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# Baseline CRP and Cardiac Troponin I Predict Outcomes of Intravenous Thrombolysis and Primary PCI in Patients with St-Segment Elevation Myocardial Infarction

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**Abstract**

**Introduction:** To study the effects of baseline cardiac troponin I and C - reactive protein levels in patients admitted with STEMI on outcomes of intravenous thrombolysis and primary PCI

**Methods:** Prospective observational study with 102 consecutive patients admitted with ST segment elevation myocardial infarction who received either intravenous thrombolysis or who underwent primary PCI. Plasma levels of CRP and cardiac troponin I was done in all patients at admission. The main outcome measures were ST-segment resolution 90 mints after thrombolysis initiation or following primary coronary angioplasty and 30-day cardiac mortality.

**Results:** Patients in the top tertiles of CRP and cTnI had a significantly lower incidence of complete ST-segment resolution compared to the lowest tertiles (third versus first i.e. 9.1% *vs.* 79.4% p<0.001) (cTnI third *vs.* first 11.8%) *vs.* 58.8% p<0.001), lower Thrombolysis in Myocardial Infarction (TIMI)3 flow in the infarct related artery (CRP tertiles : Third *vs.* first p <0.001) (cTnI tertiles : Third *vs.* first p=0.003), more compromised LV function and more incidence of multivessel CAD ( cTnI tertiles third *vs.* first p 0.02). There were more deaths in the highest tertiles of CRP and cTnI) (4 *vs.* 2 in 3$^{rd}$ *vs.* 1st tertile of CRP and 5 *vs.* 1in 3$^{rd}$ *vs.* 1$^{st}$ tertile of cTnI).

**Conclusions:** High levels of circulating CRP and cTnI at admission were associated with increased risk of intravenous thrombolysis and primary coronary angioplasty failures with increased 30-day cardiac mortality.

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## Introduction

Rapid and adequate reperfusion of jeopardized myocardium constitutes the only effective treatment in patients with ST-Segment Elevation Myocardial Infarction (STEMI) [1-3]. Early recanalization of the infarction-related artery results in the preservation of left ventricular systolic performance and subsequently in more favourable short- and long-term prognosis. Although primary percutaneous coronary angioplasty represents the preferable reperfusion strategy in patients with ST-Segment Elevation Myocardial Infarction (STEMI), intravenous thrombolysis remains the more frequently used therapy in this setting [4-6]. Although the benefits of intravenous thrombolysis are unequivocal, reperfusion fails in a significant proportion of patients, portending an adverse short and long-term prognosis [1].

The need to identify the predictors of failed thrombolysis is essential in clinical practice but is challenging. Besides well-established adverse effects of pre-hospital delay [6], several clinical, biochemical markers, and angiographic characteristics of lesions have been related to intravenous thrombolysis failure and prognosis [7-10].

The increasing role of inflammation has been brought into focus in the pathogenesis of atherosclerosis [11]. The focus is on identification of inflammatory markers, which could be easily detected and could contribute to the risk stratification in patients with coronary artery disease. C - reactive protein is a sensitive and nonspecific cytokine dependent marker of inflammation that has been implicated in adverse outcomes and in increased ischemic events in the first year after a myocardial infarction [12]. Elevated levels of CRP at admission have been implicated in poor response to thrombolysis and with worse short and long-term prognosis in patients with ST elevation myocardial infarction [12-14]. Elevated cardiac troponin I and troponin T at admission have been also found to be predictors of failed thrombolysis and increased 30 day cardiac mortality after a myocardial infarction [9,14].

Elevated cTnI levels on admission have been found to be associated with adverse outcomes of primary angioplasty in acute myocardial infarction [15].

The aim of the present study was to prospectively investigate the possible effects of elevated levels of both cTnI and CRP in an Indian cohort presenting with acute ST elevation myocardial infarction.

## Methods

102 consecutive patients with STEMI who were admitted to St Johns Medical College and Hospital Bangalore were included in the study. The inclusion criteria were (1) continuous angina chest pain of ≥30 minutes duration present on admission, which was refractory to nitrates, (2) ST-segment elevation ≥2 mm in ≥2 contiguous precordial leads, or 1 mm in ≥2 contiguous limb leads, and (3) no contraindications to intravenous thrombolysis if considered for thrombolysis. Exclusion criteria were (1) left bundle branch block (2) active infection or chronic inflammatory disease, (3) significant prior hepatic or renal dysfunction, (4) malignancy, (5) history of coronary bypass grafting surgery, or (6) Myocardial infarction or percutaneous coronary intervention in the last 6 months.

### Analysis of study biomarkers

On patient admission, venous blood samples were obtained before the intravenous administration of drugs. The samples were analysed at NABL (National Accreditation Board for Laboratories) accredited laboratory of St John's Medical College and Hospital. Plasma samples were analysed within one hour of sample collection. The analysis of plasma CRP was performed by use of Particle Enhanced Turbido Immunometric Assay (PETIA) (Siemens diagnostics Ltd) covering a range from 0.01 to 60 mg/dL. For values below the limit of detection, the lower limit value was used for statistical analysis. Cardiac specific troponin was analysed using Chemi Luminesence Immuno Assay (CLIA) (Beckman Coulter)

The higher normal limit of CRP for healthy non-pregnant adults was 0.33mg/dL.

The higher normal limit of cTnI for healthy adults was 0.04 ng/ml.

### Treatment

The thrombolytic agent used was either streptokinase or fibrin specific agent Tenecteplase (TNK). Patients who consented to PCI or had contraindications to thrombolysis were taken up for primary PCI with DES implantation. Chewable aspirin was given in a dose of 325 mg on admission and 150 mg daily was continued indefinitely. Clopidogrel loading dose of 300 mg was given at admission to all patients and they were continued on 75 mg per day for 1 year. Patients who underwent Primary PCI received 75 mg bd for 1 week and then 75 mg od. Heparin was given in a bolus dosage of 4000 units IV on admission, followed by enoxaparin subcutaneously according to body weight 12 h for a minimum of 5 days.

### Complete ST-segment resolution and electrocardiographic analysis

Complete ST-segment resolution was defined as a ≥70% reduction of the sum of ST-segment elevation [15] between the electrocardiogram on admission in the coronary care unit and the electrocardiogram 90 mints after thrombolysis initiation or post PCI as predefined by means of the protocol. All electrocardiograms were analyzed as pairs by 2 experienced cardiologists who were blinded to the patient data. The sum of ST-segment elevation was measured 20 ms after the end of the QRS complex in leads I, aVL, and $V_1$ to $V_6$ for anterior, and leads II, III, aVF, and $V_5$, $V_6$ for non-anterior MI [12]. For patients undergoing primary PCI electrocardiogram was taken post angioplasty on shifting to the CCU.

### Cardiac Catheterization, TIMI Flow and LVEF

Cardiac catheterizations were performed in patients who gave consent for the same via the femoral or radial approach as per patient preference. In patients, undergoing Primary PCI catheterization was performed on admission. Flow in the culprit arteries was graded according to the TIMI criteria [16]. TIMI flow was estimated by 2 experienced and independent angiographers who were blinded to the study. LVEF values were calculated by the 2 observers on echocardiography on day 3 using Simpsons method [17].

### Clinical follow-up

In-hospital and post discharge follow-up data were prospectively collected on predesigned case report forms. Before discharge, all patients were advised about smoking cessation, body weight reduction, regular exercise, and lipid monitoring. After discharge, patients were followed-up at 30 days on an out-

patient basis or by means of telephone interview. Cardiac death was the pre-specified primary end point. Cardiac death was considered to be any incidence of sudden unexplained death, death caused by fatal MI, and death after re-hospitalization because of heart failure or possible acute myocardial ischemia [18].

### Statistical analysis

Descriptive statistics were expressed as the mean ± SD for normally distributed variables and as the median with 25$^{th}$ and 75$^{th}$ percentiles for non-normally distributed variables. Comparisons of ST response among CRP and cTnI tertiles were made using Analysis of Variance (ANOVA) or the Kruskal-Wallis test, as appropriate. The Bonferroni in ANOVA or Mann-Whitney U test was used, as appropriate, for pair wise comparisons of continuous variables between tertiles. Associations between 2 categorical variables were tested by means of the $\chi^2$ or Fisher exact tests, as appropriate. Nonparametric Spearman's rank correlation was used for correlations between non-normally distributed variables. ANCOVA was used to compare the ST response between the CRP and cTnI tertiles adjusting for the window period as the window period was a significant confounder. P value < 5% was considered as significant. SPSS (version 18) was used for all statistical analysis.

## Results

Two hundred patients with STEMI were screened out of which 102 were recruited for the study. Patients were excluded due to late presentation beyond 12 hours without ongoing ischemia, contraindications to thrombolysis, lack of consent for Primary PCI, LBBB on ECG, chronic inflammatory conditions like rheumatoid arthritis, cancer, recent PCI in last 6 months, chronic kidney or liver disease.

### Baseline characteristics

The mean age of the study population was 54.34 ± 13.5 years (range 22-87 years). There were 85 men (83.3%) and 17 women (16.7%). Mean CRP values at admission 0.87±1.73 mg/dl. Most values were <3 as patients with chronic inflammatory states were excluded. However, one patient had an extreme value of 12.8 which was excluded in analysis where mean was required. Mean cardiac troponin I values on admission were 1.43 ± 3.49 ng/ml (range 0.01- 19.0)

The mean interval between the times of onset of pain to hospital presentation was 4.2 ± 3.19 h. (Range 20 mints -16 h).

The median door to needle time was 30 mints. The mean door to balloon time for Primary Angioplasty was 80 mints. There was no statistically significant difference between these times in various tertiles of CRP and cTnI

Prior history of hypertension was present in 47.05% of patients and a history of diabetes mellitus was present in 38.23% of patients.

50 patients i.e. 49% of the study population sustained an anterior wall STEMI. 12 patients i.e. 11.8% had suffered a previous myocardial infarction but none had undergone prior CABG or PCI. Prior stable angina was present in 10 (9.8%) of patients. There was no significant difference in the baseline characteristics in the CRP and TROP I tertiles except for the window period, which showed a statistically significant, difference (**Table 1 and 2**). The higher tertiles of trop I and CRP had a longer time delay prior to hospital presentation. This difference was accounted for in the final analysis. The mean total WBC count was 11,611 ± 3,974. There was no statistically significant difference in the total WBC count between various tertiles.

**Table 1:** Comparison of Baseline Data among Tertiles of CRP.

| Variables | CRP Tert 1 | CRP Tert 2 | CRP Tert 3 | P Value |
|---|---|---|---|---|
| CRP (tertiles)mg/dl | 0-0.05 (N=34) | 0.0501-0.58 (N=34) | >0.58 (N=33) | - |
| AGE (yrs) | 58.4 ± 14.4 | 51 ± 11.4 | 52.8±13.6 | 0.06 |
| MALE's n (%) | 30 (88.2) | 27 (79.4) | 27 (81.8) | 0.6 |
| BMI kg/m² | 25.6 ± 4.18 | 26.5±3.35 | 27.13 ± 4.14 | 0.29 |
| DM n (%) | 13 (38.2) | 11 (32.4) | 15 (45.5) | 0.54 |
| HT n (%) | 17 (50) | 14 (41.2) | 16 (48.5) | 0.73 |
| SMOKING n (%) | 13 (38.2) | 20 (58.8) | 12 (36.4) | 0.12 |
| OLD MI n (%) | 4 (11.8) | 4 (11.8) | 4 (12.1) | 0.999 |
| DLP | 31 (91.2) | 29 (85.3) | 25 (75.8) | 0.21 |
| F/H/ CAD | 5 (14.7) | 4 (11.8) | 4 (12.1) | 0.92 |
| ANT WALL MI n (%) | 16 (32.7) | 18 (36.7) | 15 (30.6) | 0.81 |
| WP | 3.62 ± 3.44 | 3.82 ± 2.49 | 5.47±3.6 | 0.043 |
| D-N time mins mean±SD | 27.8 ± 16.9 | 32.6±11.6 | 32.7 ± 11.2 | 0.32 |
| D-B time mins mean±SD | 76.25 ± 30.28 | 82.50 ± 37.7 | 83.3±12.1 | 0.45 |
| KILLIPS CLASS 2-4 n (%) | 15 (44.1) | 17 (50) | 17 (48.4) | 0.12 |
| CARDIOGENIC SHOCK n (%) | 6 (17.6) | 4 (12.1) | 7 (21.2) | 0.61 |

n: No of Patient; (%): Percentage of Patients; Values are given as MEAN±SD; BMI: Body Mass Index; MI: Myocardial Infarction; F/H/CAD: Family History of Coronary Artery Disease; WP: Window Period.

**Table 2:** Comparison of Baseline Data among Tertiles of Troponin I.

| Variables | TROPI Tert 1 | TROP I Tert 2 | TROP I Tert 3 | P Value |
|---|---|---|---|---|
| TROP I (tertiles)ng/ml | 0-0.04 (N=34) | 0.0401-0.45 (N=34) | >0.45 (N=34) | - |
| AGE(yrs) | 55.29 ± 14.0 | 55.32 ± 14.9 | 52.41 ± 11.8 | 0.6 |
| MALES n (%) | 29 (85.3) | 30 (88.2) | 26 (76.5) | 0.39 |
| BMI kg/m² | 24.6 ± 3.8 | 27.68 ± 3.7 | 26.8 ± 3.6 | 0.003 |
| DM n (%) | 11 (32.4) | 14 (41.2) | 12 (35.39) | 0.68 |
| HT n (%) | 15 (44.1) | 16 (47.1) | 17 (50.0) | 0.89 |
| SMOKING n (%) | 19 (55.9) | 14 41.2) | 12 (35.39) | 0.21 |
| OLD MI n (%) | 3 (8.8) | 6 (17.6) | 3 (8.8) | 0.42 |
| DLP | 31 (91.2) | 27 (79.4) | 27 (79.4) | 0.32 |
| F/H/ CAD | 6 (17.6) | 4 (11.8) | 3 (8.8) | 0.53 |
| ANT WALL MI n (%) | 15 (30) | 17 (34) | 18 (36) | 0.76 |
| D-N time mins mean±SD | 30.1 ± 1.2 | 38.1 ± 18.2 | 30.6 ± 9.6 | 0.28 |
| D-B time mins mean±SD | 75 ± 29.7 | 83±7 | 75.5 ± 27 | 0.85 |
| WP | 2.27 ± 1.24 | 4.42±3.5 | 6.3 ± 3.2 | <0.01 |
| KILLIPS CLASS 2-4 n (%) | 13 (38.2) | 16 (47) | 20 (58.8) | 0.38 |
| CARDIOGENIC SHOCK n (%) | 4 (11.8) | 7 (21.2) | 6 (17.6) | 0.57 |

n: No of Patient; (%): Percentage of Patients; Values are given as MEAN±SD; BMI: Body Mass Index; MI: Myocardial Infarction; F/H/CAD: Family History of Coronary Artery Disease; WP: Window Period.

### Complete ST Segment Resolution in CRP and Trop I Tertiles

62 patients (60.78%) had successful thrombolysis defined as ≥50% ST segment resolution at 90 minutes. Complete ST segment resolution was seen in 35 (34.31%) of patients. Tertiles of CRP and cardiac troponin I were associated with the non-invasive indices of myocardial reperfusion by means of univariate analysis (**Table 3 and 4**). In particular, there was a significant gradual decrease in the chance of complete ST-segment resolution with an increase in tertiles of both CRP AND cTnI.

**Table 3:** Comparison of Invasive and Noninvasive Indices of Reperfusion in the CRP Tertiles.

| VARIABLES | CRP Tert 1 | CRP Tert 2 | CRP Tert 3 | P Value |
|---|---|---|---|---|
| CRP (tertiles)mg/dl | 0-0.05 (N=34) | 0.0501-0.58 (N=34) | >0.58 (N=33) | - |
| ∑ ST1-elevation in mm | 18.7 ± 20.5 (13) | 12.42 ± 10.07 (10) | 12.42 ± 10.1 (13.68) | 0.10 |
| ∑ sT2-elevation in mm | 3.91 ± 5.57 (2.25) | 5.04 ± 3.65 (4.25) | 9.57 ± 6.04 (8.0) | <0.001 |
| Patients with >70 % ST resolution n (%) | 27 (79.4) | 5 (14.7) | 3 (9.1) | <0.001a, 0.48b, <0.001c |
| Patients with 30-69%% ST resolution n (%) | 7 (20.6) | 27 (79.4) | 15 (45.5) | - |
| Patients with <30% ST resolution n (%) | 0 (0) | 2 (5.9) | 15 (45.5) | - |
| LVEF | 47.7 ± 10.2 | 48.2 ± 8.4 | 46.9 ± 9.6 | 0.79 |
| NONINVASIVE | | | | |
| DAYS TO CAG | 2.04 ± 0.9 | 2.70 ± 1.7 | 3.1 ± 5.6 | 0.55 |
| TIMI 3 FLOW n (%) | 19 (51.4) | 11 (29.7) | 7 (18.9) | <0.01 |
| Multivessel CAD | 16 (38%) | 12 (28.6%) | 14 (33.3%) | 0.07 |

a: p Value for Comparison Between 1st and 3rd Tertile; b: p Value for Comparison Between 2nd and 3rd Tertile; c: p Value for Comparison Between 1st and 2nd Tertile.

**Table 4:** Comparisons of Invasive and Noninvasive Indices of Reperfusion in the Trop I Tertiles.

| Variables | TROP I Tert1 | TROP I Tert 2 | TROP I Tert3 | P Value |
|---|---|---|---|---|
| TROP I (tertiles)ng/ml | 0-0.04 (N=34) | 0.0401-0.45 (N=34) | >0.45 (N=34) | - |
| ∑ ST1-elevation in mm mean ± SD (median) | 14.91 ± 11.3 (11.0) | 16.05 ± 11.41 (13.5) | 17.33 ± 21.5 (12) | 0.44 |
| ∑ sT2-elevation in mm | 3.65 ± 3.69 (2.5) | 6.23 ± 5.28 (4.0) | 8.93 ± 6.8 (7.0) | <0.001 |
| Patients with >70 % ST resolution n (%) | 20 (58.8) | 11 (32.4) | 4 (11.8) | <0.001a, 0.95b, 0.02c |

| | | | | |
|---|---|---|---|---|
| Patients with 30-69%% ST resolution n (%) | 12 (35.3) | 19 (55.9) | 18 (52.9) | |
| Patients with <30% ST resolution n (%) | 2 (5.9) | 4 (11.8) | 12 (35.3) | |
| LVEF | 51.1 ± 8.7 | 46.0 ± 8.6 | 45.7 ± 10.1 | 0.03 |
| INVASIVE | | | | |
| DAYS TO CAG | 2.65 ± 1.69 | 2.95 ± 5.19 | 2.17 ± 1.13 | 0.76 |
| TIMI 3 FLOW n (%) | 19 (51.54) | 14 (37.8) | 4 (10.8) | 0.003 |
| Multivessel CAD | 14 (33.3) | 18 (42.9) | 10 (23.8) | 0.02 |

a: p Value for Comparison Between 1st and 3rd Tertile; b: p Value for Comparison Between 2nd and 3rd Tertile; c: p Value for Comparison Between 1st and 2nd Tertile.

27 out of the 34 patients(79.4%) in the lowest tertile of CRP had >70% resolution of the ST segment compared to 3 (9.1%) patients in the highest tertile. 20 out of the 34 patients (58.8%) in the lowest tertile of cTnI had >70% resolution of the ST segment compared to 4 patients (11.8%) patients in the highest tertile The p value was especially statistically significant between tertiles 3 and 1 (<0.001) of both CRP and cTnI, and this remained statistically significant even in the multivariate ancova analysis after adjusting for the window period (**Table 5 and 6**).

The statically significant difference was irrespective of whether the patients had undergone thrombolysis with fibrin specific agent, streptokinase or primary angioplasty.

The Left Ventricular Ejection Fraction was higher in patients in the first tertile of CRP 47.7 ± 10.2% versus lower tertile 46.9 ± 9.6% (p value 0.79). Between the cTnI tertiles, there was significantly higher LVEF in the lowest tertiles 51.1 ± 8.7 % in first tertile versus 45.7 ± 10.1% (p value 0.03) (**Table 7**).

**Table 5:** Adjustment for Window Period.

| Variables | CRP Tert 1 | CRP Tert 2 | CRP Tert 3 | P Value |
|---|---|---|---|---|
| CRP (tertiles) | 0-0.05 (N=34) | 0.0501-0.58 (N=34) | >0.58 (N=33) | - |
| ST SEGMENT RESOLUTION % (MEAN ± SD) | 78.19 ± 14.77A | 58.39 ± 18.35B | 36.06 ± 21.45 | <0.001 |
| Variables | TROP Tert 1 | TROP Tert 2 | TROP Tert 3 | P Value |
| TROP I (tertiles) | 0-0.04 (N=34) | 0.0401-0.45 (N=34) | >0.45 (N=34) | - |
| MEAN ST SEGMENT RESOLUTION % | 72.69 ± 23.88A | 59.62 ± 20.37B | 39.57 ± 20.58 | <0.001 |

A: Ancova Analysis done for Adjustment for Window Period with p<0.001 between Tertile 1 and 2.
B: Ancova Analysis done for Adjustment for Window Period with p<0.001 between Tertile 2and 3.

**Table 6:** 30 Day Mortality in the CRP Tertiles.

| Variables | CRP Tert 1 | CRP Tert 2 | CRP Tert 3 | P Value |
|---|---|---|---|---|
| CRP (tertiles) | 0-0.05 (N=34) | 0.0501-0.58 (N=34) | >0.58 (N=33) | - |
| 30 DAY MORTALITY | 2 (25%) | 2 (25%) | 4 (50%) | NS |

**Table 7:** 30 Day Mortality in the Trop I Tertiles.

| Variables | TROP Tert 1 | TROP Tert 2 | TROP Tert 3 | P Value |
|---|---|---|---|---|
| TROP I (tertiles) | 0-0.04 (N=34) | 0.0401-0.45 (N=34) | >0.45 (N=34) | - |
| 30 DAY MORTALITY | 1 (12.5%) | 2 (25%) | 5 (62.5%) | NS |

**Invasive Data and Tertiles of Trop I and CRP**

Coronary angiography was done in 65 patients. Of these 18 were patients who underwent primary angioplasty. There was no significant difference in the time to CAG in any of the tertiles (median 2.5 days). Of the 65 patients, 37 patients had TIMI 3 flow on CAG post thrombolysis or post angioplasty.

19 (51.4%) of patients with TIMI 3 flow were in the lowest tertile of CRP compared to only 7 (18.9%) in the highest tertile (p value- 0.006).

In the Trop I tertiles 19(51.4%) of patients with TIMI 3 flow were in the lowest tertile while only 4(10.8%) were in the highest tertile (p value- 0.003)

Mutivessel CAD was also seen in higher frequency in the higher tertiles of CRP and Trop I. However, the p value was statistically significant only between the highest and lowest cTnI tertiles.

**In-hospital complications and 30-day cardiac mortality**

4 patients expired prior to discharge and a total of 8 patients died within 30 days. The 30-day cardiac mortality was 7.84%. No mortality was seen among the patients who underwent primary angioplasty. 50% of these deaths were seen in the highest tertile of CRP. Among the Trop I tertiles 65% of deaths occurred in the highest tertile. However, as the mortality rate was low no statistically significant difference could be arrived at.

CCF was seen in a higher proportion of patients in the 3rd tertile of CRP compared to the first tertile 17 patients (37.8%) versus 12 patients (26.7%) p value 0.3. A similar trend was seen among patients in the higher 20 (43.5%) versus lowest 12 (26.1%) of patients p value 0.12

Cardiogenic shock also occurred in a higher proportion of patients in the highest tertiles of Trop I and CRP however the difference was not statistically significant (**Table 8 and 9**). The incidence of cardiac arrhythmias was however not significantly differently different between the 3 groups.

**Table 8:** Comparison Of In Hospital Complications in the CRP Tertiles.

| Variables | CRP Tert 1 | CRP Tert 2 | CRP Tert 3 | P Value |
|---|---|---|---|---|
| CRP (tertiles) | 0-0.05 (N=34) | 0.0501-0.58 (N=34) | >0.58 (N=33) | - |
| CCF | 12 (26.7%) | 16 (35.60%) | 17 (37.8%) | 0.3 |
| CARDIOGENIC SHOCK | 6 (35.3%) | 4 (23.5%) | 7 (41.2%) | 0.61 |
| ARRYTHMIAS | 10 (31.3%) | 10 (31.3%) | 12 (37.5%) | 0.72 |

**Table 9:** Comparison Of In hospital Complications in the Trop I Tertiles.

| Variables | TROP Tert 1 | TROP Tert 2 | TROP Tert 3 | P Value |
|---|---|---|---|---|
| TROP I (tertiles) | 0-0.04 (N=34) | 0.0401-0.45 (N=34) | >0.45 (N=34) | - |
| CCF | 12 (26.1%) | 14 (30.4%) | 20 (43.5%) | 0.12 |
| CARDIOGENIC SHOCK | 4 (23.5%) | 7 (41.2%) | 6 (35.3%) | 0.57 |
| ARRYTHMIAS | 13 (40.6%) | 12 (41.2%) | 6 (35.3%) | 0.57 |

## Discussion

The primary finding of this study is that elevated plasma CRP and cardiac troponin I levels on hospital admission in patients with STEMI are strongly associated with thrombolysis failure. This relationship remains significant even after adjustment for the window period. There is also an increase in the incidence of adverse cardiac events and 30-day hospital mortality although the numbers were not large enough to reach statistical significance.

Many prospective studies have been conducted to evaluate the role of CRP in the prognosis of patients with stable or unstable coronary syndromes [10,12,18,19]. There is however, paucity of data about a possible association of plasma CRP levels on admission with response to thrombolysis.

Tanasijevic et al [7] and Stewart et al [8] have shown that an elevated cTn (I or T) circulating level on presentation was inversely related rate of TIMI (Thrombolysis in Myocardial Infarction) 3 flow in coronary angiography at 60 and 90 mints, respectively. Stubbs et al [9] have shown that an elevated circulating level of cTnT on presentation was a negative predictor of the presence of the noninvasive signs of reperfusion. Alban Dibra et al [20]. Found that CRP levels on admission may predict the efficacy of reperfusion in patients with AMI and that the predictive ability is dependent on the form of reperfusion therapy.

Zairis et al [13] found that plasma levels of CRP on admission might be a predictor of reperfusion failure and of worse short and long-term prognosis in patients with ST elevation myocardial infarction.

Sg Foussas et al [14] found that high circulating levels of both cardiac troponin I and hs-CRP are related with an independent increased risk of intravenous thrombolysis failure and increased 30-day cardiac death in patients who receive intravenous thrombolysis in the first 6 hours of STEMI. This study was done in Greece. However, no such study has been done in the Indian population.

The possible relationship of plasma CRP levels with short- and long-term prognosis in patients with acute MI has been investigated and a positive association has been reported in all the studies.

Gheno et al [19], who studied 205 consecutive elderly women without thrombolysis, have reported that a high plasma CRP on admission was independently and positively related to in hospital mortality Tomoda et al [21] have found that elevated CRP levels in the first 6 hours of acute MI were positively associated with more in hospital adverse outcome, including cardiac death after primary percutaneous coronary intervention.

Pietilä et al [22] have demonstrated a gradual inverse relationship between peak plasma levels of CRP, estimated during the first days of STEMI, and the 24-month survival probability. In Pietilä's study, CRP measurements were made late in the course of MI, and subsequently, CRP values were significantly influenced by the extent of intercurrent myocardial necrosis.

In this study blood, sampling was done on admission and hence were not significantly different in the anterior and non-anterior wall MI groups, however a longer prehospital delay was significantly associated with higher CRP and cTnI levels at admission. However, in spite of adjusting for this error CRP and cTnI levels significantly predicted poor outcomes of thrombolysis.

Although the exact pathophysiological mechanisms for the present results are not completely known, it has been speculated that elevated circulating levels of cTnI or CRP may reflect the presence of an infarct related thrombus more resistant to either fibrinolytic or primary coronary angioplasty [23,24].

Elevated cTnI on admission appears to be an independent marker of an early and extensive myocardial damage, which in turn is associated with an increased risk of primary angioplasty failure and a more complicated clinical course [24]. This more resistant thrombus and greater microvascular damage [7,8,9,14] as observed in the present study may account for the

failure of intravenous thrombolysis or primary angioplasty and increased in hospital complications and 30 day mortality.

**Clinical implications**

Our results have demonstrated that a high CRP and cTnI value before the start of intravenous thrombolysis is strongly associated with reperfusion failure, as measured by means of ST-segment resolution, TIMI 3 flow, or LVEF and short term cardiac mortality. The additional information derived from combined cTnI and CRP measurements was independent of the other studied clinical variables, with possible influence in risk stratification and treatment of patients with STEMI. Patients with elevated CRP and cTnI levels on admission may need special attention for the identification of thrombolysis failure and possibly the appropriate adjustment of treatment.

**Limitations of the study**

Although the study was designed to study possible association of CRP and cTnI there was no random allocation of several therapies like thrombolytic or PCI. The more sensitive hs-CRP was not used in the study due to cost considerations and technical difficulties. The study patients had not undergone catheterization immediately after the administration of intravenous thrombolysis. Therefore, the estimated TIMI grades do not represent the flow in the infarction-related artery early after thrombolysis administration. However, complete ST-segment resolution is a reliable predictor of myocardial reperfusion and is well related to TIMI 3 flow in the infarction-related artery after thrombolysis [25,26].

Permanent ST-segment elevation and impaired TIMI flow in the infarction-related artery may accompany previous MI. Therefore, our results might have been influenced by the inclusion of such patients. However, no significant differences were observed for the prevalence of previous MI among the CRP and cTnI tertiles. A more accurate estimation of LVEF after dissolution of acute phase of myocardial stunning and with a more appropriate method like radionuclide angiography may have altered the predictive value of this parameter.

The cardiac mortality in the study and the adverse cardiac events in hospital were not in numbers significant enough to reach any statistically significant conclusion, hence longer duration and continuation of the study is proposed.

## Conclusions

The results of the present study indicate that high levels of circulating CRP and cTnI at admission are associated with increased risk of failure of intravenous thrombolysis and primary coronary angioplasty and increased 30-day cardiac mortality. The present study suggests that combined use of biomarkers may help in better risk stratification of patients presenting with ST elevation myocardial infarction in first 12 hours and may thus be a surrogate marker for worse prognosis prompting more aggressive treatment strategies in such patients.

## References


1. CH Davies, OJM Ormerod. Failed coronary thrombolysis. The Lancet. 1998; 351: 1191- 1196.
2. The GUSTO Angiographic Investigators. The effect of tissue plasminogen activator, streptokinase, or both on coronary-artery patency, ventricular function, and survival, after acute myocardial infarction. N Engl J Med. 1993; 329: 311-322.
3. Van't Hof AW, Liem A, de Boer MJ, Zijlstra F. Clinical value of 12-lead electrocardiogram after successful reperfusion therapy for acute myocardial infarction. Lancet. 1997; 350: 615-619.
4. ACC/AHA guidelines for the management of patients with ST-Elevation. J. Am. Coll. Cardiol. 2004;44;671-719
5. ACCACC/AHA guidelines for the management of patients with ST-Elevation/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction-Executive Summary Circulation. 2004; 110: 588-636.
6. 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) Thomas J. Ryan, Elliott M. J. Am. Coll. Cardiol. 1999; 34; 890-911.
7. Myoglobin, creatine-kinase-MB and cardiac troponin-I 60-minute ratios predict infarct-related artery patency after thrombolysis for acute myocardial infarction: Results from the Thrombolysis in Myocardial Infarction Study (TIMI) 10B Milenko J. Tanasijevic, Christopher P J. Am. Coll. Cardiol. 1999; 34: 739-747.
8. T Stewart, JK French, Théroux P, Ramanathan K, Solymoss BC, Early noninvasive identification of failed reperfusion after intravenous thrombolytic therapy in acute myocardial infarction. J. Am. Coll. Cardiol. 1998; 31: 1499-1505.
9. Peter Stubbs, Paul Collinson, David Moseley, Trevor Greenwood, Mark Noble. Prognostic Significance of Admission Troponin T Concentrations in Patients with Myocardial Infarction Circulation. 1996; 94: 1291-1297.
10. C-reactive protein is a potent predictor of mortality independently of and in combination with troponin T in acute coronary syndromes: A TIMI 11A sub study. Thrombolysis in Myocardial Infarction. J. Am. Coll. Cardiol. 1998; 31: 1460-1465.
11. Ross R. Atherosclerosis-an inflammatory disease. N Engl J Med. 1999; 340: 115-126.
12. C-Reactive protein levels on admission are associated with response to thrombolysis and prognosis after ST-segment elevation acute myocardial infarction American Heart Journal. 2002: 144.
13. C-reactive protein as a marker for cardiac ischemic events in the year after a first, uncomplicated myocardial infarction American Journal of Cardiology. 1999; 83: 1595-1599.
14. SG Foussas, MN Zairis, SS Makrygiannis, SJ Manousakis, FA Anastassiadis, et al. The significance of circulating levels of both cardiac troponin I and high-sensitivity C reactive protein for the prediction of intravenous thrombolysis outcome in patients with ST-segment elevation myocardial infarction. Heart. 2007; 93: 952-956.
15. Schroder R, Wegscheider K, Schroder K, Rüdiger Dissmann, Wolfgang Meyer-Sabellek. Extent of early ST elevation resolution: a strong predictor of outcome in patients with acute myocardial infarction and a sensitive measure to compare thrombolytic regimens. J Am Coll Cardiol. 1995; 26: 1657-1664.
16. Chesebro JH, Knatterud G, Roberts R, J Borer, LS Cohen, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial, phase 1: A comparison between intravenous tissue plasminogen activator and intravenous streptokinase: Clinical findings through hospital discharge. Circulation. 1987; 76: 142-154.
17. Evaluation of systolic function of left Ventricle-Feigenbaum's Echocardiography, seventh edition. 123-157.

18. Danesh J, Whincup P, Walker M, L Lennon, A Thomson, et al. Low-grade inflammation and coronary heart disease: prospective study and updated meta-analyses. BMJ. 2000; 321: 199-204.

19. Gheno G, Libardoni M, Zeppellini R, F Cucchini. C-reactive protein as a predictor of in-hospital death in the elderly with acute myocardial infarction. Cardiologia. 1999; 44: 1023 - 1028.

20. Predictive value of basal C-reactive protein levels for myocardial salvage in patients with acute myocardial infarction is dependent on the type of reperfusion treatment Alban Dibra, Julinda Mehilli, Markus Schwaiger. European Heart Journal. 2003; 24: 1128-1133.

21. Tomoda H, Aoki N. Prognostic value of C-reactive protein levels within six hours after the onset of acute myocardial infarction. Am Heart J. 2000; 140: 324-328.

22. KO Pietila, AP Harmoinen, J Jokiniitty, AI Pasternack. Serum C-reactive protein concentration in acute myocardial infarction and its relationship to mortality during 24 months of follow-up in patients under thrombolytic treatment. European Heart Journal. 1996; 17: 1345-1349.

23. Nikfardjam M, Mullner M, Schreiber W, E Oschatz, M Exner, et al. The association between C-reactive protein on admission and mortality in patients with acute myocardial infarction. J Intern Med. 2000; 247: 341-345.

24. Shlomo Matetzky, Tali Sharir, Michelle Domingo, Marko Noc, Kuang-Yuh Chyu, et al. Elevated Troponin I Level on Admission Is Associated With Adverse Outcome of Primary Angioplasty in Acute Myocardial Infarction. Circulation. 2000; 102: 1611-1616.

25. Topol E. Acute myocardial infarction: thrombolysis. Heart. 2000; 83: 122-126.

26. de Lemos JA. ST-Segment resolution as a marker of epicardial and myocardial reperfusion after thrombolysis: Insights from the TIMI 14 and in TIME-II trials. J Electrocardiol. 2000; 33: 67-72.