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Assessment of risk stratification and prognosis among patients of myocardial infarction by cardiac biomarkers

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Abstract

Introduction: Biomarkers are a large range of quantitative and repeatable biological sign features. They are defined as "a trait that is objectively measured and analysed as a sign of normal biological mechanisms, pathogenic processes, or pharmacological reactions to a therapeutic strategy" in its broadest definition. Many novel biomarkers are still through early development, but it is still unclear how these indicators' roles and biochemistry connect to the likelihood of subsequent cardiac disease in people with and without coronary artery disease (CAD), as well as how useful they are clinical.

Aims and Objective: The study aims to find the association of cardiac biomarkers with the occurrence of myocardial infarction (MI) and attempts to apply them in risk and prognostic determination.

Methods: This is a prospective study that was conducted on 220 patients who visited our hospital in the outpatient department of cardiology or emergency department and were examined for biomarkers of MI along with their clinical features. The diagnosis of MI was made by applying criteria set by World Health Organization. The patients with diagnosed MI were considered in the MI group while those who did not have MI, were taken as control. The laboratory parameters were statistically analysed between the two groups to associate the risk of MI with each variable.

Results: The study found that the cardiac biomarkers like hsCRP, CKMB, TnT, and MPO, were all significantly ($p<0.05$) more in the MI group as compared to the control group. It was shown that the biomarkers were significantly higher in the MI group than in the Control group ($p<0.05$).

Conclusion: The study concluded that there is a high risk of having MI if these cardiac biomarkers come higher level and can be considered the risk and prognostic marker of MI.

Keywords: Myocardial infarction, Cardiac biomarkers, Cardiovascular disease, Troponin

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Introduction

Across the entire world, cardiovascular disease (CVD) is the primary cause of both mortality and impairment. Conventional CVD risk factors including cigarettes, pressure, diabetes mellitus, & hypercholesterolemia have sparked significant advances in both therapy and risk prediction models. Yet, 40.2% of people with cardiovascular problems have just one typical risk factor, and up to 20.4% have none (1).

Biomarkers are a large range of quantitative and repeatable biological sign features. They are defined as "a trait that is objectively measured and analysed as a sign of normal biological mechanisms, pathogenic processes, or pharmacological reactions to a therapeutic strategy" in its broadest definition. The following requirements must be met by effective biomarkers: (1) Accuracy, or the capacity to spot at-risk persons; (2) Reliability, or the consistency of outcomes, when tested again; and (3) Therapeutic Impact with Primary Prevention (2,3).

Biomarkers of myocardial infarction

Cardiac troponin: The globular contractile regulatory protein complex known as troponin, which consists of troponin T, I, and C, is found at frequent intervals inside a striated muscle's fine fibre. Troponin hinders by trying to prevent myosin & actin from interacting during contractions, a process that is a key step in muscle contraction (4). Cardiovascular only inside the heart, troponins I & T are highly specific and distinct biomarkers of myocardial necrosis. cTnI and cTnT are generated from necrotic myocardium in acute myocardial infarction (AMI) together as whole proteins & by products of protein degradation (5). The level of cardiac biomarkers in peripheral circulation both indicates & quantifies cardiomyocyte injury. Myoglobin, creatine kinase (CK), and its MB isoenzyme is less specific and sensitive indicators of cardiomyocyte injury than cardiac troponins (6).

High-sensitive cardiac troponin (hs-cTn): Technological advancements have enhanced the capacity to identify and quantify cardiomyocyte damage and have refined cTn assays. With the development of these hs-cTn assays, cTn's function has shifted from that of a marker only employed mostly in acute disease diagnosis to one that evaluates continuing cardiac impairment in stable patients or even individuals that appear to be healthy (7). Cardiac troponin concentrations rise quickly in AMI patients, typically if elevated tests were utilized as well as the levels remain higher for an indeterminate period, within 1 hour (8).

Heart-type fatty acid binding protein (H-FABP): Fatty acid transfer via membranes is made possible by a class of transport proteins called cytoplasmic FABP. FABP is tissue-specific, hence there seem to be different types for the liver, intestines, brain, and heart. H-FABP, a protein with a small molecular weight and 132 amino acids, is implicated inside the myocardium's metabolism for fatty (9,10). H-FABP seems to be either better for the sternum or provides extra value to quantitation inside the early diagnosis of the acute coronary syndrome, according to several investigations, as demonstrated by ROC analysis (ACS). In AMI patients who reported

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within 4 hours of the start of complaints, Kabekkodu *et al.* (11) found that the responsiveness of H-FABP was 60.7%, which is substantially higher than greater compared to CK-MB and cTnI.
Many novel biomarkers are still through early development, but it is still unclear how these indicators' roles and biochemistry connect to the likelihood of subsequent cardiac disease in people with and without CAD, as well as how useful they are clinically (12). As a result, it is challenging to make explicit inferences about the mechanisms by which a biomarker can alter the prognosis based on the available evidence. Although there is proof that merging biomarkers can enhance the reliability of some tests, it is still necessary to identify the best combinations for prognosis or diagnosis (13,14).

Materials and Methods

Research design

This is a prospective study that was conducted on 220 patients, who visited SRVS Government Medical College Shivpuri hospital in the department of Pathology from March 2022 to February 2023. The patients were examined for biomarkers of MI along with their clinical features. The diagnosis of MI was made by applying criteria set by World Health Organization (10,12). The diagnosis of MI was confirmed by two experienced cardiologists independently. The patients were divided into 2 groups, namely, the MI group and Control group. The patients with diagnosed MI were considered in the MI group while those who did not have MI, were taken as control. The laboratory parameters like High-sensitivity C-reactive protein (hsCRP), Creatine kinase-MB (CKMB), Troponin T (TnT), Myeloperoxidase (MPO) were statistically analyzed between the two groups to associate the risk of MI with each variable.

Inclusion and Exclusion criteria

The patients who visited the hospital with chest pain and other features of MI as per the WHO criteria were only included in this study. The patients, who were diagnosed with MI by both doctors as mentioned above were only included. The patients who did not cooperate, had chronic conditions, especially pulmonary disease, and did not follow our study protocol, were excluded from the study.

Statistical Analysis

The study used SPSS 22 for effective statistical analysis. The continuous data were expressed as mean±sd, while discrete data were expressed as frequency and its respective percentage. The study employed ANOVA to associate the occurrence of MI with each variable. The level of significance was $p<0.05$.

Ethical Approval

The study process has been explained clearly to each patient and the authors obtained written consent from each patient. The study was approved by the Ethical Committee of the concerned hospital before the collection of data.

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Results

Figure 1 shows the gender distribution in this study. The study found that there are much more males in each of these groups and there are more males in the MI group than in the control group.

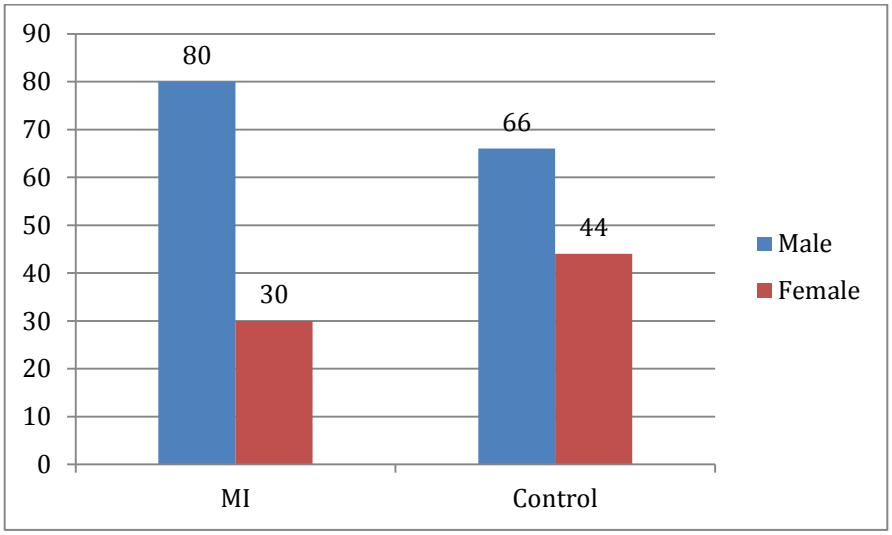

Figure 1: Gender distribution in each group of this study

The mean values were calculated between the groups. It was shown that the biomarkers were significantly higher in the MI group than in the Control group ($p<0.05$). It was found that MI has male preponderance. Other biomarkers including hsCRP, CKMB, TnT, and MPO, were all significantly ($p<0.05$) more in the MI group as compared to the control group. Table 1 shows the details of the mean values of each parameter while Table 2 shows the result of the significance test.

Table 1: Mean values of the parameters in each group

Parameters	MI	Control
AGE	44.2±4.98	45.31±4.17
hs-CRP	4.6±1.54	0.50±0.22
CKMB	166.20±27.05	2.04±1.23
TnT	135.17±8.65	96.57±2.85
MPO	156.77±29.16	42.47±15.077

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Table 2: Pearson's Chi-Square Test between each variable

Parameters	$\chi 2$	F-value	p-value
hs-CRP	220	925.65	.000
CKMB	218	685.766	.000
TnT	220	1973.325	.000
MPO	220	1333.084	.000
Age	23.60	3.252	0.73
Sex	3.99	4.028	0.046

Table 2 presents the results of Pearson's Chi-Square Test, which was used to examine the association between each variable and the presence of MI. The test is commonly used to evaluate the relationship between two categorical variables. The p-value is the probability of observing the results obtained by chance alone, with a p-value less than 0.05 indicating statistical significance. The first four variables (hs-CRP, CKMB, TnT, and MPO) show a highly significant association with the presence of MI, as indicated by the very low p-values (all at 0.00) and high $\chi 2$ values (all at 220). These variables are biomarkers that are commonly used in clinical practice to evaluate patients with MI. hs-CRP (high-sensitivity C-reactive protein) is an inflammatory marker that increases in response to inflammation in the body. CKMB (creatine kinase MB) and TnT (troponin T) are enzymes that are released when heart muscle is damaged. MPO (myeloperoxidase) is an enzyme that is produced by white blood cells and plays a role in inflammation. Age shows a weak association with the presence of MI, with a p-value of 0.21, which is not statistically significant. This suggests that age alone may not be a good predictor of MI risk. However, it is important to note that age is a well-established risk factor for cardiovascular disease, and it may have a stronger association with MI when combined with other risk factors. Sex also shows a significant association with the presence of MI, with a p-value of 0.04. This suggests that sex may play a role in MI risk, with males being more likely to develop MI than females. This finding is consistent with previous research, which has shown that males are at a higher risk of developing cardiovascular disease than females.

Table 3 suggests that hs-CRP, CKMB, TnT, and MPO are strong predictors of MI risk, while age and sex have weaker associations with MI risk. These findings have important implications for the diagnosis and treatment of MI, as they suggest that biomarkers may be more useful for predicting MI risk than age and sex alone.

Table 3: Pearson Correlation Coefficient among Myocardial Infarction case

Correlations						
		AGE	**hsCRP**	**CKMB**	**TnT**	**MPO**
AGE	Pearson Correlation	1	-0.067	-.170*	-0.131	-0.098
	Sig. (2-tailed)		0.325	0.011	0.052	0.147
	N	220	220	220	220	220
hsCRP	Pearson Correlation		1	.750**	.824**	.804**
	Sig. (2-tailed)			0.000	0.000	0.000

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	N		220	220	220	220
CKMB	Pearson Correlation			1	.865**	.836**
	Sig. (2-tailed)				0.000	0.000
	N			220	220	220
TnT	Pearson Correlation				1	.900**
	Sig. (2-tailed)					0.000
	N				220	220
MPO	Pearson Correlation					1
	Sig. (2-tailed)					
	N					220

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Table 3 displays the Pearson correlation coefficients between age and four biomarkers: hsCRP, CKMB, TnT, and MPO. The correlation coefficient ranges from -1 to 1, where -1 indicates a perfect negative correlation, 0 indicates no correlation, and 1 indicates a perfect positive correlation. The results indicate that age is negatively correlated with hsCRP (r=-0.06, p= 0.32), CKMB (r=-0.17, p=0.01), TnT (r=-0.13, p=0.05), and MPO (r=-0.09, p= 0.14). The negative sign indicates that as age increases, the levels of these biomarkers decrease. However, the correlations are weak, with r ranging from -0.098 to -0.170, and none of them are statistically significant at the 0.05 level except for CKMB. The correlations between hsCRP, CKMB, TnT, and MPO are all positive and strong, with r ranging from 0.750 to 0.900, and all are statistically significant at the 0.01 level. This suggests that as one biomarker increases, the others tend to increase as well. Specifically, hsCRP is highly positively correlated with CKMB (r=0.75, p<0.01), TnT (r=0.82, p<0.01), and MPO (r=0.80, p<0.01), CKMB is highly positively correlated with TnT (r=0.865, p<0.01) and MPO (r=0.83, p<0.01), and TnT is highly positively correlated with MPO (r=0.90, p<0.01). The results suggest that age is weakly negatively correlated with hsCRP, CKMB, TnT, and MPO. On the other hand, hsCRP, CKMB, TnT, and MPO are strongly positively correlated with each other. These findings may have implications for understanding the relationships between age and biomarkers of cardiovascular disease. However, further research is needed to confirm these relationships and to determine their clinical significance.

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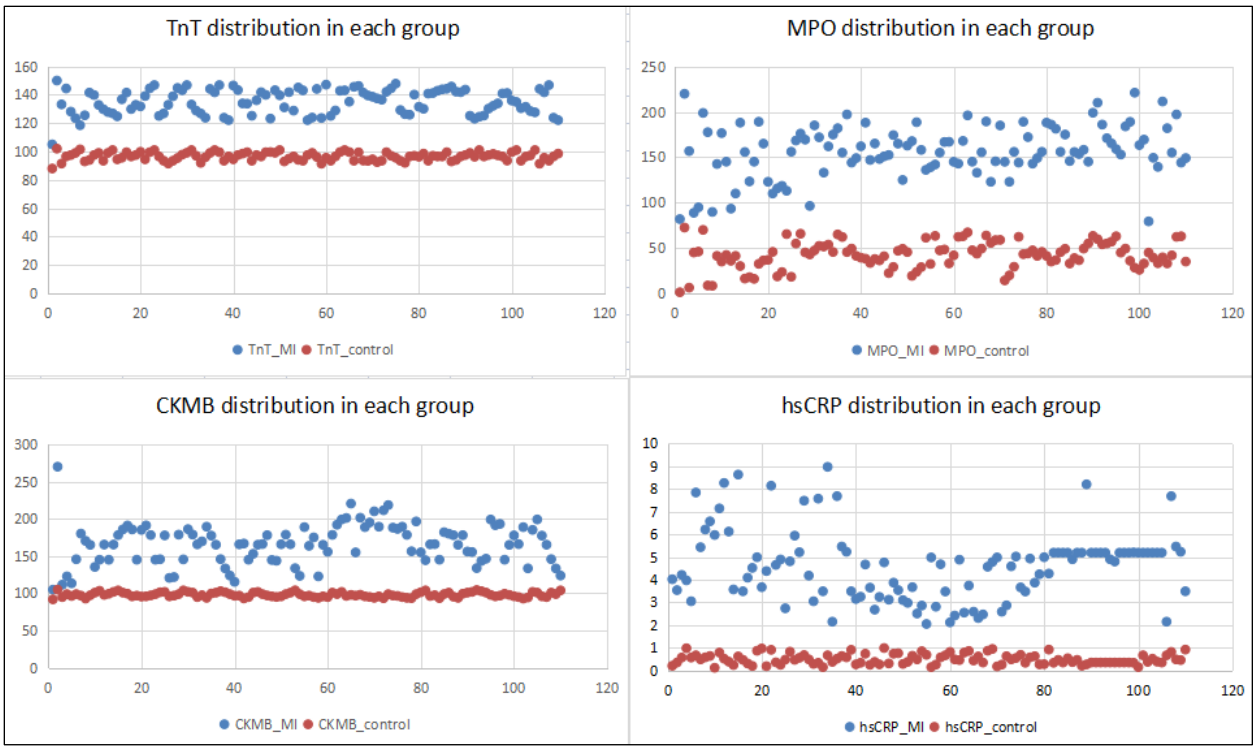

Figure 2: Scatter diagram showing distribution of TnT, MPO, CKMB and hsCRP in each group

Discussion

Biomarkers were biological variables that can be objectively analyzed and quantified for indicators of diseased processes, human primary functioning, or responses to treatments. Biomarkers, which are frequently thought of as instruments for the progression of disease screening, diagnosis, or monitoring, can also be used to assess disease eligibility and susceptibility to a particular therapy (15). When myocardial damage occurs, proteins that are part of cardiac markers, which are cell-based indicators, are released into the blood. These are essential in the identification, evaluation, and care for people who have chest pain & suspected acute coronary syndrome, in addition to people who have acute heart failure exacerbations (20).

Several cardiac biomarkers that are clinically evident have proven useful in predicting prognosis in individuals with acute coronary syndromes. However, neither separately nor in combination, their respective prognostic importance in stable people has indeed been prospectively verified (16,17). The study's goal was to evaluate the possible predictive usefulness of high-Quality products protein, myeloperoxidase, & B-type natriuretic peptide in patients getting elective diagnostic angioplasty that do not suffer from episodes of the acute coronary syndrome. Finally, a thorough examination of cardiac troponins may have idealist prognostic value for patients with stable cardiac conditions who experience long-term unfavourable clinical outcomes (21).

CAD risk is increasing. Conventional markers like troponins & creatine kinase, while crucial in the diagnosis, vulnerability assessments, & therapy of cardiovascular disease, cannot detect myocardial ischemia in the absence of necrosis (18). As a result, the subject of how to identify ischemia in people who have acute coronary syndrome is still very important. In this context,

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high-sensitivity troponin is developing as a trustworthy biomarker that has been integrated into clinical practice. There is currently a great deal of curiosity in biomarkers since they not only aid in illness diagnosis and therapy but also in understanding the pathophysiology of the disease state. Moreover, multimarker analysis has shown to be a highly helpful technique for risk categorization. Troponins and CK, two common conventional biomarkers, have been crucial in the identification, risk assessment, and treatment of ACS. Potential novel biomarkers, including MPO and H-FABP, have been developed as a result of extensive study, and they are currently the subject of active validation studies. Complementary analysis employing a multimarker technique is a very helpful tool in risk classification with the advent of additional markers (22).
ST-elevated myocardial infarction (STEMI) is among the primary reasons for mortality & morbidity worldwide. In addition to the conventional biomarker NT-proBNP, other biomarkers, including Pentraxin-3 (Ptx-3) & ST2, have been developed as potential tools for risk classification in cardiac patients (19). The potential clinical impact of multimarker techniques to predict the prognosis of STEMI patients must be investigated. As a result of STEMI, Moreover, multimarket approaches improved the accuracy of CV fatality prediction. ST2, Ptx-3, & NT-proBNP have also been connected to the incidence of CV death (23).

Conclusion

In patients with high risk of having MI, if these cardiac biomarkers come higher level can be considered a risk and prognostic marker of MI. The study has also evidently shown that there is male preponderance in MI cases and, shows that age cannot be a reliable risk factor or parameter. The study is limited by the variety of the population. So, this can be achieved by conducting more similar studies with varied populations. Overall, this current study has highlighted an important clinical aspect of MI that would contribute to early diagnosis, management, and prognosis of MI.

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