=0.04$), history of CAD ($p=0.03$), and presentation after 12 hours ($p=0.009$). Age greater than 60 years, diabetes, and current smoking were associated with ST elevation on electrocardiogram ($p=0.06$, $p=0.09$, $p=0.04$ respectively) whereas, a prior history of CAD was associated with ST depression ($p=0.001$). Patients more likely (borderline significance) to have in-hospital complications were diabetics ($p=0.07$), those having low HDL ($p=0.05$) and those having a prior history of in-hospital complications. ($p=0.001$).

Mortality on Follow-up

Three hundred and seven patients were discharged; 216 patients were available for follow-up. By 6 January, 2000, 28 percent patients had expired. Gender did not influence mortality. Among the initial presenting symptoms, dyspnea (OR: 0.4, 95% CI: 0.2-0.8, $p=$

Discussion

When analyzing the age distribution of patients with AMI, the mean age of 60 years correlated well with the Western demographics²⁷, but disagreed with the past studies in Pakistan, which reported that Pakistani patients are young, aged 40 and 45, and therefore affected by premature CAD²⁸. The in-hospital mortality rate was 10.8% and increased with age greater than 60. This is comparable to that of developed countries, where, in-hospital mortality rate in the best centers ranges from 7.4% to 8%⁷. Most patients presented with chest pain (76%). Only one-third (37%) of the patients presented in less than 2 hours, and most of these patients had chest pain. Thus, chest pain is readily recognized as a symptom of “heart attack” and early hospital care is sought. It has been shown that the greatest benefit of thrombolytic therapy occurs if treatment is initiated within the first 1 - 3 hours, when a 50% or greater reduction in mortality can be achieved¹². The magnitude of benefit declines rapidly thereafter. Unfortunately, nearly one-third (36%) of the patients presented after 12 hours, and most of them had symptoms of dyspnea (32%), or “ghabrahat” (apprehension), which are not readily recognized as symptoms of “heart attack”, by the layman. This leads to the late presentation to the hospital. Hence, the need arises to increase public awareness regarding symptoms associated with the painless infarction (like dyspnea, diaphoresis, apprehension). More than half (52%) of the patients’ population had previous coronary artery disease. About one-fifth of the patients were already taking aspirin, beta-blockers and nitrates when they presented while a few (13 to 15%) were on CCB and ACE!. The lack of secondary prevention, which aims at delaying the progression and complication of CAD after it is manifest, is highlighted by the fact that only 5% of the patients at presentation were on lipid lowering drugs. Hypertension (HTN) (47%) and diabetes (40%) were major co-morbid in almost one-half of our patients. Epidemiological studies have already identified these as important risk factors for coronary heart disease²⁹. In-hospital complications were more likely in those who had diabetes and low HDL (<35mg/dl). In the ER, aspirin, IV and sublingual nitrates, IV heparin and oxygen was the mainstay of treatment. Thrombolytic therapy (streptokinase) was given to 29% of the patients. A study conducted in the USA in 1993, reported that 35.1% of the AMI patients received thrombolytic therapy³⁰. In our study, the mean this could be the multi-purpose ER, which caters to all kinds of patients. This thus calls for the establishment of Chest Pain Units. (CPU) within the ER where a rigorous assessment of patients presenting with chest pain can be carried out and they can be rapidly triaged and dealt accordingly. A prospective randomized trial established that a CPU located in the ER and managed by the ER staff; can be a safe, effective and cost saving means of assuring that patients with chest pain receive appropriate care³¹. We also found that 33% of the patients who were eligible for streptokinase, (no contraindications, nor late presentation), did not receive it. The reasons for this remain obscure.

Mean length of stay in CCU was 4 days, comparable to the reported mean of 3.3 in the United States⁷. Smokers stayed in the CCU for a longer duration as compared to non-smokers. Hence, smoking is associated with increased morbidity and cost of healthcare³². In-hospital mortality was 5.8 times more likely in patients who presented with syncope and cardiac arrest. This finding agrees with previous studies, as most hypotensive patients have moderate to severe left ventricular dysfunction and thus a poor prognosis²³. Fifty eight percent of the patients had Q wave MI, similar to the Western figure of 51.5%⁷. The magnitude of peak creatinine kinase elevation in serum was higher in those

who died. Similar association has been reported in past studies⁷. A series of clinical trials have demonstrated the importance of elevated LDL cholesterol in the pathogenesis of atherosclerosis and the substantial benefit of treating hyperlipidemia in preventing this condition¹⁸. Only about one-third of the patients (n130) had their lipid profiles documented in their medical records. This might have been due to late presentation, (>24 hours) when the lipid profiles become unreliable.

Echocardiography provides a convenient bedside assessment of left ventricular, global and regional function. It has been used successfully to make judgments about admission and management of patients with suspected infarction²³. Despite this, echo was performed only on 67% patients and wall motion abnormality was seen in 84% of these cases. The reasons behind this low rate of investigation could be a failure to document the echo reports, cost issues or technical difficulties.

The goal of preventing reinfarction and death, postMI has led to strategies to evaluate risk. Early after infarction, this evaluation involves the use of non-invasive testing. In stable patients, sub-maximal Exercise Tolerance Test (E1'T) may be carried out prior to hospital discharge to detect residual ischemia and ventricular ectopy, and to provide the patient with a guideline for exercise. Stress testing may also help in building the patient's confidence towards a reasonable exercise tolerance³³. Our study demonstrated an under utilization of this useful investigation. Only 16% patients underwent a predischarge ETT with more than half (59%) being positive (ST changes, chest pain). This might have been due to lack of patient compliance, cost issues, documentation errors, or doubts in the physician's mind regarding the efficacy of this tool. The most common in-hospital procedures were cardiac catheterization and CABG. Both were associated with increased survival on follow-up. This could be due to timely identification of the culprit artery and appropriate intervention.

In-hospital use of aspirin, oral beta-blockers, oral nitrates and ACE inhibitors, significantly decreased in-hospital mortality. This result is compatible with known effects of aspirin and beta-blockers^{12,13}. On discharge, aspirin, oral nitrates, and oral beta-blockers were given to a great majority (61 to 78%) of the patients and half the patients received ACE inhibitor. Despite the proven efficacy of lipid lowering agents in primary and secondary prevention of CAD¹⁸, only about one-fourth of the patients (28%), received lipid lowering agents on discharge.

Two hundred sixteen (70%) of the patients who were discharged home were contacted again by telephone, and the 1-year mortality rate among them was 28%. The high mortality rate could be because of poor follow-up, comorbid, lack of compliance to treatment, or may reflect the need to re-examine the present management strategies.

Limitations

Small size of the patient population available for our study, in our view, is the main limitation of our study. It is a retrospective survey, with inability to control the quality of the data. The exact reason for patient-to-patient variability regarding treatment was not noted. This is an important factor, which should be considered if any subsequent management protocol is to be developed in the future on the basis of our study results. The general epidemiology, risk factor profile, mortality and management of AMI in our population was in coherence with the studies from the developed countries.

Improvements can be made in triaging patients with chest pain by establishing CPUs. An organized plan for rehabilitation of Post-MI patients can be made, using predischarge

investigations for risk stratification of these patients. Furthermore, public awareness programs are needed to increase the awareness regarding primary and secondary prevention, and the presenting symptoms of CAD. Treatment practices in other hospitals of Pakistan should also be studied to assess the mortality rate and identify any needs for improvement in the management strategies.

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References

- 1.Manson JE, Tosteson H, Ridker PM, et al. The primary prevention of myocardial infarction. *N. Eng. J. Med.*, 1992;326:1406-16.
- 2.Kannel WB, Thom TJ. Incidence, prevalence and mortality of cardiovascular diseases. In: Hurst JW, eds. *The Heart* 8th ed. New York, McGraw-Hill, 1994, pp. 185-97.
- 3.Samad A. (Editorial). 12th Asian Pacific Congress of Cardiology. *Pak.J.Cardiol.*, 1999;10:81-2.
- 4.Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation*, 1 998;97:596-601.
- 5.Friedman BM. Early investigations in the management of acute uncomplicated myocardial infarction. *West. i. Med.*, 1995;162:19-27.
- 6.Sullivan H, Floras iS. Early management of acute myocardial infarction. *Br. J. Hosp. Med.*, 1988;40:449-58.
- 7.Gheorghiad M, Ruzamna P, Borzak S. et al. Decline in the rate of hospital mortality from acute myocardial infarction: impact of changing management strategies. *Am. Hearti.*, 1996;131:250-7.
- 8.Giogar D, Yang P, Steurer G. Management of acute myocardial infarction: evaluating the past, practicing in the present, elaborating the future. *Am. Heart. J.*, 1996;132:465-70;.
- 9.Vincent R. Advances in the early diagnosis and management of acute myocardial infarction. *J. Accid. Emerg. Med.*, 1 996;1 3:74-9.
- 10.Grover A, Rihal CS. The importance of early patency after acute myocardial infarction. *Curr. Opin. Cardiol.*, 1995;10:361-6,
- 11.Lieu TA, Gurley Ri, Lundstrom RJ, et al. Primary angiography and thrombolytics for acute myocardial infarction: an evidence summary. *i. Am. Coil. Cardiol.*, 1996;27:737-50.
- 12.ISIS-2 Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet*, 1988;ii:349.
- 13.Goldstein S. Beta-blocking drugs and coronary heart disease. *Cardiovasc. Drugs Ther.*,1997;11:219-25.
- 14.Reeder GS. Adjunctive therapy in the management of patients with acute myocardial infarction. *Mayo. Clin. Proc.*, 1995;70:464-8.

15. Hall AS, Ball SG. Adjunctive therapy in the management of patients with acute myocardial infarction. *J. Cardiovas. Risk*, 1995 ;2:396-405.
16. Goldstein S. Beta blockers in hypertensive and coronary heart disease. *Arch. Intern. Med.*, 1996;156:1267-76.
17. GISSI-3 investigation myocardial infarction: when and how should we initiate treatment with ACE inhibitors? *Cardiology*, 1996;87 (Suppl. 1): 16-22.
18. 4S Randomized trial of cholesterol in 4444 patients with coronary heart disease. *Lancet*, 1994;344:1383-9.
19. Leupker RV, Herlitz J. Differences in the treatment of AMI between regions of Countries and the impact on prognosis. *J. Cardiovasc. Risk.*, 1999;6:77-87.
20. George E, Hunsberger S, Savitha D et al. Treatment of AMI: does the type of hospital makes a difference? PPAMI Study Group. *Ind. Heart J.*, 51:161-6.
21. Venturini F, Romero M, Tognoni G. Patterns of Practice of AMI in a population from ten countries. *Eur. J. Clin. Pharmacol.*, 1999;54:877-86.
22. Hills LD, Formas S, Braunwald E. The thrombolysis in myocardial infarction (TIMI). Phase III co-investigators. Risk stratification before thrombolytic therapy in patients with acute myocardial infarction. *J. Am. Coll. Cardiol.*, 1990;16:313-15.
23. Iona M, Grossman E, Boyko V et al. Relation of early one-year outcome after acute myocardial infarction to systemic arterial blood pressure on admission. *Am. J. Cardiol.*, 1999;84:162-65.
24. Herlitz J, Karlson BW, Lindquist J, et al. Predictors of death and mode of death during long term follow up among patients with unconfirmed acute myocardial infarction, *Clin. Cardiol.*, 1999;22: 179-83.
25. Herlitz J, Karlson BW, Lindquist J. et al. Predictors of death over 5 years among patients admitted raising suspicion of acute myocardial infarction. *J. Intern. Med.*, 1998;243:41-8.
26. Topol EJ, Burek K, O'Neil WW, et al. A randomized controlled trial of hospital discharge three days after myocardial infarction in the era of reperfusion. *N. Eng. J. Med.*, 1998;338:1083-8.
27. Kanm MA, Mehmood SF, Akhter J, Qureshi AR. Thrombolytic therapy in AMI in Pakistan. *J. Pak. Med. Assoc.*, 1995;45:54-58.
28. American Heart Association. Heart and Stroke facts, 1998. Dallas:AHA,1998.
29. Kannel WB, McGee DL. Atherosclerosis risk factors. *Pharmacol. Ther.*, 1987;32:207-35.
30. Rogers WJ, Bowlby U, Chandna NC, et al. For the participants of the national registry of myocardial infarction: treatment of myocardial infarction in United States. (1990-1993); observation from the National Registry of Myocardial Infarction. *Circulation.*, 1989;21 03-14.
31. Farkouh MA, Smars PA, Reeder GS, et al. A clinical trial of a chest pain observation unit for patients with unstable angina: chest pain evaluation in the emergency room (CHEER) Investigators. *N. Eng. J. Med.*, 1998;339: 1882-8.
32. U.S. Department of Health and Human Services. Targeting Tobacco use: the nation's leading cause of death at a glance. Bethesda, MD: Centers of Disease Control and Prevention, 1998.
33. Antman EL, Braunwald E. Myocardial Infarction. In: Fauci AS, Braunwald E, eds.

Harrison's principles of international medicine. 14th ed. New York, McGraw-Hill, 1998, pp. 1352-65.