Original Article

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Pathology Section

Assessing the Role of MAPH Score in Predicting Acute Coronary Syndrome: A Cross-sectional Study

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ABSTRACT

Introduction: Incorporating the concepts of hyperviscosity, platelet hyperactivity, and age-related risk of Acute Coronary Syndrome (ACS), a new score has been put forward-the Mean platelet volume-Age-total Protein-Haematocrit (MAPH) score, which can determine the increased thrombotic tendency associated with ST-Segment Elevation Myocardial Infarction (STEMI). The MAPH score includes parameters such as Mean Platelet Volume (MPV), age, total protein, and haematocrit. Researchers have found that a high MAPH score is associated with a high thrombus burden in cases with STEMI and Non ST-Elevation Myocardial Infarction (NSTEMI). However, the association between MAPH score and ACS is undefined.

Aim: To assess the role of MAPH score in predicting ACS.

Materials and Methods: This cross-sectional study was conducted in the Department of Pathology, Srinivas Institute of Medical Sciences and Research Centre Mangalore, Karnataka, India for six months. The study included 100 clinically diagnosed cases of ACS and 100 healthy controls. The demographic data, MPV, total protein, and haematocrit values of all cases and controls were collected and tabulated, and statistical analysis was performed. Receiver Operating Characteristic (ROC) curve analysis was performed on each MAPH score parameter, and cut-off values for each parameter were obtained based on the Youden index. After calculating the MAPH score of cases and controls, multivariate logistic regression analysis was performed to evaluate the role of the MAPH score as an independent predictor of ACS.

Results: A statistically significant increase in MPV (p-value=0.017) and total protein (p-value <0.001) was noted among the cases. The calculated cut-off values for MPV, age, total protein, and haematocrit were 8.4 fL, 54 years, 6.8 g/dL, and 49.1%, respectively. A statistically significant increase in the MAPH score was noted among the cases compared to the controls. Finally, multivariate logistic regression analysis identified the MAPH score as an independent predictor of ACS.

Conclusion: This was the first study investigating the association between MAPH scores in patients with ACS. The MAPH score was identified as an independent predictor of ACS and can be used as a screening tool to predict and diagnose the condition in primary healthcare settings. This helps to ensure early coronary revascularisation and reduce Coronary Artery Disease (CAD)-related mortality and morbidity to a greater extent.

Keywords: Coronary artery disease, Haematocrit, Myocardial infarction, Primary healthcare, Thrombosis

INTRODUCTION

Cardiovascular Diseases (CVD) are the leading cause of mortality and morbidity worldwide, accounting for 31% of all deaths globally. CAD, secondary to atherosclerosis and its complications, contributes to most of these deaths. Atherosclerotic plaques undergo erosion or rupture with added thrombus formation, leading to a complete or partial blockage of coronary arteries. The resulting cardiac ischaemia often leads to alarming clinical manifestations. The most baleful clinical presentation of CAD is ACS [1,2]. ACS covers the spectrum comprising STEMI and NSTEMI, and Unstable Angina (UA) [3]. ACS requires immediate medical intervention to relieve the occlusion in coronary arteries. Partial occlusion leads to NSTEMI and UA, but complete occlusion leads to STEMI. The aetiopathogenesis of thrombosis, leading to arterial occlusion, is discussed in depth in the current era [4]. Many studies are evaluating the role of hyperviscosity in thrombus formation [5]. Studies conducted by Çınar T et al., and Caimi G et al., describe an association between acute myocardial infarction and hyperviscosity [6,7]. Cellular components, erythrocyte deformability, and plasma viscosity are the factors that determine blood viscosity. It is found that high molecular weight proteins in the plasma and haematocrit play a major role in contributing to hyperviscosity [8,9].

Platelets play a significant role in the induction of atherosclerotic lesions and thrombus formation. The metabolically and enzymatically active larger platelets have a higher potential to create thrombosis, and the extent of platelet activation can be evaluated by assessing the Mean Platelet Volume (MPV). Researchers have found that MPV is higher in cases with ACS. Hence, they consider that MPV can be a biomarker in differentiating chest pains of cardiac origin from others [10,11]. Incorporating the concepts of hyperviscosity, platelet hyperactivity, and age-related risk of ACS, a recent study by Abacioglu OO et al., has put forward a new score-"The MAPH score"-that can determine the increased thrombotic tendency associated with STEMI. The parameters included in the MAPH score are MPV, age, total protein, and haematocrit [4]. Researchers have found that a high MAPH score is associated with a high thrombus burden in cases with STEMI and NSTEMI [4,12]. However, the association between the MAPH score and ACS is yet to be defined. Hence, the present study aims to assess the role of the MAPH score in predicting ACS.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Pathology, Srinivas Institute of Medical Sciences, Mangaluru, Karnataka, India, from January 2023 to June 2023. Data collection and analysis were completed in July 2023. Ethical clearance was obtained (SIEC/SIMS&RC/05(39)/2023).

Inclusion criteria: All clinically diagnosed cases of ACS were included in the study as cases. Subjects who came for routine health check-ups without any clinical complaints and having complete blood count and biochemical parameters such as liver function tests and total cholesterol values within normal limits were included as controls.

Exclusion criteria: Cases with severe hepatic disease, end-stage renal disease, febrile illness, thrombocytopenia, severe anaemia, those who received chemotherapy, and those with missing clinical data were excluded from the study. Controls who were on cholesterol-lowering drugs were also excluded from the study.

Sample size calculation: The estimated minimum sample size was 85, with a confidence interval of 95%, prevalence of 8% [13,14], and an attributable error of 6%. The current study included 100 cases of ACS and 100 controls. Patient files of all cases and controls were reviewed. Complete blood counts and liver function were analysed using automated haematology and biochemistry analysers. The demographic data, MPV, total protein, and haematocrit values of all cases and controls were collected and tabulated.

Calculation of MAPH score: ROC curve analysis was performed on each MAPH score parameter, and each parameter's cut-off values were obtained based on the Youden index. Values equal to or more than the cut-off were given a score of one, and values less than the cut-off were given a score of zero. The total score was obtained by adding the score of each parameter [4].

STATISTICAL ANALYSIS

Statistical analysis was performed using Microsoft Excel 2021 and and stats.pvalue.io. A comparison between the cases and controls was conducted with the Welch t-test. The significance of individual parameters in the MAPH score was analysed. A p-value <0.05 was considered statistically significant. After calculating the MAPH score in cases and controls, p-values, cut-off values, and ROC analysis were performed. Finally, multivariate logistic regression analysis was conducted to evaluate the role of the MAPH score as an independent predictor of ACS.

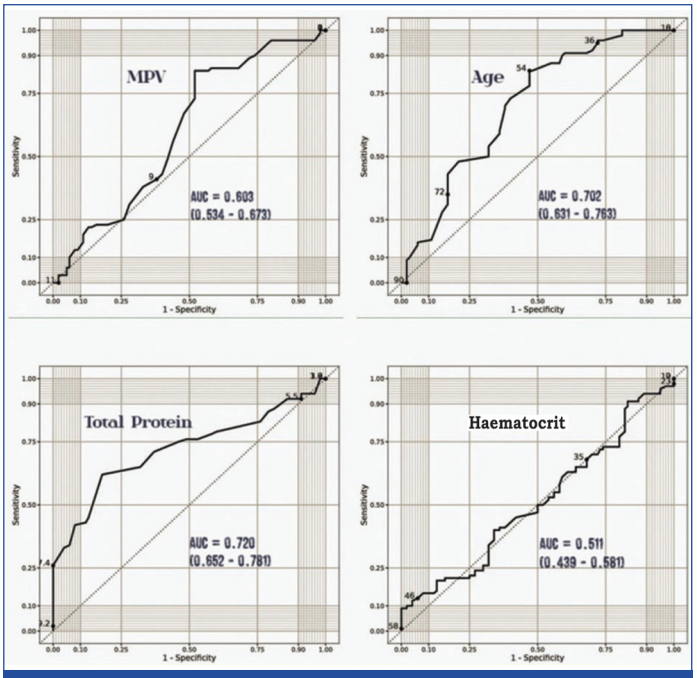
RESULTS

The current study included 100 cases of ACS and 100 controls. A male predominance was noted among the cases (n=62, 62%) and controls (n=68, 68%). Most cases were aged 71 to 80 years (n=33, 33%), followed by 61 to 70 years (n=27, 27%). The mean age of the cases with ACS (65.19±13.63 years) was higher than the control (51.22±20.27 years) group. Laboratory parameters such as MPV, total protein, and haematocrit were higher among the cases. This difference in MPV, age, and total protein was statistically significant (p-value=0.017, p-value <0.001, p-value <0.001, respectively). The statistical significance of higher haematocrit in cases was not established (p-value=0.61). The mean values and statistical significance of individual MAPH score parameters (MPV, age, total protein, and haematocrit) in cases and controls are summarised in [Table/Fig-1].

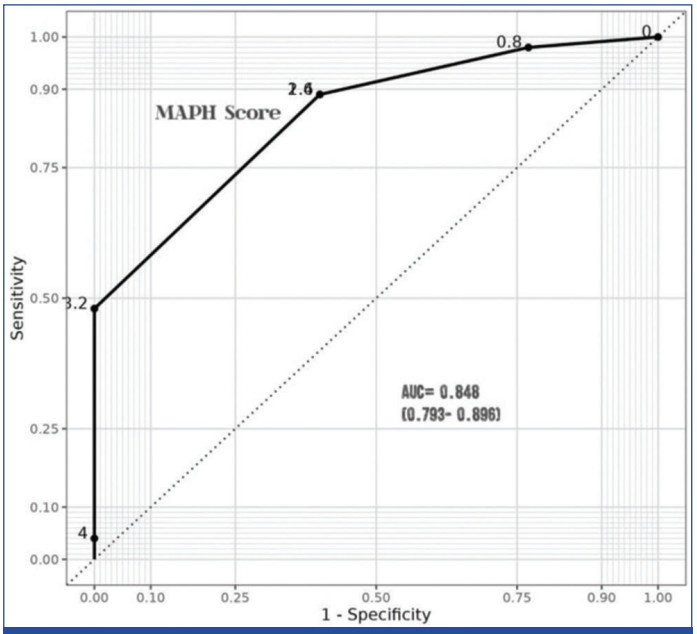
Parameters	Cases (n=100)	Controls (n=100)	p-value (Welch test)
MPV, mean±SD	8.89±0.829	8.59±0.941	0.017
Age, mean±SD	65.19±13.63	51.22±20.27	<0.001
Total protein, mean±SD	6.89±0.899	6.28±0.578	<0.001
Haematocrit, mean±SD	38.2±6.94	37.7±6.09	0.61
MAPH score, mean±SD	2.39±0.79	1.17±0.77	<0.0001

[Table/Fig-1]: MAPH score parameters in cases and control.

ROC analysis was performed on each parameter in the MAPH score [Table/Fig-2], and cut-off values to predict ACS were calculated based on the Youden index. The cut-off and Area Under the Curve (AUC) values for MPV, age, total protein, and haematocrit were (8.4 fL; 0.603), (54 years; 0.702), (6.8 g/dL; 0.720), and (49.1%; 0.511), respectively. Based on the cut-off values, the MAPH score was calculated, and ROC analysis of the MAPH score [Table/Fig-3] was performed. The mean MAPH score was higher in cases (2.39±0.79) than in the controls (1.17±0.77). This difference was found to be statistically significant (p-value <0.001). The cut-off value to predict ACS, calculated based on the Youden index, was two, and AUC was 0.848. MAPH score sensitivity was 89%, and specificity was 60% when the cut-off value was 2. The ROC curve analysis and cut-off values of the MAPH score and individual parameters, with sensitivity and specificity, are summarised in [Table/Fig-4].



[Table/Fig-2]: ROC analysis of individual parameters in MAPH score.



[Table/Fig-3]: ROC analysis of MAPH score.

Parameters	AUC	95% CI	Cut-off	Sensitivity	Specificity
MPV	0.603	0.534-0.673	8.4 fL	84%	48%
Age	0.702	0.631-0.763	54 years	84%	53%
Total protein	0.720	0.652-0.781	6.8 g/dL	62%	82%
Haematocrit	0.511	0.439-0.581	49.1 %	9%	99%
MAPH Score	0.848	0.793-0.896	2	89%	60%

[Table/Fig-4]: ROC analysis and cut-off values of MAPH score and its individual parameters.

Finally, multivariate logistic regression analysis identified the MAPH score as an independent predictor of ACS (Odds ratio 0.260 and p-value <0.001) [Table/Fig-5].

Parameters	Odds-ratio	95% CI	p-value
MPV	0.823	0.505-1.34	0.43
Age	0.967	0.938-0.994	0.022
Total protein	0.461	0.250-0.802	<0.01
Haematocrit	0.972	0.972-1.04	0.4
MAPH score	0.260	0.123-0.511	<0.001

[Table/Fig-5]: Multivariate logistic regression analysis to predict ACS.

DISCUSSION

Ischaemic Heart Disease (IHD) records a significant mortality rate, morbidity rate, and socio-economic burden in the present era. IHD has caused more than two million deaths globally in the past two decades. According to recent World Health Organisation (WHO) statistics (2019), the leading cause of death in India is IHD, accounting for 90 deaths per 100,000 female population and 130 deaths per 100,000 male population [15]. Hence, reducing the mortality and morbidity associated with IHD has to be prioritised in the current era. Researchers have identified various non modifiable risk factors for IHD and thus for ACS, which include male gender, age, genetics, and family history. A sedentary lifestyle with an unhealthy diet, smoking, obesity, diabetes mellitus, hypertension, and dyslipidaemia are the modifiable risk factors associated [16,17]. Among these risk factors, age strongly predicts mortality associated with ACS [18]. Tal S et al., and Maden O et al., observed that individuals over 65 years are at an increased risk of developing thromboembolic events [19,20]. Similarly, in the current study, 60% of the cases were aged above 60 years. Enzymatically active large platelets with an increased MPV play a crucial role in the development of atherosclerosis and ACS. Therefore, MPV is an excellent indicator for identifying patients at risk of developing ACS [21,22]. Similarly, the current study also identified a statistically significant increase in MPV in patients with ACS. Studies have reported the association between blood hyperviscosity and ACS. Higher haematocrit and high molecular weight proteins in the plasma are significant factors leading to hyperviscosity [5,7,8,23]. The current study observed a statistically significant increase in total protein in ACS, but the statistical significance of the rise in haematocrit in ACS was not established.

Incorporating the concepts of advancing age, hyperviscosity, and platelet activation, Abacioglu OO et al., put forward the new MAPH score in 2021, which helps to determine the higher thrombus burden in cases with STEMI. Their study compared various parameters between the high thrombus grade group and low thrombus grade group and found that a MAPH score of more than two predicts a high thrombus load. Similarly, the current study predicts a high-risk of ACS, which can be secondary to a high thrombus load, when the MAPH score is more than two. According to Abacioglu OO et al., the sensitivity and specificity at a MAPH score >2 were 56.3% and 92.2%, respectively. The authors also identified that the MAPH score performs better than known biomarkers, such as High Shear Rate (HSR) and Low Shear Rate (LSR) [4]. HSR and LSR are markers derived from haematocrit and total protein values, indicating serum viscosity and thrombotic tendencies [6,24].

Çakmak Karaaslan Ö et al., suggest that the MAPH score is an independent predictor of high thrombus burden in cases of NSTEMI. Their study compares various parameters between the low thrombus burden group and the high thrombus burden group. The authors identified the best cut-off value of the MAPH score as two, which yields a sensitivity and specificity of 67.9% and 69.3%, respectively. The authors also suggest that this simple scoring tool helps in choosing appropriate clinical management and decreasing adverse consequences [12]. Similarly, the current study identifies the MAPH score as an independent predictor of ACS, which can manifest as a result of a high thrombus load.

Akhan O and Kış M, consider the MAPH score an indicator of blood viscosity. Therefore, they suggest that the score can predict the Coronary Slow Flow phenomenon. Similarly, findings from the current study also imply that the MAPH score can be considered as an indicator of blood viscosity. Akhan O and Kış M, compared parameters between the coronary slow flow group and the normal flow group. According to the authors, at an MAPH score cut-off of 2.5, the sensitivity and specificity are 43% and 86%, respectively [25]. The coronary slow flow phenomenon is a unique clinical situation with specific angiographic diagnostic criteria, where there is a delay in the distal opacification of the coronaries during angiography. Several studies have identified a relationship between hyperviscosity and CSF [26-29]. The MAPH score cut-offs with sensitivity and specificity given by various studies are summarised in [Table/Fig-6] [4,12,25].

Study	Place and publication year of study	Study population with sample size	MAPH score cut-off	Sensitivity (%)	Specificity (%)
Abacioglu OO et al., [4]	Turkey, 2022	High thrombus grade (71) and Low thrombus grade (402) groups	2	56.3	92.2
Çakmak Karaaslan Ö et al., [12]	Turkey, 2022	High thrombus burden (283) and Low thrombus burden (339) groups	2	67.9	69.3
Akhan O and Kış M, [25]	Turkey, 2023	Coronary slow flow (98) and normal flow(168) groups	2.5	43	86
Current study	India, 2024	ACS (100) and control (100) groups	2	89	60

[Table/Fig-6]: Comparing the MAPH score cut-off, sensitivity and specificity with other studies [4,12,25].

Limitation(s)

The present study had limitations as it was conducted at a single institute. Therefore, multicentre prospective studies, including a more extensive study population, are needed to overcome these limitations.

CONCLUSION(S)

The MAPH score has been identified as an independent predictor of ACS. Therefore, the MAPH score can be used as a screening tool to predict and diagnose ACS in primary healthcare settings. This helps ensure early coronary revascularisation and reduces CAD-related mortality and morbidity to a greater extent.

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