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ORIGINAL ARTICLE

Association between Plasma Procalcitonin with Onset of MACE, in Patients with Acute ST elevated MI: An Unicentric Prospective Observational Comparative Study

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Abstract:

Background: *Cardiovascular diseases (CVDs) pose a significant global health threat, with South Asia, including Bangladesh, experiencing a substantial burden. Procalcitonin (PCT), a marker associated with bacterial infections and inflammatory responses, has been studied for its potential correlation with acute myocardial infarction (AMI). However, its role in predicting major adverse cardiac and cerebrovascular events (MACCE) in ST-segment elevation myocardial infarction (STEMI) remains underexplored in the Bangladeshi population.*

Methodology: *This prospective observational study, conducted at the Department of Cardiology, BSMMU, aimed to investigate the prognostic significance of PCT in 54 STEMI patients within a one-month follow-up period. Enrollment criteria included admission within 12 hours of symptom onset. PCT levels were measured using chemiluminescence immunoassay (CLIA) technology. Comprehensive demographic, clinical, and diagnostic data were collected, and statistical analyses were performed, including univariate and multivariate logistic regression.*

Results: *The study observed a significant association between high admission PCT levels and MACCE. In the high PCT group, 7 out of 27 patients experienced MACCE, compared to 3 out of 27 in the low PCT group ($p = 0.038$). Univariate and multivariate logistic regression analyses revealed elevated PCT as an independent predictor of MACCE (OR: 4.541, 95% CI: 2.119–6.521; AOR: 3.475, 95% CI: 1.962–5.546).*

Discussion: *This study establishes the predictive role of procalcitonin in MACCE following STEMI. Elevated PCT levels on admission independently correlate with a heightened MACCE risk, showcasing its potential as a prognostic biomarker. The study's observed MACCE rate of 18.5% within 30 days aligns with regional data, emphasizing the challenges in timely revascularization procedures. Correlations with Troponin and C-reactive protein emphasize the inflammatory response's role in adverse outcomes, contributing valuable insights for risk stratification in STEMI patients.*

Conclusion: *This study contributes valuable insights into the prognostic significance of elevated PCT levels in predicting MACCE in STEMI patients. The independent association between high admission PCT and adverse outcomes suggests its potential as a prognostic biomarker. These findings emphasize the importance of PCT in risk stratification and decision-making for STEMI management in the Bangladeshi population.*

Keywords: *Procalcitonin, ST-segment elevation myocardial infarction, Major Adverse Cardiac and Cerebrovascular Events, Bangladesh*

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Introduction:

Cardiovascular diseases (CVDs) represent a leading cause of premature mortality globally. It contributes to 17.7 million deaths annually which is anticipated to rise to 23.6 million by 2030.[1] Although some developed countries have observed a decline in mortality from cardiovascular diseases

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in recent times, developing countries are still facing an escalating burden.[2] In South Asia, ischemic heart disease is the leading cause of mortality. It accounts for 10.6% of total reported fatalities, equating to 1.8 million deaths, and contributes to more than half of cardiovascular mortality.[3] Despite this scenario, very little is known about the exact prevalence of coronary artery disease in Bangladesh. Recent data suggests that coronary artery disease prevalence ranges from 1.85% to 3.4% in rural areas and 19.6% in urban settings.[4] According to the Global Burden of Disease Study, as of 2020, the South Asian region, which includes India, Pakistan, Bangladesh, and Nepal, was projected to bear a disproportionate burden of atherothrombotic cardiovascular disease than any other region.[5]

Procalcitonin (PCT) is a 116-amino acid polypeptide precursor of calcitonin and is elevated in conditions associated with bacterial infections, such as sepsis[6] and post-cardiac surgery.[7] Given the inflammatory response accompanying acute myocardial infarction (AMI), multiple studies have explored the potential association between PCT levels and AMI severity and prognosis. While some studies found no clear association,[8] others demonstrated correlations between PCT release and established prognostic markers[9] as well as its elevation being associated with severe heart failure, resuscitated cardiac arrest, or concurrent bacterial infection.[10]

Subsequent research delved into the role of PCT in acute coronary syndrome (ACS) finding its notable associations with major adverse cardiac and cerebrovascular events (MACCE). Observational studies indicate significantly higher PCT levels in ACS patients being identified as a 'higher risk' group of ACS patients for short and long-term mortality and experiencing cardiogenic shock post-ST-elevation acute myocardial infarction (STEMI).[11] Moreover, prospective cohort studies highlight a nearly 50% higher relative risk of MACCE at 12 months post-myocardial infarction (MI) in individuals with elevated PCT levels, with a predominant association with patient mortality during follow-up.[12] Larger prospective studies further confirm elevated plasma PCT levels in patients experiencing MACCE, underscoring its potential prognostic value in ACS.[13]

There is a paucity of data regarding acute phase major adverse cardiac and cerebrovascular events (MACCE) following ST-segment elevation myocardial infarction (STEMI) in Bangladesh. A recent study at the National Institute of Cardiovascular Disease (NICVD), revealed that 6.2% of patients encountered an in-hospital adverse event, and 7.5% experienced events within the 30 days following discharge.[14] Another cross-sectional observational study also had similar findings where about 7.8% of the patients had MACCE events.[15]

However, the role of peripheral PCT concentration in predicting ST-segment elevation myocardial infarction (STEMI) prognosis in Bangladeshi individuals remains unexplored. Our study aims to examine the relationship between PCT levels at admission and clinical outcomes post-STEMI to get a more comprehensive understanding of PCT's prognostic significance. This study focuses on MACCE as the primary endpoint during a one-month follow-up, utilizing chemiluminescence immunoassay (CLIA) technology to measure PCT levels.

Materials and methods:

Study Design and Setting:

Our study was a prospective observational study that was conducted at the Department of Cardiology at BSMMU from October 2020 to September 2021 after receiving approval from the Institutional Review Board (IRB).

Sample size and population:

The sample size was predetermined to be 54 using an appropriate formula for comparative study. Enrollment involved STEMI patients who were admitted within the first 12 hours of symptom onset. STEMI was defined clinically as chest pain lasting >20 minutes, ECG evidence of ST elevation >1mm in >2 contiguous leads, or presumably new LBBB or true Posterior MI with ST depression of >1mm in >2 contiguous anterior leads V1-V3 with a positive terminal T wave. Posterior MI was further confirmed by concomitant ST-segment elevation ≥0.5 mm recorded in leads V7–V9.

Data collection:

The purpose of the study was thoroughly explained to each participant and informed written consent was obtained. Detailed demographic information, risk factors, and clinical history were recorded. Various diagnostic measures, including 12-lead ECG, Troponin I, CK-MB, serum creatinine, serum procalcitonin, HbA1c, and echocardiography, were conducted during the enrollment. Blood samples, collected aseptically, underwent biochemical investigations, including the measurement of procalcitonin using LIAISON BRAHMS PCT II GEN assay with chemiluminescence immunoassay (CLIA) technology. The study employed rigorous procedures to ensure data integrity and quality throughout the process.

Statistical analysis:

Statistical analyses of the study were planned and reviewed by the investigators and guide. Following data editing, statistical analysis was conducted using the Statistical Package for Social Science (SPSS) version 25.0 for

Windows. Numerical data were presented as mean with standard deviation (SD) and assessed using the Student's t-test. Categorical data were expressed as frequencies and percentages, and the Chi-Square test was employed for analysis. To identify independent predictors of Major Adverse Cerebrovascular Events (MACE), both univariate and multivariate logistic regression analyses were employed. A significance level of $p < 0.05$ was considered statistically significant.

Results:

Table-I

Distribution of MACCE according to admission PCT

MACCE Status	Group 1 (n=27) Low PCT	Group 2 (n=27) High PCT	P value
MACCE n(%)	24 (54.5)	20 (45.5)	0.038
Non MACCE n(%)	3 (30)	7 (70)	

Table-II

Association of plasma procalcitonin with the onset of MACCE through univariate & multivariate logistic regression analysis

	Univariate			Multivariate[b]		
	Odds Ratio	95% CI[a]	P value	Adjusted Odds Ratio	95% CI	P value
Age	1.171	0.874-2.745	0.762	1.065	0.649-1.928	0.819
Gender	0.723	0.308 - 1.837	0.981	0.638	0.482 - 1.742	0.762
BMI[a]	1.420	1.021-3.264	0.034	1.099	0.819-2.532	0.468
Smoker	2.180	0.949-3.146	0.485	1.843	0.842-2.946	0.655
HTN	1.923	0.824-2.860	0.357	1.645	0.698-2.510	0.467
DM	2.415	1.249-3.228	0.001	2.089	1.054-2.678	0.001
Dyslipidemia	3.142	1.098-5.024	0.001	2.564	0.956-4.662	0.068
Family History	1.185	0.894-2.210	0.339	0.841	0.688-1.658	0.384
Troponin I	0.292	0.081-1.829	0.519	0.189	0.041-1.015	0.954
Procalcitonin	4.541	2.119-6.521	0.001	3.475	1.962-5.546	0.001
LVEF[a]	3.689	1.056-4.969	0.026	2.958	1.01- 3.412	0.034
CRP[a]	1.902	0.873-3.021	0.398	1.428	0.592- 2.429	0.867

[a]CI: confidence interval; BMI: body mass index; DM: diabetes mellitus; LVEF: Left ventricular ejection fraction; CRP: C reactive protein

[b]Multivariable adjusted odds ratio were adjusted with rest of the other variables

Table-III

Adjusted odds ratio for MACCE considering Procalcitonin, Treatment Modalities, and STEMI Surface involvement

	95% CI			
	AOR	Lower	Upper	P value
Low PCT	1			
High PCT	2.608	1.337	7.674	0.001
Modalities				0.991
Thrombolysis	1			
Pharmacoinvasive	0.974	0.155	6.111	0.977
Routine PCI	0.736	0.118	4.615	0.744
Medical Management	0.024	0.001	1.054	0.999
Surface				0.949
Anterior	1			
Inferior	0.622	0.130	2.967	0.551
Lateral	0.384	0.114	1.214	0.954
Posterior	0.062	0.021	1.022	0.994

[a]AOR: adjusted odds ratio

[b]CI: confidence interval

In Table I, MACCE was evident in 3 patients in the low PCT group and 7 patients in the high PCT group, with a significant P-value of 0.038 from the chi-square test.

Table II shows that higher admission PCT levels pose a higher risk of MACCE (OR: 4.541, 95% CI: 2.119 – 6.521; AOR: 3.475, 95% CI: 1.962 - 5.546), indicating a 3.5 times increased risk per unit PCT increase. Confounders include age, sex, BMI, hypertension, dyslipidemia, smoking, family history, troponin-I, CRP, and reduced ejection fraction (LVEF<40%).

In Table III, higher admission PCT levels are seen associated with a higher risk of MACE (AOR: 2.608, 95% CI: 1.337-7.674), suggesting a 2.608 times increased risk per unit PCT increase. Confounders include treatment modalities and STEMI surface involvement.

Discussion:

In this study, we investigated the prognostic significance of procalcitonin (PCT) in patients with ST-segment elevation myocardial infarction (STEMI), focusing on its role as a predictive biomarker for major adverse cardiac and cerebrovascular events (MACCE). PCT, a recognized inflammatory marker is commonly associated with various infections and stress conditions. However, in recent times, it has shown dynamic changes in acute coronary syndrome (ACS). Several studies have reported elevated PCT levels as predictors of poor prognosis in ACS which prompted our exploration to contribute further evidence to this area.

Our study observed a notable association between procalcitonin (PCT) levels and major adverse cardiac and cerebrovascular events (MACCE) in ST-segment elevation myocardial infarction (STEMI) patients. In the low PCT group, MACCE occurred in 3 out of 10 patients, while in the high PCT group, MACCE occurred in 7 out of 44 patients. The chi-square test yielded a P value of 0.038, signifying a significant difference in MACCE incidence between the two PCT groups. Among the total 54 STEMI patients, 10 experienced MACCE, indicating an 18.5% occurrence rate. Comparisons with a large prospective study in China revealed a mean admission procalcitonin level of 1.4 µg/L, with higher MACCE incidence in the high PCT group (20%) compared to the low PCT group (15.5%).[16] These findings can be potentially explained by the longer follow-up duration in that study (12 months vs. 30 days). These results underscore the potential prognostic value of PCT in predicting MACCE in STEMI patients.

A previous study conducted at a prominent cardiac hospital in Bangladesh reported a 13% incidence of MACCE within 30 days post-discharge for patients admitted with STEMI[14]. This rate was comparatively lower than the 23% MACCE observed in another study in a rural setting.[16] Notably, none of the patients in our study underwent primary percutaneous coronary intervention (PCI). This instance is possibly related to delayed arrival at the hospital following prolonged symptom onset. The delay in revascularization procedures in Bangladesh, where a significant portion of healthcare expenses is borne out-of-pocket, underscores challenges in aligning with acute myocardial infarction treatment guidelines recommended by the European Society of Cardiology.[16]

Our multivariate logistic regression analysis, adjusted for confounders, demonstrated that high admission PCT levels independently increased the risk of MACCE (OR: 4.541, 95%CI: 2.119–6.521; AOR: 3.475, 95% CI: 1.962–5.546). This implies that for each unit increase in PCT, there is about a 3.553 times higher risk of MACCE. Our results are consistent with existing literature, such as a prospective cohort study showing a 50% higher relative risk of MACCE at 12 months post-MI with elevated PCT levels.

Our study calculated the mean admission PCT level, revealing it to be 1.35 µg/L, and established a linear correlation between plasma PCT and C-reactive protein (CRP) levels on admission. Higher levels of Troponin and CRP were found to be associated with an increased risk of MACCE. In addition, our study revealed a similar increasing trend of CRP and reported a linear correlation between plasma CRP level and plasma PCT level on admission. Our observation of PCT as an indicator of the inflammatory response severity in patients with coronary heart disease reflects the potential prognostic significance linked to inflammation.

To ensure the reliability of our conclusions in our study, we adhered to international diagnostic criteria for STEMI, maintained robust subject compliance during follow-up, and utilized a mature and reliable method for measuring PCT. In summary, our study contributes to the growing body of evidence supporting serum procalcitonin as a valuable biomarker for predicting MACCE in STEMI patients and highlights its potential clinical significance in risk stratification and management decisions.

Conclusion:

In conclusion, our study highlights a significant association between elevated serum procalcitonin (PCT) levels as an increased risk of major adverse cardiac and cerebrovascular events (MACCE). This underscores the potential independent predictive value of peripheral PCT

concentration for adverse outcomes in STEMI, emphasizing its relevance as a prognostic biomarker. These findings contribute to the understanding of risk stratification in STEMI patients and suggest the utility of serum PCT in predicting poor prognosis.

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