Prognostic Significance of Troponin-T and Clinical Variables in Acute Coronary Syndrome

S.M.N.A. Nadeem, K. Kazmi, I. Chandna, N. Basir, A. Pathan
Cardiology Section, Department of Medicine, The Aga Khan University Hospital, Karachi.

Abstract

Objectives: Troponin T (TnT) is an independent predictor for short and long-term adverse cardiac event. We evaluated the prognostic significance of TnT in our patients and also tested the prognostic significance of other early available clinical risk indicators, after adjustment for TnT.

Methods: We studied 255 consecutive patients admitted with the diagnosis of Unstable Angina (UA) and Non-ST-Segment elevation myocardial infarction (NSTEMI). All patients had a baseline TnT estimation at presentation and repeated twelve hours later, in case of an initial negative result. Follow-up was available in 233 patients (91%) with a mean duration of 13 $\pm$ 6 months.

Results: By Kaplan Meier estimates; survival free of myocardial infarction was 92.8% in TnT- vs. 66.9% in TnT+ group (p = 0.001) at 18 months. By multivariate Cox- regression analysis, independent predictors of death and myocardial infarction (MI) were positive TnT (HR 2.96, 95% CI 1.34-6.56), increasing age (HR for one year increase 1.05, 95% CI 1.02-1.08), history of congestive heart failure (CHF) (HR 6.17, 95% CI 2.40 - 15.87) and peak CK (HR for one IU/L rise 1.00, 95% CI 1.00-1.001)

Conclusion: Positive Troponin T in patients with UA/NSTEMI is a strong, independent risk predictor of future death and MI. In addition, history of CHF, peak CK and age were also associated with increased risk of death and MI. Conventional risk predictors like pulse rate, ST depression, gender and diabetes were not identified as independent risk predictors (JPMA 53:280;2003).

Introduction

Acute coronary syndrome is a useful operational term, referring to clinical situations with symptoms suggestive of acute myocardial ischemia. It encompasses acute myocardial infarction including ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction (NSTEMI), unstable angina (UA) and sudden ischemic death. Patients with acute ST-elevation myocardial infarction constitute a distinct group with distinct management strategies including immediate reperfusion therapy either by fibronolytic agents or by catheter based interventional procedures, as dictated by patient's hemodynamic state, availability of treatment modalities and other logistic considerations.

Several studies have shown that patients with UA and NSTEMI are a heterogeneous group with a variable subsequent adverse outcome. At the time of presentation, patients with UA and NSTEMI may be indistinguishable and are managed on similar lines. Early risk stratification is therefore important to identify high-risk patients requiring aggressive management strategies including early revascularization procedures. Recent prognostic studies have shown that both short and long term mortality and risk of subsequent reinfarction are largely determined by myocardial damage at initial presentation. Cardiac specific Troponin-T (TnT) and Troponin-I assays are highly sensitive in detecting myocardial damage.[1] Recent clinical data has suggested TnT as an independent predictor for short and long term adverse cardiac events.[2]

Most of the prognostic studies done on TnT have been reported from west.[3-9] Reports from the developing world addressing the role of TnT in patients with acute coronary syndrome are scarce.[10-12] To our knowledge none of the report from developing world has so far discussed long-term prognostic significance of TnT.

The purpose of this study was to validate the prognostic significance of this novel marker of myocardial injury in a cohort from Pakistan, a developing county. We also sought to test the independent prognostic significance of other early available clinical risk indicators after adjustment for Troponin Status.

Methods

Study design: This was a single center, prospective, observational, follow-up study conducted at The Aga Khan University Hospital, a tertiary care referral center. All consecutive patients admitted to coronary care and step down units between November 1, 1997 and October 31, 1998 with the diagnosis of acute coronary syndrome (ACS) without ST-segment elevations were screened for eligibility. ACS was defined as typical resting chest pain symptoms or sudden acute respiratory distress suggestive of coronary insufficiency. A dynamic ST deviation on electrocardiogram was considered supportive but not mandatory for inclusion. Diagnosis of NSTEMI was later confirmed by total

creatinine kinase (CK) greater than twice-upper limits of normal or an elevated CK-MB fraction.

Patient Selection: During the study period 350 consecutive patients with acute coronary syndrome without ST-Segment elevations were screened for eligibility. Exclusion criteria included significant renal impairment defined as serum creatinine greater than 2.0 mg/dl (n=36), left bundle branch block (n=24), cardiogenic shock (n=3), revascularization either percutaneous or surgical in last six months (n=5), recent myocardial infarction in last two months (n=4), acute coronary syndrome precipitated by secondary causes like anemia (n=8) and Non cardiac chest pain on subsequent evaluation during hospital stay (n=15). After exclusion, 255 patients were found eligible for inclusion.

Troponin-T Assay: All patients had a baseline TnT estimation at presentation and repeated, in case of an initial negative result, at least 12 hours from onset of symptoms. Strips manufactured by Roche for specific detection of cardiac TnT through quantitative immunological tests were used. This test contains two monoclonal antibodies specific for cardiac TnT: one gold-labeled, the other biotinylated. Test strips were analyzed by using optical system of cardiac reader provided by Roche. The quantitative range for cardiac TnT detection extends from 0.1ng/ml to 2ng/ml. The reader interprets TnT concentration below or above this range qualitatively (low or high respectively). The cutoff used in our study for positive TnT assay was 0.1ng/ml.

End Points: Follow-up information was collected by telephone contact and review of medical records, with a mean follow-up of 13 $\pm$ 6 months (33 days to 30 months). The prospectively determined primary end point was a composite of all cause mortality and non-fatal Myocardial Infarction at long-term follow-up.

Statistical Analysis: Data was analyzed using Statistical software SPSS Version 10.0. Descriptive data will be expressed as mean$\pm$SD for variables with normal distribution and median with range for all other variables. Chi-square test was done for categorical variables to assess differences among baseline clinical features, while student's t test for continuous variables. Overall survival and event free survival were computed according to the Kaplan-Meier method. Comparison of survival between subgroups was performed by the log-rank test. Independent determinants of prognosis were identified by multivariate Cox-regression proportional hazard model using all-important biological variables and variables with a p value less than 0.2 by univariate analysis. A difference in log likelihood was used to test significance of added variables. Statistical significance would be inferred at a two-tailed p value <0.05.

Results

From the initial 255 patients selected for study, follow-up was available in 233 (91.4%). Follow up was available in 92.7% of patients with positive Troponin-T assay and 90.3% of patients with negative Troponin-T test, signifying no differential loss to follow up. There were more males (p=0.03) and smokers (p=0.002) among patients with positive TnT as compared to those with negative TnT (Table 1). Rest of the baseline characteristics were equally distributed between the two groups. Significantly higher proportions of patients with negative TnT were talking either beta-blockers or Calcium antagonists at the time of index cardiac event (Table 1).

Table 1. Baseline characteristics according to Troponin-T status.

	Positive troponin-T (n=102)	Negative troponin-T (n=131)	P value
Age (yrs)	62 $\pm$ 11	61 $\pm$ 11	NS
Male	64 (62.7%)	63 (48.1%)	0.03
Coronary risks:			
Diabetes[1]	57 (55.9%)	64 (48.9%)	NS
Hypertension	51 (50.0%)	79 (60.3%)	NS
Elevated Cholesterol	53 (52.0%)	69 (52.7%)	NS
Current smokers[2]	20 (19.6%)	18 (13.7%)	NS
Ever Smoked[3]	44 (43.1%)	31 (23.7%)	0.002
Family History of CAD	24 (23.5%)	38 (29.0%)	NS
History of:			
Exertional angina	70 (68.6%)	95 (72.5%)	NS
Prior MI	27 (26.5%)	44 (33.6%)	NS
Prior PTCA	2 (2.0%)	3 (2.3%)	NS
Prior CABG	6 (5.9%)	12 (9.2%)	NS
Previous stroke	3 (2.9%)	8 (6.1%)	NS
CHF	7 (6.9%)	8 (6.1%)	NS
Medications at presentation:	n = 86	n = 100	
Aspirin	49 (57.0%)	67 (67.0%)	NS
Beta-blockers	24 (27.9%)	42 (42.0%)	0.04
Calcium antagonists	25 (29.1%)	53 (53.0%)	0.001
ACE-I	24 (27.9%)	31 (31.0%)	NS
Diuretics	16 (18.6%)	19 (19.0%)	NS
Lipid lowering	11 (12.8%)	17 (17.0%)	NS

Data are expressed as mean $\pm$ SD or number (%) of patients. NS > 0.05.

MI=Myocardial Infarction, PTCA=percutaneous transluminal coronary angioplasty.

CABG = Coronary artery bypass grafting, CHF=Congestive Heart Failure, CAD = Coronary artery disease.

ACE-I = Angiotensin converting enzyme inhibitor.

1. Diabetes is defined as history of diabetes, need for oral hypoglycemic agents or insulin or fasting blood glucose of greater than 126 mg/dl.

2. Current smoker is defined as smoking within one month of presentation.
3. Ever smoked means any prior history of smoking.

Table 2. Clinical presentation and hospital course.

	Positive troponin-T (n=102)	Negative Troponin-T (n=131)	P value
Pulse (b/min)	97 ± 24	88 ± 21	0.004
SBP (mm Hg)	133 ± 27	143 ± 26	0.003
DBP (mm Hg)	82 ± 18	84 ± 14	NS
ST depressions ω	43 (42.2%)	18 (13.7%)	<0.001
Non-ST-elevation MI ψ	58 (56.9%)	13 (9.9%)	<0.001
LVEF (%)ϕ	48 ± 15	58 ± 12	<0.001
CCU stay (days)	2.2	1.4	<0.001
Hospital stay (days)	6.5	4.2	<0.001
Readmission CCU/CSDUΦ	6 (5.9%)	1 (0.8%)	0.04
In-hospital evaluation			
Echocardiogram	62 (60.8%)	53 (40.5%)	0.002
ETT	12 (11.8%)	25 (19.2%)	NS
Angiogram	28 (27.5%)	12 (9.2%)	<0.001
In-hospital outcome			
Death	3 (2.9%)	-	0.08*
Reinfarction	1 (1.0%)	-	NS
PTCA	3 (2.9%)	1 (0.8%)	NS
CABG	-	1 (0.8%)	NS
Stroke	2 (2.0%)	1 (0.8%)	NS
CHF	45 (44.1%)	18 (13.7%)	<0.001
Recurrent angina	30 (29.4%)	26 (19.8%)	0.09
Arrhythmia	9 (8.8%)	4 (3.1%)	0.05
In hospital medications			
Aspirin	102 (100%)	129 (8.5%)	NS
Heparin	97 (95%)	125 (95.4%)	NS
Beta-blockers	59 (57.8%)	94 (71.8%)	0.02
Calcium antagonists	38 (37.3%)	52 (39.7%)	NS
Nitrates	100 (98.0%)	130 (99.2%)	NS
ACE-I	58 (56.9%)	52 (39.7%)	0.009
Lipid lowering	46 (45.1%)	57 (43.5%)	NS
Anticoagulants	7 (6.9%)	3 (2.3%)	NS
Anti-arrhythmic	6 (5.9%)	4 (3.1%)	NS

NS > 0.05. * P value according to Fisher's exact test.

SBP=Systolic blood pressure, DBP=Diastolic blood pressure, ETT=Exercise tolerance test,

PTCA= percutaneous transluminal coronary angioplasty,

CABG=Coronary artery bypass grafting, CHF=Congestive Heart Failure, ACE-I=Angiotensin converting enzyme inhibitor.

ω Dynamic ST depression of greater than 0.5 mm.

ψ Non-ST-elevation MI based on conventional CPK >twice upper limit of normal or CK-MB. 6.0 ng/ml, irrespective of Troponin status. See text for details.

Φ Defined as patients requiring repeat visit to coronary care unit (CCU) or coronary step down unit (CSDU) in same index hospitalization.

ϕ LVEF=Left ventricular ejection fraction (%), data available for 62 patients with positive TnT and 53 with negative TnT.

Patients with positive TnT had significantly higher pulse rate at presentation (p=0.004) higher proportion had dynamic ST depressions ($p < 0.01$) and comparatively lower left ventricular ejection fraction ($p<0.001$). Patient with positive TnT also required longer stay at Coronary Care or step down units ($p < 0.001$) and more frequent need for repeat visits to Coronary Care or step down units during same hospitalization (Table 2).

Patients with positive TnT had significantly higher incidence of heart failure ($p < 0.001$) during hospital stay, a trend toward higher incidence of recurrent angina (p=0.09) and arrhythmia requiring treatment (p=0.05). Three patients died during hospital stay, all with evidence of Troponin leak (Table 2). Among patients with negative TnT, 13 had evidence of NSTEMI based on conventional criteria of two-fold or greater rise of total CK or CK-MB greater than upper limits of normal (Table-II). However none of these patients had any adverse outcome, including death, myocardial infarction or need for revascularization, on long-term follow-up (data not shown).

In the 30-day follow-up no patient with negative TnT died. Higher incidence of heart failure and recurrent angina was observed among patients with positive TnT (Table 3) along with higher need for repeat hospitalization for cardiac reasons.

Table 3. Short term (30-day) clinical outcome.

	Positive troponin-T (n = 102)	Negative troponin-T (n =131)	P value
Death	3 (2.9%)	-	0.08*
Reinfarction	4 (3.9%)	1 (0.8%)	NS*
Angiogram	15 (14.9%)	5 (3.8%)	0.003
PTCA	6 (5.9%)	3 (2.3%)	NS*
CABG	2 (2.0%)	1 (0.8%)	NS*
Stroke	3 (2.9%)	1 (0.8%)	NS*
CHF	16 (15.8%)	7 (5.3%)	0.008
Recurrent angina	55 (54.5%)	40 (30.5%)	<0.001
Cardiac hospitalizations	15 (14.7%)	9 (6.9%)	0.05

* P value according to Fisher's exact test. NS > 0.05

PTCA = percutaneous transluminal coronary angioplasty

CABG = Coronary artery bypass grafting

CHF = Congestive heart failure.

Overall survival was significantly reduced in patients with positive TnT. By Kaplan-Meier analysis (Figure 1) survival probability at 18 months for patients with negative TnT was 93.6% vs. 75.1% for those with

Table 4. Cox regression by univariate analysis for predictors of Death or Non-Fatal Myocardial Infarction on Long Term Follow-up.

Variable	HR	95% CI for HR	P value
Age (yrs) *	1.05	1.02 - 1.08	0.001
Diabetes	1.79	0.87 - 3.60	0.1
Males	1.23	0.64 - 2.40	0.5
Hypertension	0.66	0.34 - 1.29	0.2
Smoking history	1.49	0.76 - 2.92	0.2
Elevated Cholesterol	0.50	0.25 - 0.99	0.04
Prior MI	1.91	0.99 - 3.68	0.05
Prior CHF	4.21	1.74 - 10.12	0.001
Beta Blockers use =	0.62	0.29 - 1.29	0.2
Calcium Antagonists use =	0.96	0.49 - 1.89	0.9
Lipid lowering therapy ω	0.49	0.24 - 1.01	0.05
Beta-Blockers use ω	0.58	0.30 - 1.10	0.1
ACE- Inhibitorsω	1.88	0.96 - 3.67	0.07
Pulse (per minute) *	1.02	1.01 - 1.03	< 0.001
SBP (mm Hg) *	0.99	0.97 - 1.00	0.05
ST-Depression ψ	2.05	1.05 - 4.02	0.03
Positive Troponin ϕ	4.04	1.95 - 8.38	< 0.001
Peak CK (IU/L) *	1.01	1.00 - 1.00	< 0.001
LVEF π (%) *	0.94	0.91 - 0.97	< 0.001

NS > 0.05

* Continuous variables, Hazard ratios are for per unit increase.

CHF=Congestive Heart Failure, SBP=Systolic blood pressure.

ω Use during hospital stay and / or at discharge.

ψ Dynamic ST depression of greater than 0.5 mm.

= Medication in use by patients at presentation.

π LVEF=Left ventricular ejection fraction (%), data available for 115 patients.

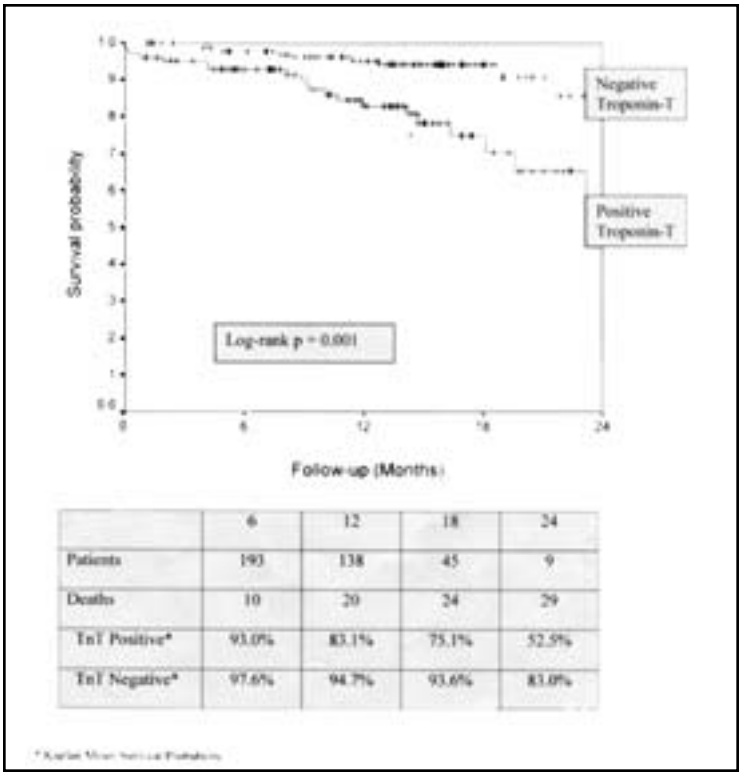
ϕ Troponin - T ≥ 0.1ng/ml

positive TnT (p=0.001). The incidence of composite end

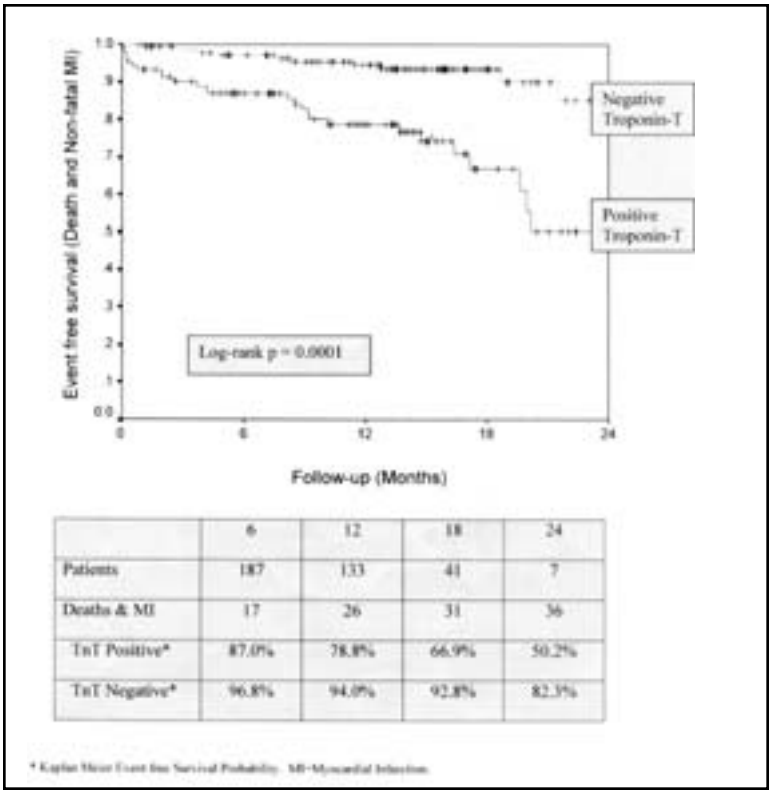
Table 5. Multivariate Cox-Regression Proportional hazard analysis for predictors of long-term mortality and non-fatal myocardial infarction.

	HR	95% CI for HR	P value
Positive Troponin T =	2.96	1.34 - 6.56	0.007
Age (yrs) *	1.05	1.02 - 1.08	0.002
History of CHF	6.17	2.40 - 15.87	< 0.001
Peak CK (IU/L) *	1.00	1.00 - 1.001	0.002

* Hazard ratio's are for per unit increase.
= Troponin - T > 0.1ng/ml



	6	12	18	24
Patients	193	138	45	9
Deaths	10	20	24	29
TnT Positive*	93.0%	83.1%	75.1%	52.5%
TnT Negative*	97.6%	94.7%	93.6%	83.0%



	6	12	18	24
Patients	187	133	41	7
Deaths & MI	17	26	31	36
TnT Positive*	87.0%	78.8%	66.9%	50.2%
TnT Negative*	96.8%	94.0%	92.8%	82.3%

point of death and non-fatal MI (Figure-2) was significantly low in patients with negative TnT 7.2% vs. 33.1% among those with positive TnT (p< 0.001).

Age, previous history of CHF, pulse rate at presentation, positive TnT, peak CK and a low LVEF had strong positive association with primary composite outcome by univariate analysis (Table 4). Prior MI, systolic blood pressure at presentation and ST-depression were also positively associated with subsequent death and non-fatal MI, whereas elevated cholesterol and use of lipid lowering therapy (mostly statins) showed negative association. High association was observed between elevated cholesterol and subsequent use of lipid lowering therapy (p<0.001) explaining the probable cause of observed protective effect of elevated cholesterol on univariate analysis. Similar associations were observed between history of CHF and use of Angiotensin converting enzyme Inhibitors (p<0.001). Strong linear correlation was observed between pulse rate at presentation and systolic blood pressure at presentation (p = 0.005). All variables with p<0.2 and gender being clinically important, were entered into multivariate analysis by Cox regression proportional hazard analysis using time to death or non-fatal MI as dependant variable. Independent predictors for primary outcome by multivariate analysis are listed in Table 5. Low LVEF, although strongly associated with primary outcome on univariate testing was not used for multivariate analysis because information was missing in significant proportion of patients.

Discussion

This study confirms that the presence of myocardial damage identified by elevation of TnT is a strong prognostic indicator in patients with unstable acute coronary syndromes. Elevation of TnT ≥0.1mg/ml was associated with a 3.5 fold increase in the relative risk of death and non-fatal MI at one year (Figure 2). The curve starts to diverge very early in first 30 days, with no death observed among patients with negative TnT, however the difference was not statistically significant due to small number of events (Table 3). The curves continue to separate with time, with relative risk increasing to 4.5 fold at 18 months between the groups (Figure 2). These results are in accordance with the previously reported cohorts.[3-9] Similar results have recently been reported from India showing significantly worse in hospital outcome among those patients with an initial TnT leak at admission.[11]

Troponin-T has been used in emergency rooms for triage of patient with acute chest pain.[13] It has also been shown to have independent prognostic value in patients without ischemic electrocardiographic changes, a subset otherwise believed to have low-prevalence of coronary artery disease and good prognosis.[14] In our study ischemic ST-depression, were not identified as an independent predictor. Previous reports have shown that ST segment depression in patients with acute myocardial infarction was associated with increased short-term mortality[15], however reports on long-term survival are conflicting.[15-17] The multi-cent Diltiazem post infarction trial research group showed approximately doub one-year mortality in patients with ST segment depression with or without waves[17] and ST segment depression as an independent predictor of mortali over 4-years of follow-up period[17], whereas others have failed to demonstra such effects on long term survival.[15]

CHF (HR 6.17; 95% CI 2.4-15.8, <0.001) and age (HR 1.05; 95% C 1.02-1.08; p = 0.002) were identified as an independent risk predictor (Tab 5) in our group. These findings are consistent with most of the previous reported studies.[18,19] The excess relative mortality associated with CHF h previously been reported to be associated with every age strata and absolu excess mortality most pronounced in the elderly than in young.[18] LVEF w found to be a powerful predictor of subsequent adverse outcome in our stud on univariate analysis, however due to substantial amount of missing data o LVEF, we were not able to test in multivariate analysis, one of the major lim itation of our study. Previous reports have clearly shown LVEF to be a stron independent predictor, and its interaction with transient or persistent CHF h also been reported.[19]

Positive TnT was an independent predictor in our study (Table 5). It estimated that approximately 30% of patients who present with rest pa without ST-segment elevation and would otherwise be diagnosed as havin unstable angina because of a lack of CK-MB elevation actually have non-S elevation myocardial infarction when assessed with cardiac specific Tropon assay.[20, 21] Case reports exists that confirm histological evidence of foc myocyte necrosis or micro infarction in patient with elevated cardia Troponin levels and normal CK-MB or CK values indicating that myocardi necrosis can be recognized with increased sensitivity.[22,23] Myocardial infar tion has recently been redefined, incorporating rise of Troponin as one of th diagnostic criteria for acute MI.[24]

Peak CK was also an independent predictor in our study (Table 5 Both early and late peak CK has been described as a marker of successf reperfusion with myocardial salvage in patients with acute ST segment elev tion myocardial infarction receiving thrombolytic therapy[25,26], predictin favorable long-term clinical outcome. However, prognostic value of peak-C in patients with NSTEMI has not been frequently studied. Peak CK has als been reported as predictor of in hospital CHF with subsequent increase adverse cardiac events on late follow-up.[27]

Gender was not identified to be associated with subsequent clinic outcome. Based on previous studies, estimates of the relative risk of woma as opposed to men have varied from unity to as high as 1.5.[28-31] Since the di ease occurs average 10 years later in women and because women have a hig er incidence of other risk factors and co-morbid features-particularly hype tension, diabetes and obesity - it is difficult to assess the effect of female ge der per se.[32] A report from China has suggested higher short-term mortali in women after myocardial infarction even after adjustment for age, hyperte sion and other associated co-morbid, however 10-year cumulative mortali was not significantly different between both genders.[33]

Pulse rate at presentation was significantly associated with subseque death and myocardial infarction on univariate analysis. Pulse rate was als highly correlated with age (p=0.001) and associated with prior history CHF (p< 0.001). When entered with model containing age and CHF, pul

It has been recognized for several decades that diabetic patients have a two to three fold increased risk for cardiovascular disease compared with their non-diabetic counterparts. Prevalence of diabetes mellitus in cohorts with acute coronary syndrome reported from west, ranges from 11-27%[34-36], whereas the proportion of diabetes in our cohort was 51.9%, further raising the concerns of alarming epidemic of diabetes in Asia.[37,38] In our study diabetes was not identified as predictor of death or MI at long-term follow-up. This is in contrast to most previous reports suggesting diabetes as an independent predictor of subsequent mortality after unstable angina and non-Q-wave myocardial infarction.[39,40] However a report from Sweden suggest that although overall one year mortality rate was higher among diabetes with MI, adjusted multivariate analysis failed to show diabetes as predictor of death or reinfarction.[41]

References

1. Olatidoye AG, Wu AH, Feng FJ, et al. Prognostic role of Troponin-T versus Troponin-I in unstable angina pectoris for cardiac events with meta-analysis comparing published studies. Am J Cardiol 1998;81:1405-10.
2. Van Domburg RT, Cobbaert C, Kimman GJ, et al. Long term prognostic value of serial Troponin T bedside tests in patients with acute coronary syndromes. Am J. Cardiol 2000;86:623-7.
3. Hamm CW, Ravkilde J, Gerhardt W, et al. The prognostic value of serum Troponin-T in unstable angina. N Eng J Med 1992;327:146-50.
4. Pertijohn TL, Doyle T, Spiekerman AM, et al. Usefulness of positive Troponin-T and negative creatine kinase levels in identifying high-risk patients with unstable angina pectoris. Am J Cardiol 1997;80:510-11.
5. Lindahl B, Venge P, Wallentin L. Relation between Troponin-T and the risk of subsequent cardiac events in unstable coronary artery disease. The FRISC study group. Circulation 1996;93:1651-7.
6. Stubbs P, Collinson P, Mosetey D, et al. Prospective study of the role of cardiac Troponin T in patients admitted with unstable angina. BMJ 1996;313:262-64.
7. Luscher MS, Thygesen K, Ravkilde J, et al. Applicability of cardiac Troponin T and I for early risk stratification in unstable coronary artery disease: TRIM study group. thrombin inhibition in myocardial ischemia. Circulation 1997; 96:2578-85.
8. Antman EM, Sacks DB, Rifai N, et al. Time to positivity of a rapid bedside assay for cardiac specific Troponin T predicts prognosis in acute coronary syndromes: thrombolysis in myocardial infarction (TIMI 11A) sub study. J Am Coll Cardiol 1998; 31:326-30.
9. Ohman EM, Armstrong PW, Christenson RH, et al. Cardiac Troponin T levels for risk stratification in acute myocardial ischemia. GUSTO IIA Investigators. N Engl J Med 1996; 335:1333-41.
10. Hawkins RC, Tan HL. Comparison of the diagnostic utility of CK, CK-MB (activity and mass), Troponin T and Troponin I in patients with suspected acute myocardial infarction. Singapore Med J 1999;40::680-4.
11. Kane GR, Keshavamurthy CB, Sethi RB, et al. Troponin-T in unstable angina - a clinical and angiographic study. J Assoc Physicians India 2000;48:1074-7.
12. Leowattana W, Mahanonde N, Bhuripanyo K, et al. Serum cardiac Troponin-T in unstable angina pectoris patients. J Med Assoc Thai 2000;83 (Suppl 2):S61-5.
13. Hamm CW, Goldmann BU, Heeschen C, et al. Emergency room triage of patient with acute chest pain by means of rapid testing for cardiac Troponin T or Troponin I. N Eng J Med 1997; 337:1648-53.
14. Christopher RF, Tocchi M, Parmer RJ, et al. Cardiac Troponin T in chest pain unit patients without ischemic electrocardiographic changes: angiographic correlates and long-term clinical outcomes. J Am Coll Cardiol 2000;35:1827-34.
15. Miller WL, Sgura FA, Kopecky SL, et al. Characteristics of presenting electrocardiograms of acute myocardial infarction from a community based population predict short and long-term mortality. Am J Cardiol 2001;87:1045-50.
16. Lim LL, Kinlay S, Fisher JD, et al. Can ECG changes predict the long term outcome in patients admitted to hospital for suspected acute myocardial infarction? Cardiology 1997;88:460-7.
17. Krone RJ, Greenberg H, Dwyer EM, et al. Long-term prognostic significance of ST-segment depression during acute myocardial infarction. The Multicenter Diltiazem Post Infarction Trial Research group. J Am Coll Cardiol 1993;22:361-7.
18. Kober L, Torp-Pederson C, Ottesen M, et al. Influence of age on the prognostic importance of left ventricular dysfunction and congestive heart failure on long-term survival after acute myocardial infarction. TRACE Study Group. Am J Cardiol 1996;78:158-62.
19. Kober L, Torp-Pederson C, Pederson OD, et al. Importance of congestive heart failure and interaction of congestive heart failure and left ventricular systolic function on prognosis in patients with acute myocardial infarction. Am J Cardiol 1996;78:1124-8.
20. ACC/AHA Guidelines for the management of patients with unstable angina and non-ST-Segment elevation myocardial infarction. J Am Coll Cardiol 2000;36:970-1062.
21. Heeschen C, Hamm CW, Bruemmer JS, et al. ML for the CAPTURE investigators. Predictive value of C-reactive protein and troponin-T in patients with unstable angina: A Comparative Analysis. J Am Coll Cardiol 2000;35:1535-42.
22. Antman EM, Grudzien C, Mitcheu RN, et al. Detection of unsuspected myocardial necrosis by rapid bedside assay for cardiac troponin T. Am Heart J 1997;133:596-8.
23. Apple FS, Falahati A, Paulsen PR, et al. Improved detection of minor ischemic myocardial injury with measurement of serum cardiac Troponin I. Clin Chem 1997;43:2047-51.
24. Alpert JS, Thygesenn K, Antman E, et al. Myocardial infarction redefined - a consensus document of the Joint European Society of Cardiology / American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000;36:959-69.
25. Corbalan R, Prieto JC, Chavez E, et al. Bedside markers of coronary artery patency and short-term prognosis of patients with acute myocardial infarction and thrombolysis. Am Heart J 1999;138:533-9.
26. Kosuge M, Kimura K, Ishikiwa T, et al. Early peak Creatine Kinase activity is not always a marker of successful reperfusion with myocardial salvage in patients with reperfused anterior myocardial infarction. Am Heart J 2001;141:759-64.
27. Ali AS, Rybicki BA, Alam M, et al. Clinical predictors of heart failure in patients with first acute myocardial infarction. Am Heart J 1999;138:1133-9.
28. Vaccarino V, Krumholz HM, Berkman LF, et al. Sex differences in mortality after myocardial infarction: Is there evidence for an increased risk for women? Circulation 1995;91:1861-71.
29. Tofler GH, Stone PH, Muller JE, et al. Effects of gender and race on prognosis after myocardial infarction: Adverse prognosis for women, particularly black women. J Am Coll Cardiol 1987;9:473-82.
30. Dittrich H, Gilpin E, Nicod P, et al. Acute myocardial infarction in women: influence of gender on mortality and prognostic variables. Am J Cardiol 1988;62:1-7.
31. Jenkins JS, Flaker GC, Nolte B, et al. Causes of higher in hospital mortality in women than in men after acute myocardial infarction. Am J Cardiol 1994;73:319-22.
32. Alexandar RW, Schlant RC, Fuster V, et al. The heart, arteries and veins, 9th ed. New York; McGraw-Hill:1998, pp. 1127-28.
33. He J, Klag MJ, Whelton PK, et al. Short and long-term prognosis after acute myocardial infarction in Chinese men and women. Am J Epidemiol 1994;139:693-703.
34. Armstrong PW, Fu Y, Chang WC, et al. Acute Coronary Syndromes in the Gusto-IIb Trial. Circulation 1998;98:1860-8.
35. Frank VA, Liwa TY, Bernard RC, et al. Early and 1-year clinical outcome of patients evolving Non-'Q'-wave versus Q wave myocardial infarction after thrombolytics. Results from the TIMI-II study. Circulation 1995;91:2541-8.
36. Mihai G, Paui R, Steven B, et al. Decline in the rate of hospital mortality from acute myocardial infarction. Impact of changing management strategies. Am Heart J 1996;131:250-56.
37. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. Diabet Med 1997;14(Suppl 5):S1-85.
38. Hameed K, Kadir M, Gibson T, et al. The frequency of known diabetes, hypertension and ischemic heart disease in affluent and poor urban populations of Karachi, Pakistan. Diabet Med 1995;12:500-3.
39. Jacoby RM, Nesto RW. Acute myocardial infarction in the diabetic patient: Pathophysiology, clinical course and prognosis. J. Am Coll Cardiol 1992;20:736-44.
40. Malmberg K, Yusuf S, Gerstein HC, et al. Impact of diabetes on long term prognosis in patients with Unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for IschemiMc Syndromes) Registry. Circulation 2000;102:1014-9.
41. Karlson BW, Herlitz J, Hjalmarson A. Prognosis of acute myocardial infarction in diabetic and non-diabetic patients. Diabet Med 1993;10:449-54.