RESEARCH PAPER

Prognostic and Predictive Biomarkers in Patients Undergoing PCI: Comparative Evaluation in MACE and Non-MACE Patients

Minesh Patel[1*], Dr. Shyamalendu Tripathy[2]

[1]Research Scholar, Parul University, Vadodara, Gujarat 391760, India
[2]Associate Professor, School of Pharmacy, Parul University, Vadodara, Gujarat 391760, India
*[*]**Corresponding Author:** Minesh Patel*
Email: minesh.ad99@gmail.com
ORCID: 0000-0002-5793-7879

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ABSTRACT

Background: Percutaneous Coronary intervention (PCI) is commonly used in patients with coronary artery disease (CAD). However, Post PCI patients are found to have adverse events associated which are termed as MACE (Major adverse cardiac events). These events are seen either in a year of PCI or seen much later.

Aims: The research was aimed to perform a comparative analysis of various biomarkers in patients undergoing Percutaneous Coronary Intervention (PCI) with or without Major Adverse Cardiac Events (MACE)

Methods: A Prospective cohort study was carried out in Hospital, Gandhinagar, Gujarat, India. All the data was collected from the patients' IP and OP medical records from Hospitals and was recorded on the Case Report Form. The total number of samples was 500 with outpatient patients 250 and in patients- 250. Inclusion and exclusion criteria were followed to select the patients.

Results: Baseline biomarkers did not show any difference between MACE and non-MACE in pre PCI patients. All the markers showed no statistical significance. Baseline biomarkers did not significantly differ between MACE and non-MACE patients in post PCI. Among post-PCI biomarkers, only cTnI and TMAO demonstrated statistically significant differences between groups. However, neither biomarker independently predicted MACE after adjustment for demographic variables. The hypothesis was partially supported, indicating significant differences only in select post-PCI biomarkers.

Conclusion: The study found that selective biomarkers could be used for prediction of MACE events. However, these were marginally significant and when correlated with demographic variables had no significance. These markers could be used as complementary markers along with other methods for detection of MACE related events post PCI.

Keywords: Percutaneous Coronary Intervention; Biomarkers; Major Adverse Cardiovascular Events; Prognosis; Inflammation.

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I. INTRODUCTION

1.1 Clinical Context of PCI and the Need for Risk Stratification

Coronary Artery Disease (CAD) is the leading cause of mortality worldwide. CAD possesses a significant health risk globally. There has been an increasing trend in CAD related mortality worldwide in the last few decades [1-2]. Percutaneous coronary intervention (PCI) is a widely used method in patients suffering with CAD. The PCI technique utilizes a balloon to widen the narrowed blood vessels [3]. Though the core principle of PCI has not changed with the advances in digital technology there have been a lot of changes associated with imaging, therapy and device manufacturing that have resulted in preventing major adverse events [4-5]. A significant population of patients who undergo PCI suffer with Major adverse cardiac events (MACE). MACE or major adverse cardiovascular event/cardiac event is a cornerstone in cardiovascular research and trials. MACE is a complex endpoint which includes a wide spectrum of conditions such as non-fatal Myocardial Infarct (MI), non-fatal stroke, and death related. Revascularization, unstable angina and heart failure hospitalization also are included in MACE [6-7].

MACE is observed in these patients either in a few months to one year of PCI or may be observed very late after years of PCI [8]. Late onset of MACE is mostly associated with chronic disease progression and underlying changes that are associated with disease failure [9]. Thus, it is essential

**Author for Correspondence: minesh.ad99@gmail.com*

to do risk stratification while monitoring the post PCI patients for MACE. The risk stratification is dependent on several factors. One of the major factors is the levels of cardiac biomarkers which could help in assessing the severity of risk and subsequent protocol to be followed to prevent the adverse outcome.

1.2 Biomarkers in Cardiovascular Disease

There are different cardiac biomarkers that are considered to be elevated during stressful events. The most important markers that are indicative of cardiac injury include Troponins (cTnI, cTnT). The presence of these in serum is indicative of cardiac injury or necrosis. The use of highly sensitive detection methods for these is helpful in risk stratification and further planning of therapy in both acute and chronic settings. Heart-type fatty-acid binding protein (H-FABP) is another distinct marker which shows significant elevation within 3 hrs of cardiac injury. The markers are useful to evaluate the cardiac status in cases where troponin levels are not helpful for predicting the risk [11]. Natriuretic peptides such as B-type natriuretic peptide (BNP), N-terminal proBNP (NT-proBNP), and mid-regional pro-atrial natriuretic peptide (MR-proANP) are released into circulatory system when there is a stretch of ventricular wall or there are changes in pressure of the heart chambers. The levels of this correlate with the extent of severity of cardiac damage [12]. Another set of distinct markers for cardiovascular damage include High-sensitivity C-reactive protein (hs-CRP), and interleukins [12]. Apart from these well-established markers that are used for risk analysis and stratification other non-established biomarkers such as Trimethyl N- Oxide (TMAO), micro-RNA, specialized lipoproteins such as Lp-PLA_2 and oxidative stress related biomarkers such as GDF-15, pentraxin-3 are also considered for cardiac injury. However, these non-established markers need further validation and extensive research [13].

1.3 Rationale and Knowledge Gap

Patients who are undergoing PCI the management of MACE remains a clinical challenge that needs to be addressed. Due to the dynamic and complex nature of cardiovascular diseases it is essential to consider a nuanced approach for post PCI complications to reduce the morbidity and mortality. The use of proper tools to perform risk stratification and subsequent treatment is vital to reduce the post PCI complications [14]. One of the tools that has emerged in various studies include the use of biomarkers as a predictive framework for MACE in post PCI patients. Biomarkers are associated with the cardiac status and hence any changes would reflect the ongoing changes in the tissue helping in predicting the adverse outcomes. Their role is important and stretches beyond detection with help in prognosis and stratified approach to patient care [15]. In the context of PCI, the ability to predict MACE through biomarkers such as cardiac troponins, natriuretic peptides, inflammatory markers (like C-reactive protein), and novel markers like microRNAs, presents an opportunity for presumptive and targeted intervention [16].

II AIM OF THE STUDY

The research was aimed to perform a comparative analysis of various biomarkers in patients undergoing Percutaneous Coronary Intervention (PCI) with or without Major Adverse Cardiac Events (MACE).

III. OBJECTIVES OF THE STUDY

3.1 Research Objectives

This research is poised to fill critical knowledge gaps regarding the predictive and prognostic value of various biomarkers in patients undergoing PCI. By achieving its objectives, this study hopes to enhance the understanding of the underlying mechanisms that contribute to the success or failure of PCI procedures

Primary

- To Analysis of Various Biomarkers in Patients undergoing PCI with MACE
- Comparison of Various Biomarkers in Patients undergoing PCI with MACE with those without MACE

Secondary

- Outcome Analysis of Patients undergoing PCI with or without MACE
- Comparison of Various Biomarkers in Patients undergoing PCI with or without MACE with bassline
- Analysis of Risk Factors in Patients undergoing PCI with or without MACE

3.2 Research questions

1. What are the baseline levels of cardiac biomarkers, including but not limited to troponin, C-reactive protein (CRP), and brain natriuretic peptide (BNP), in patients undergoing PCI, and how do these levels correlate with the occurrence of MACE?
2. Does the occurrence of MACE post-PCI associate with specific changes in biomarker profiles when compared to patients without MACE, adjusting for confounders such as age, gender, comorbidities, and baseline cardiac function?
3. How do patient demographics and comorbidities modify the relationship between biomarker levels and the incidence of MACE post-PCI, and can personalized biomarker-guided strategies improve patient outcomes?

IV. HYPOTHESES

H1: Patients who develop MACE post-PCI have significantly different baseline and post-procedure biomarker profiles compared to those who do not develop MACE.

V. METHODS

Study design

Prospective cohort study

Source of Data: All the data will be collected from the patients' IP and OP medical records from Hospitals and will be recorded on the Case Report Form.

Related Approval: The approval will be taken from the Hospitals Ethics Committee.

Sample Description: The total number of samples is 500 with outpatient patients 250 and in patients- 250.

Selection Criteria

Inclusion Criteria

- **Age and Gender:** Patients aged 18 years or older, regardless of gender.
- **Clinical Diagnosis:** Patients diagnosed with coronary artery disease (CAD) and scheduled for Percutaneous Coronary Intervention (PCI).
- **Consent:** Patients who have given written informed consent to participate in the study.

  Biomarker Baseline: Patients with baseline measurements of biomarkers of interest prior to undergoing PCI.
- **Follow-Up Commitment:** Patients who are available for and commit to follow-up evaluations as specified by the study protocol.

Exclusion Criteria

- **Previous Major Cardiovascular Events:** Patients with a history of Major Adverse Cardiac Events (MACE) within six months prior to the study's enrollment period.
- **Concurrent Medical Conditions:** Patients with acute or chronic inflammatory diseases, severe liver or renal dysfunction, malignancy, or any medical condition that could interfere with the biomarker levels or impact the study's outcome.
- **Medication Use:** Patients currently using medications known to significantly impact biomarker levels unrelated to the study's pharmacotherapeutic intervention.
- **Pregnancy:** Pregnant or lactating women due to potential for needing different treatment protocols or the effects on pregnancy outcomes.
- **Prior Intervention:** Patients who have undergone a PCI or any coronary artery bypass graft (CABG) surgery within the last year, to eliminate effects of previous interventions on the study's biomarkers and outcomes.
- **Participation in Other Studies:** Patients currently participating in other clinical research that could influence the outcomes of this study.

METHODOLOGY

The enrollment of patients was done after approval from the ethics committee. Cases were selected based on inclusion and exclusion criteria. All the necessary information was collected from patient files. Face to face interviews were done with parents of subjects only if needed. Data collection was done based on Case report form.

Selection of Hospital/Clinic

Site selection was done based on the infrastructure, resources, staff experiences and patient population. The ethical, safety and adherence to regulations for performing various procedures was considered for selection of site as well. Patient demographic was enquired and the number of patients visiting hospital was checked. Based on the review of the hospital the site was selected.

Designing a Research Protocol, Informed Consent form and Case report form

Once the protocol was approved by the ethics committee, an informed consent form was prepared in three languages and its approval was subsequently applied. Case report forms were prepared and necessary data was extracted from the patient files.

Approaching the doctor at selected hospital site

Doctors who were interested in our study were contacted and protocol, informed consent and case report form were discussed. If they agreed for the work then they were enrolled as a part of the team and the necessary data was taken post the permission of the doctor and hospital.

Ethics committee submission (if required)

This was applied for and obtained from the hospital based on the guidelines and protocols wherever needed. All the ethical protocols were followed in accordance with the Declaration of Helsinki. The ethics approval number is 200800404003 and date is 18 November 2024

Data collection

A predefined case report form was prepared. Data was collected in case report form by referring to patients file based on the designed protocol and defined criteria. Cases were selected based on inclusion and exclusion criteria. The patient's demographic data, social data, clinical data, lab reports, biomarker level results, past medical history and Questionnaire related aspects were collected. Questionnaire based data was essential and based on face-to-face interview if needed.

Statistical Analysis

Descriptive stats calculations were done such as Mean, Standard deviation. Continuous variables were assessed using t-test or any other suitable test. Frequency related variables were analyzed by intra group comparison using Chi-square test. Statistical analysis was done using SPSS version 26. Data was presented in tabular form with outcomes and important data in the form of charts.

Feasibility issues

No special instruments or gadgets were required for the conduct of the study so it was carried out with minimum expenditure. After getting the patient's consent for

enrollment, the patient's medical records were checked, and the following information was updated in CR.

VI. RESULTS

Baseline Characteristics of the Study Cohort.

Gender distribution

In the current study predominant male patients were observed for percutaneous coronary intervention (PCI). Of the total 500 patients around, 67.4 percent were males and 32.6 percent were females. This gender distribution has been in line with the established epidemiological trends of coronary artery disease (CAD) in which men are more commonly afflicted and they normally appear at a younger age than women.

Age range and central tendency

The age of the sample used in the given research indicates that the predominant age group of patients that had undergone PCI. The age range was between 37 and 92 years, with a definite focus on 55-66 years. This trend is consistent with the natural history of coronary artery disease (CAD), which generally shows clinical expression in later decades of life as a result of the cumulative impact of atherosclerosis, endothelial dysfunction, and protracted exposure of the cardiovascular risk factor.

Anthropometrics (BMI, height, weight)

It is the anthropometric profile of the research population which gives relevant background on the cardiovascular risk and post-PCI outcomes. The mean age of the participants in the current study was 60.69 ± 7.87 years, which will support the idea that PCI was mostly carried out on an older adult population. Mean body weight of individuals comprising the sample was 70.36 kg with standard deviation of 7.71 kg. The average height was 167.12cm with standard deviation of 5.59 cm. The values are generally in agreement with norms of the adult population in regional cardiovascular cohorts. But taken together to come up with BMI, the mean of 25.32 ± 3.71 kg/m 2 puts the average population in the overweight range as defined by World Health Organization (WHO). This result is of clinical importance because excess body weight has been confirmed as a well-established risk factor of the development and progression of coronary artery disease.

Comparative Biomarker Analysis

pre-PCI and Post PCI and MACE status

Descriptive statistics was performed for correlating the biochemical markers and mace status. The error values varied significantly showing differences across the MACE status and the biochemical markers. The skewness was negative in most of the cases. cTnT_PostPCI. CK_MB_PostPCI, BNP_PostPCI and TMAO_PostPCI showed positive values for skewness.

Pre PCI biomarker levels between MACE and non-MACE

A Mann–Whitney U test was performed to test the hypothesis. A comparison of baseline (pre-PCI) biomarker levels between patients who subsequently developed major adverse cardiac events (MACE) and those who did not. The results showed no statistically significant differences between the two groups for any of the measured pre-PCI biomarkers.

The values for each of the biomarkers is shown below:

- Troponin T (Pre-PCI): p = 0.530
- CK-MB (Pre-PCI): p = 0.274
- BNP (Pre-PCI): p = 0.559
- hs-CRP (Pre-PCI): p = 0.949
- TMAO (Pre-PCI): p = 0.540
- H-FABP (Pre-PCI): p = 0.294

Thus, in each case, the p-value exceeded the significance threshold of 0.05. This indicated that the baseline distribution of these biomarkers did not differ across MACE status categories in pre-PCI patients.

Post PCI biomarker levels between MACE and Non-MACE

On the contrary, Post PCI biomarkers were tested with MACE status using the MAnn-Whitney U test. The testing of various hypothesis showed that two biomarkers namely Troponin I and TMAO—showed statistically significant differences between MACE and non-MACE groups, with cTnI_PostPCI (p = 0.048) and TMAO_PostPCI (p = 0.020) being significantly higher among patients who developed MACE. Thus, the findings suggest that acute myocardial injury and post-procedural metabolic alterations may contribute to the risk of adverse cardiac events. In contrast, all other post-PCI biomarkers demonstrated non-significant differences. The biomarkers such as including cTnT_PostPCI with p-value of 0.975), CK_MB_PostPCI with p value of 0.912, BNP_PostPCI with p- value of 0.445), hsCRP_PostPCI with p value of 0.166, and HFABP_PostPCI with p value of 0.266. These results indicate that, apart from Troponin I and TMAO, the remaining biomarkers did show any significant patterns that could be considered.

Analysis of the change in biomarker levels from pre- to post-PCI (Delta values)

The analysis showed no significant differences. All markers failed to reach statistical significance. These findings indicate that the magnitude of biomarker elevation or reduction following PCI was similar between MACE and non-MACE groups. Thus, it suggests that Delta values—reflecting physiological change induced by the procedure—did not effectively discriminate against patients based on subsequent adverse cardiac outcomes in this cohort. Although Delta cTnI and Delta TMAO approached statistical significance, the null hypothesis was retained for all variables (p > 0.05). Therefore, the magnitude of biomarker changes alone did not significantly differentiate MACE from non-MACE patients.

Binary logistic regression for MACE status and variables.

In order to predict if post-procedural biomarkers and demographic variables such as age, gender, BMI have any correlation to predict MACE a binary logistic regression was carried out. The overall model, which included cTnI_PostPCI, TMAO_PostPCI, age, gender, and BMI, was not statistically significant with Omnibus chi square value of 5.375, and p value of 0.372. This combination of predictors did not reliably distinguish between MACE and non-MACE patients. Further, the model was only able to explain 5.2% of the variance in MACE occurrence. The model explained only 5.2% of the variance in MACE occurrence as evident from Nagelkerke $R^2 = 0.052$ which was not significant. The overall analysis demonstrated poor predictive performance, correctly classifying 100% of non-MACE cases but none of the MACE cases. This could be associated with imbalance in the data sheet. Examination of individual predictors showed that cTnI_PostPCI with a p value of 0.172), TMAO_PostPCI with p value of of 0.078), age with p value of 0.876), gender with a p value of 0.637, and BMI with a p value of 0.562 were not significant independent predictors of MACE. Although TMAO_PostPCI values were close to significance it still did not meet the required threshold. These results suggest that while certain biomarkers showed group-level differences in earlier analyses, none of the variables included in the logistic regression independently predicted MACE after adjusting for demographic factors.

Discriminatory Performance

ROC curve

Troponin I and TMAO—showed statistically significant differences between MACE and non-MACE groups in Post PCI patients. Thus, to evaluate the sensitivity of the markers ROC curve analysis was done. Receiver Operating Characteristic (ROC) curve analysis was conducted to evaluate the discriminative ability of cTnI_PostPCI in predicting MACE. The Area Under the Curve (AUC) was 0.579 with a 95% CI and range of 0.499–0.658. The p value for prediction was 0.048. An AUC of 0.579 indicates poor discriminatory ability, only slightly better than chance (0.5). Although statistically significant, the clinical predictive performance of cTnI_PostPCI alone is limited. The ROC curve demonstrates modest sensitivity–specificity trade-off, suggesting that while cTnI levels differ between groups, they do not provide strong standalone predictive accuracy. Troponin I (cTnI_PostPCI) to differentiate patients who developed MACE from those who did not. The curve yielded an AUC of 0.579 with SE of 0.041, p value of 0.048. The overall confidence rate was 95% CI: 0.499–0.658. The overall result shows a poor discriminative ability. However, the p value was less than 0.05 indicating statistical significance. This suggests that post-procedural cTnI levels provide limited yet meaningful predictive information regarding MACE occurrence. Sensitivity and specificity trade-offs across cut-off values show that a threshold around 0.05 -- 0.07 ng/mL and maintain relatively high sensitivity of 0.97 -- 0.91. The specificity was low indicating that biomarkers are sensitive to identifying at-risk patients. However, it lacks specificity in ruling out non-MACE cases. Overall, cTnI_PostPCI demonstrates modest predictive value, which supports its role as a weak standalone biomarker but not a strong classifier of MACE.

Hypothesis for study and the observations

H1: Patients who develop MACE post- PCI have significantly different baseline and post-procedure biomarker profiles compared to those who do not develop MACE.

According to the Mann–Whitney U test results, there were no significant differences in baseline (pre-PCI) biomarker levels between patients who developed MACE and those who did not ($p > .05$). However, post-PCI Troponin I ($U = 7315.50$, $Z = -1.97$, $p = .048$) and TMAO ($U = 3391.00$, $Z = -2.33$, $p = .020$) showed statistically significant differences between the two groups. These findings suggest that elevations in Troponin I and TMAO after PCI are associated with MACE occurrence. Thus, post-procedure biomarkers demonstrated greater predictive value for adverse cardiac events. Overall, H1 was partially supported, indicating significant differences only in select post-PCI biomarkers.

V. DISCUSSION

5.1 Interpretation of Principal Findings

The findings from the study confirm that PCI induces measurable biochemical responses reflecting myocardial injury, inflammation, and metabolic alterations. Baseline biomarkers did not show any difference between MACE and non-MACE in pre-PCI patients. All the markers showed no statistical significance. Baseline biomarkers did not significantly differ between MACE and non-MACE patients in post PCI. Among post-PCI biomarkers, only cTnI and TMAO demonstrated statistically significant differences between groups. However, neither biomarker independently predicted MACE after adjustment for demographic variables. Additionally, ROC analysis showed poor discriminative ability of cTnI alone. These findings suggest that while peri-procedural myocardial injury and metabolic response may be associated with adverse outcomes, their standalone predictive utility is limited in this cohort. Elevations in Troponin I and TMAO after PCI are associated with MACE occurrence. Thus, post-procedure biomarkers demonstrated greater predictive value for adverse cardiac events. Overall, hypothesis for study was partially supported, indicating significant differences only in select post-PCI biomarkers.

5.2 Comparison with Existing Literature

In the present study the predominant age range was between 55-66 years. This trend is consistent with the observations from literature wherein the occurrence of CAD is seen in this age group. Most older adults show clinical expression in later decades of life due to

atherosclerosis, endothelial dysfunction, and protracted exposure of the cardiovascular risk factor [17]. The present study in pre-PCI analysis of biomarkers showed that initially, baseline biochemical status was not a reliable discriminant of patients in high-risk category in respect of adverse outcomes after PCI in this cohort. THe present observations correlate well with existing studies. In their study they observed that hs-CRP was not a reliable indicator for MACE however IL-6 was a good predictor. The present study thus differs from the observation that none of the markers are significant predictors of MACE in pre-PCI. Post PCI only two markers were found to have predictive value which included cTnT and BNP. Studies conducted by [18-19] have shown that post PCI troponin can be used as a marker for adverse cardiac events. However, the levels need to be significantly higher and not just above baseline. The use of other markers such as CK-MB was more reliable instead of Troponin in such cases. TMAO can be useful to predict adverse events post PCI in short term periods [16]. Meta analysis done by Zhang et al., showed that TMAO levels are associated with increased incidence of MACE post PCI. Thus, the present study correlates well with observations obtained from previous published studies.

5.3 Clinical Implications and Translational Potential

The use of biomarkers for establishing the incidence of MACE in PCI patients has significant impact on the risk stratification. The assay of biomarkers is simple and it needs only a collection of appropriate samples. Thus, all biomarkers can be assessed from relatively less sample amounts and provide an easier approach. Thus, the present study has huge translational potential in terms of using biomarkers for risk stratification.

5.4 Study Strengths and Limitations

The study utilises the established cardiac biomarkers and their levels in distinguishing MACE vs non-MACE patients for risk stratification. Of the several biomarkers tested none of them could predict MACE before PCI. However, post PCI only two markers were found to be associated with MACE which include TnT and TMAO. However, these were also weak predictors when adjusted with cohort and demographic variables. Thus, these markers could be helpful in prediction but can serve as only standalone for other methods for confirming the risk for MACE. The study was done on a specific cohort and most dependent on the available data and their results. This is the basic limitation associated with the study. Further, increasing the sample size and working on a diverse group of population could enhance the findings of the present study.

VI. CONCLUSIONS AND FUTURE DIRECTIONS

The study has a huge potential in terms of utilizing biomarkers for predicting the MACE events post PCI. However, the two markers identified in this study were marginally significant and could not correlate with age confounded variables. Thus, these could serve as standalone markers along with other methods for detection. The study host potential however it needs to be done on larger cohorts so that the implications from this study are meaningful.

Conflict of interest

None

VII. REFERENCES

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VIII FIGURES

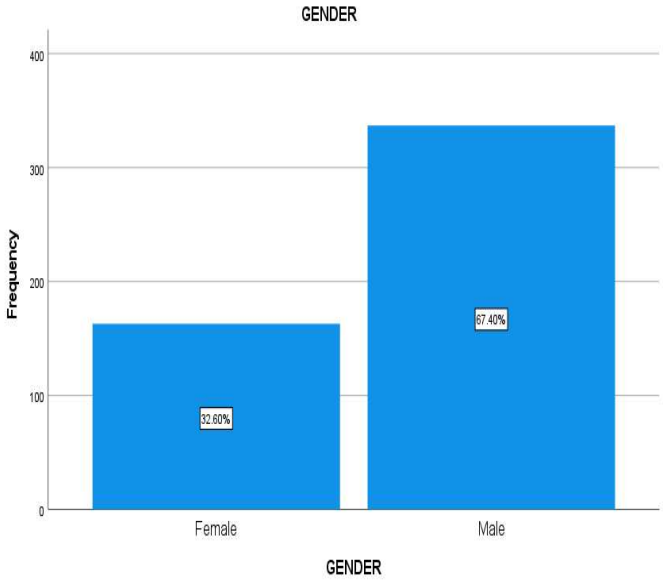

Fig 1. Summary of the gender distribution across sample population

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of cTnT_PrePCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.530	Retain the null hypothesis.
2	The distribution of CK_MB_PrePCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.274	Retain the null hypothesis.
3	The distribution of BNP_PrePCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.559	Retain the null hypothesis.
4	The distribution of hsCRP_PrePCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.949	Retain the null hypothesis.
5	The distribution of TMAO_PrePCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.540	Retain the null hypothesis.
6	The distribution of HFABP_PrePCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.294	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Fig 2. Hypothesis testing for markers correlation in MACE and Non-MACE pre pCI.

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of cTnI_PostPCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.048	Reject the null hypothesis.
2	The distribution of cTnT_PostPCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.975	Retain the null hypothesis.
3	The distribution of CK_MB_PostPCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.912	Retain the null hypothesis.
4	The distribution of BNP_PostPCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.445	Retain the null hypothesis.
5	The distribution of hsCRP_PostPCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.166	Retain the null hypothesis.
6	The distribution of TMAO_PostPCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.020	Reject the null hypothesis.
7	The distribution of HFABP_PostPCI is the same across categories of MACE_Status.	Independent-Samples Mann-Whitney U Test	.266	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Fig 3. Hypothesis testing for markers and their association between MACE and non- MACE post PCI

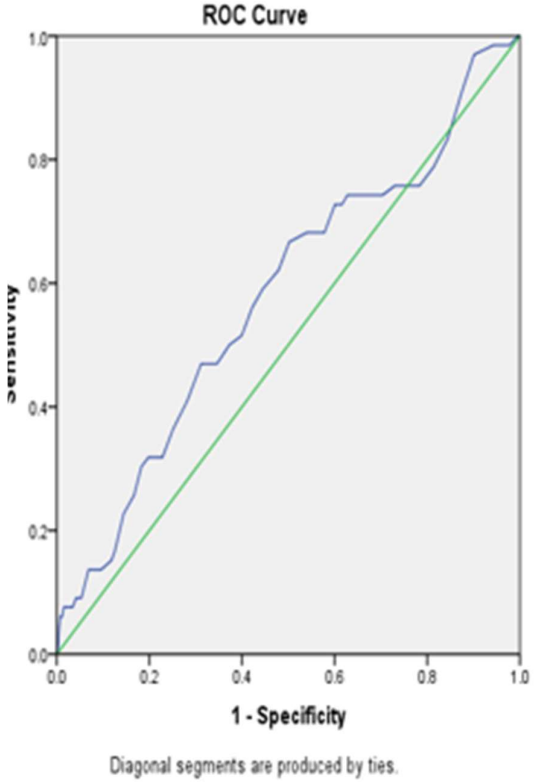

Fig 4. ROC curve analysis

VIII TABLES

Table 1. Summary of the gender distribution across sample population

GENDER					
		Frequency	Percentage	Valid Percentage	Cumulative Percentage
Valid	Female	163	32.6	32.6	32.6
	Male	337	67.4	67.4	100.0
	Total	500	100.0	100.0	

Table 2. Table summarizing the age and central tendency

AGE					
		Frequency	Percentage	Valid Percentage	Cumulative Percentage
Valid	37	1	0.2	0.2	0.2
	38	2	0.4	0.4	0.6
	43	2	0.4	0.4	1
	44	1	0.2	0.2	1.2
	45	5	1	1	2.2
	46	2	0.4	0.4	2.6
	47	13	2.6	2.6	5.2

	48	9	1.8	1.8	7
	49	15	3	3	10
	50	6	1.2	1.2	11.2
	51	9	1.8	1.8	13
	52	12	2.4	2.4	15.4
	53	12	2.4	2.4	17.8
	54	10	2	2	19.8
	55	13	2.6	2.6	22.4
	56	26	5.2	5.2	27.6
	57	21	4.2	4.2	31.8
	58	22	4.4	4.4	36.2
	59	23	4.6	4.6	40.8
	60	26	5.2	5.2	46
	61	26	5.2	5.2	51.2
	62	26	5.2	5.2	56.4
	63	31	6.2	6.2	62.6
	64	35	7	7	69.6
	65	30	6	6	75.6
	66	28	5.6	5.6	81.2
	67	23	4.6	4.6	85.8
	68	17	3.4	3.4	89.2
	69	9	1.8	1.8	91
	70	15	3	3	94
	71	1	0.2	0.2	94.2
	72	10	2	2	96.2
	73	3	0.6	0.6	96.8
	74	1	0.2	0.2	97
	75	1	0.2	0.2	97.2
	77	1	0.2	0.2	97.4
	78	3	0.6	0.6	98
	81	2	0.4	0.4	98.4
	84	2	0.4	0.4	98.8
	87	2	0.4	0.4	99.2
	88	2	0.4	0.4	99.6
	90	1	0.2	0.2	99.8
	92	1	0.2	0.2	100
	Total	500	100	100	

Table 3. Summary of various anthropometric parameters

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	500	37	92	60.69	7.870
WEIGHT	500	54	103	70.36	7.705
HEIGHT (cm)	500	149	193	167.12	5.593
BMI (Calculated)	500	21.71	44.89	25.3180	3.70563
Valid N (listwise)	500				

Table 4. Summary of the binary logistic regression analysis done

Variables in the Equation									
		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1a	cTnI_PostPCI	2.462	1.804	1.863	1	0.172	11.73	0.342	402.429
	TMAO_PostPCI	0.414	0.235	3.099	1	0.078	1.513	0.954	2.399
	AGE	0.006	0.036	0.024	1	0.876	1.006	0.937	1.079
	GENDER(1)	-0.221	0.468	0.223	1	0.637	0.802	0.32	2.006
	BMICalculated	0.062	0.107	0.336	1	0.562	1.064	0.863	1.311
	Constant	-7.738	4.516	2.936	1	0.087	0		
a. Variable(s) entered on step 1: cTnI_PostPCI, TMAO_PostPCI, AGE, GENDER, BMICalculated.									

Table 5. AUC analysis summary presented in table 6

Area Under the Curve				
Test Result Variable(s): cTnI_PostPCI				
Area	Std. Errora	Asymptotic Sig.b	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.579	0.041	0.048	0.499	0.658
The test result variable(s): cTnI_PostPCI has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.				

Table 6. Coordinates of the curve presented in Table 7

Coordinates of the Curve		
Test Result Variable(s): cTnI_PostPCI		
Positive if Greater Than or Equal Toa	Sensitivity	1 - Specificity
0	1	1
0.025	1	0.996
0.035	0.985	0.977
0.045	0.985	0.943
0.055	0.97	0.901
0.065	0.909	0.875
0.075	0.833	0.844
0.085	0.788	0.814
0.095	0.758	0.783
0.105	0.758	0.76
0.115	0.758	0.73
0.125	0.742	0.703

0.135	0.742	0.673
0.145	0.742	0.65
0.155	0.742	0.627
0.165	0.727	0.616
0.175	0.727	0.601
0.185	0.682	0.578
0.195	0.682	0.54
0.205	0.667	0.502
0.215	0.621	0.479
0.225	0.591	0.445
0.235	0.561	0.422
0.245	0.515	0.399
0.255	0.5	0.373
0.265	0.47	0.346
0.275	0.47	0.312
0.285	0.409	0.281
0.295	0.364	0.251
0.305	0.318	0.228
0.315	0.318	0.198
0.325	0.303	0.183
0.335	0.258	0.167
0.345	0.227	0.144
0.355	0.167	0.125
0.365	0.152	0.118
0.375	0.136	0.095
0.385	0.136	0.068
0.395	0.091	0.053
0.405	0.091	0.042
0.415	0.076	0.034
0.425	0.076	0.023
0.435	0.076	0.019
0.445	0.076	0.015
0.46	0.061	0.011
0.475	0.061	0.008
0.53	0.03	0.004
0.665	0.015	0.004
1	0	0

The test result variable(s): cTnI_PostPCI has at least one tie between the positive actual state group and the negative actual state group.

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Table 7. Summary of the analysis done for correlation of markers

Test Statistics[a]														
	Troponin I Level Before PCI (ng/mL)	Troponin T Level Before PCI (ng/L)	Creatine Kinase MB Before PCI (IU/L)	B-type Natriuretic Peptide Before PCI (pg/mL)	High-sensitivity C-reactive Protein Before PCI (mg/L)	Trimethylamine N-oxide Before PCI (µM)	Heart Fatty Acid Binding Protein Before PCI (ng/mL)	Troponin I Level After PCI (ng/mL)	Troponin T Level After PCI (ng/L)	Creatine Kinase MB After PCI (IU/L)	B-type Natriuretic Peptide After PCI (pg/mL)	High-sensitivity C-reactive Protein After PCI (mg/L)	Trimethylamine N-oxide After PCI (µM)	Heart Fatty Acid Binding Protein After PCI (ng/mL)
Mann-Whitney U	7440.5	7237	10399	10010.5	12927	6173.5	6543.5	7315.5	5409.5	6378	5017.5	4964.5	3391	4241.5
Wilcoxon W	44841.5	8890	63049	52496.5	16008	7551.5	38421.5	42031.5	29062.5	7809	29327.5	30842.5	22306	22962.5
Z	-0.105	-0.628	-1.094	-0.584	-0.064	-0.613	-1.049	-1.974	-0.032	-0.11	-0.764	-1.387	-2.333	-1.113
Asymp. Sig. (2-tailed)	0.916	0.53	0.274	0.559	0.949	0.54	0.294	0.048	0.975	0.912	0.445	0.166	0.02	0.266
a. Grouping Variable: MACE_Status														