International Journal of Cardiology Sciences 2025; 7(1): 98-103

ISSN Print: 2664-9020
ISSN Online: 2664-9039
Impact Factor: RJIF 5.42
IJCS 2025; 7(1): 98-103
www.cardiologyjournals.net
Received: 02-01-2025
Accepted: 06-02-2025

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The correlation and clinical outcome between H2FPEF score and thrombus burden in STEMI patient

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DOI: https://www.doi.org/10.33545/26649020.2025.v7.i1b.99

Abstract
Background: Intracoronary thrombus burden (TB) in ST elevation myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI) increases the risk of adverse outcomes. The H$_2$FPEF score, initially designed for heart failure with preserved ejection fraction (HFpEF), may help predict TB severity and clinical prognosis.
Objectives: To investigate the interplay between H$_2$FPEF score and TB in STEMI patients undergoing PCI and its impact on clinical outcomes, particularly major adverse cardiovascular events (MACE).
Methods: In this prospective observational study conducted across two centers, a total of 100 consecutive patients presenting with STEMI who underwent primary PCI at Benha University Hospital and Mataria Teaching Hospital were enrolled. Based on angiographic assessment, participants were stratified into two groups: low TB (Grades 1–3) and high TB (Grades 4–5).
Results: Hypertension (HTN) was substantially more prevalent in the high TB group ($P = 0.011$). The H$_2$FPEF score was significantly higher in the high TB group ($P = 0.03$). MACE incidence was 25% in high TB patients vs. 7.5% in low TB patients ($P = 0.026$). ROC analysis identified an H$_2$FPEF score >2 as a predictor of high TB ($AUC = 0.694$, $P = 0.001$) and MACE ($AUC = 0.744$, $P = 0.004$). Multivariate regression confirmed H$_2$FPEF as an independent predictor of high TB ($OR = 1.958$, $P = 0.006$).
Conclusions: The H2FPEF scoring system holds clinical utility in predicting both TB and MACE in patients with STEMI, with scores above 2 effectively delineating high-risk cases.

Keywords: H$_2$FPEF score, Thrombus burden, STEMI, MACE

Introduction

ST-elevation myocardial infarction (STEMI) represents the most common subtype of MI and remains a leading cause of mortality among individuals with cardiovascular disease. PCI has been documented as the preferred therapeutic approach over fibrinolysis, offering superior outcomes in reducing mortality and rates of reinfarction. Nevertheless, despite successful PCI, STEMI patients often continue to face various physical and psychological complications, with all-cause mortality remaining a significant concern [1].

Primary PCI remains the cornerstone of treatment for STEMI; however, its efficacy may be limited in the presence of a substantial intracoronary thrombus. Despite advancements in potent antiplatelet and anticoagulant therapies, intracoronary thrombus continues to pose significant risks, including distal embolization, stent thrombosis, no-reflow phenomenon, and adverse long-term cardiovascular outcomes [2].

The H$_2$FPEF score is current; however, it helps distinguish between non-cardiac reasons and preserved ejection fractional heart failure as the etiological cause of unexplained shortness of breath. Clinical (age, obesity, hypertension "HTN", and atrial fibrillation "AF") and echocardiographic data (systolic pulmonary artery "sPAP" and left ventricular "LV" filling pressure indicators) are used to calculate the H$_2$FPEF score [3].

Several investigations have established links between these individual variables and the extent and intricacy of CAD, in addition to their relationship with unfavorable cardiovascular events [4, 5].

As far as can be ascertained from existing literature, no prior research has specifically examined the association between the H2FPEF score and TB in patients presenting with STEMI, nor its potential impact on clinical outcomes. Therefore, this investigation aims to investigate relation between the H2FPEF score and TB in STEMI patients and to evaluate its potential as a prognostic indicator.

Patients and methods

Study design and population

Conducted across two centers, this prospective observational study took place at the Cardiology Department of Benha University and Mataria Teaching Hospital from August 2023 to December 2024. The study included 100 consecutive STEMI patients undergoing primary PCI, who were categorized into 2 groups according to TB: 60 patients with high TB and 40 with low TB.

Patient Selection

All subjects aged above 18 years, regardless of sex, were eligible for inclusion upon meeting the diagnostic standards for STEMI, which included ST-segment elevation in at least two contiguous leads (≥2 mm in precordial leads, ≥1 mm in limb leads), new-onset left bundle branch block (LBBB), ischemic chest pain lasting more than 30 minutes, and elevated cardiac biomarkers (CK-MB and troponin) at least twice the upper reference limit [6].

Patients were excluded if they had a history of CABG, valve surgery, or prior PCI. Additional exclusion criteria included heart failure with LVEF ≤40%, history of stroke, chronic kidney disease (eGFR <30 ml/min/1.73m²), active infection, coagulopathy, or malignancy. Patients with mitral annular calcification, chronic pulmonary embolism, pulmonary HTN, permanent pacemakers, moderate-to-severe valvular disease, mitral valve repair, or prosthetic valves were also excluded.

Methods

All patients were subjected to detailed assessment, including age, gender, and cardiovascular risk factors such as HTN, dyslipidemia, diabetes mellitus (DM), smoking, and family history of CAD. Previous medical conditions, including prior cardiovascular interventions and cerebrovascular events, were recorded along with current medication use.

Echocardiography

Echocardiography was conducted using a Vivid 7 Pro device (GE, Vingmed, Horten, Norway), with patients positioned in the left lateral decubitus. Images were digitally stored for offline analysis. Echocardiographic measurements were obtained and analyzed following the standards outlined by the American Society of Echocardiography. [7] Stroke volume (SV) was measured by subtracting LVESV from LVEDV, then LVEF was calculated through this formula: LVEF = (SV/EDV) × 100. sPAP was calculated using the following formula sPAP = 4 × (highest tricuspid regurgitation velocity)² + right atrial pressure. LV filling pressures were estimated using the E/e′ ratio, E; representing early mitral flow velocity and e′; early diastolic mitral annular velocity [7].

H_2FPEF Score Calculation

H_2FPEF score was determined using Reddy *et al.* [3] scoring system, incorporating obesity (Body mass index "BMI" >30 kg/m² = 2 points), HTN (≥2 antihypertensive medications = 1 point), AF (paroxysmal or persistent = 3 points), age >60 years (1 point), pulmonary HTN (sPAP >35 mmHg = 1 point), and elevated LV filling pressure (E/e′ >9 = 1 point) [8].

Coronary Angiography

Primary PCI was performed using the Judkins technique via femoral or radial access, with angiographic images recorded in multiple projections to ensure a comprehensive assessment of coronary anatomy. Two independent cardiologists evaluated the TB, which was classified according to Sianos *et al*. grading [9]. The classification included grade 0, indicating the absence of thrombus, and grade 1, representing a possible thrombus with features such as irregular lesion contour, turbidity, or reduced contrast density. Grade 2 was assigned when thrombus occupied less than half of the vessel diameter, whereas grade 3 referred to thrombus dimensions exceeding half but remaining less than two vessel diameters. Grade 4 was defined by a thrombus extending beyond two vessel diameters, and grade 5 indicated total vessel occlusion due to thrombus. Based on this classification, patients were categorized into low TB (Grades 1–3) and high TB (Grades 4–5) groups.

Follow-Up and Outcome Assessment

Coronary flow post-PCI was assessed using the TIMI grading system, with impaired flow defined as TIMI <3. In-hospital outcomes included acute heart failure (Killip 2–3), cardiogenic shock (Killip 4), malignant arrhythmias, and recurrent AMI, diagnosed by clinical symptoms, ECG changes, and biomarker re-elevation [10]. Six-month follow-up evaluated MACE defined as a composite of total mortality, MI, stroke, and HF-related hospitalizations [11].

Statistical methods

Data analysis was conducted using IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY, USA). To determine the distribution pattern of continuous data, the Shapiro–Wilk test was applied. Based on the results, data were described as mean ± standard deviation or median with range, as appropriate. Frequencies and percentages were used to summarize categorical data. Depending on the distribution pattern, comparisons of quantitative variables were performed using either the independent samples t-test or the Mann–Whitney U test. Categorical comparisons were performed using the Chi-square or Fisher's exact test, as appropriate. ROC curve analysis was employed to determine the discriminatory ability of the H2FPEF score for predicting high TB levels, including calculation of the AUC, optimal threshold, and diagnostic accuracy measures. Correlations were examined using Spearman's rank correlation coefficient. Logistic regression models—both univariate and multivariate—were constructed to identify predictors of elevated TB, presenting results as ORs with 95% confidence intervals. Results were deemed statistically significant at a threshold of $p < 0.05$.

Results

HTN was significantly more frequent in high TB group (88.3% vs. 67.5%, P = 0.011). Other variables, including age (P = 0.744), gender (P = 1), DM (P = 0.868), dyslipidemia (P = 0.218), smoking (P = 1), family history (P = 1), heart rate (P = 0.729), systolic blood pressure (P =

0.864), diastolic blood pressure (P = 0.671), and BMI (P = 0.181), showed no substantial variations between the groups (Table 1).

Most of the patients with high TB had an intermediate H_2FPEF score. However, patients with low TB had intermediate and low H_2FPEF score (P = 0.03). Other echocardiographic parameters, including LVEF (P = 0.444), pulmonary artery systolic pressure (P = 0.105), E/e′ ratio (P = 0.408), and the presence of wall motion abnormalities (P = 0.868), showed no significant differences. Additionally, no significant differences were found regarding the number of stents deployed (P = 0.918), stent type, or TIMI flow post-PCI (P = 0.6) (Table 2 and Figure 1).

Six months MACE was substantially higher in high TB group (25% vs.7.5%, P = 0.026). However, no notable variations were detected between the groups regarding in-hospital outcomes, including heart failure, shock (P = 0.645), malignant arrhythmia (P = 0.148), stroke (P = 1.0), re-infarction (P = 1.0), and mortality (P = 1.0). Similarly, no significant differences were found in long-term outcomes, including heart failure (P = 0.273), shock (P = 1.0), malignant arrhythmias, stroke (P = 0.648), re-infarction (P = 0.309), and mortality (P = 0.515) (Table 3).

Univariate analysis revealed that HTN (OR = 3.646, 95% CI: 1.303–10.202, P = 0.014) and H_2FPEF score (OR = 1.748, 95% CI: 1.238–2.469, P = 0.002) were significant predictors of high TB, indicating that a higher score increased the likelihood of high TB. However, multivariate analysis showed that H_2FPEF score is a significant independent predictor with an increased OR (OR = 1.958, 95% CI: 1.21–3.168, P = 0.006), demonstrating its strong association with the outcome after adjusting for other variables (Figure 2).

Receiver operating characteristic (ROC) curve analysis was conducted to assess the ability of the H2FPEF score to discriminate cases with high TB. It showed a significant AUC of 0.694 (95% CI: 0.591–0.797, P = 0.001). The best cutoff point was >2, yielding a sensitivity of 46.7%, specificity of 85%, PPV of 82.5%, and NPV of 51.5%.

Patients with high TB were classified according to MACE. Those with MACE had significantly higher H_2FPEF score (P= 0.004). Additionally, ROC analysis was done to assess the diagnostic accuracy of H_2FPEF score for predicting MACE in high TB patients. It demonstrated a significant AUC of 0.744 (95% CI: 0.591–0.897, P = 0.004). The best cutoff point was >4, with 60% sensitivity, 86.6% specificity, 60% PPV, and 86.7% NPV (Figure 3).

Discussion

Despite the improvements in primary PCI techniques, managing a significant intracoronary thrombus burden in STEMI remains challenging, as it predisposes patients to no-reflow, stent thrombosis, and adverse cardiovascular outcomes [12]. Identifying high-risk patients early is crucial for optimizing management and improving outcomes, so we aim to assess interrelation between the H_2FPEF score and TB in STEMI patients undergoing PCI.

The present study revealed that most STEMI patients with high TB had intermediate H_2FPEF score. However, those with low TB had low and intermediate H_2FPEF score. Moreover, univariate regression analysis identified HTN and H_2FPEF score as significant predictors of high TB. Multivariate regression analysis revealed that H_2FPEF score is the significant independent predictor of TB. ROC analysis confirmed that H_2FPEF score is a predictor of high TB, with a cut-off >2 demonstrating high specificity and PPV, making it useful for identifying high-risk patients. However, its lower sensitivity and NPV limit its effectiveness in ruling out low-risk cases. Similarly, Kucuk and Volina [13] revealed a substantial relationship between H_2FPEF score and TB. Also, they found that H_2FPEF score and red cell distribution width (RDW) were significant predictors of high TB. Their ROC analysis (AUC = 0.724) showed 78% sensitivity and 50% specificity at a cut-off ≥2 for predicting HTB, reinforcing the H_2FPEF score's role in thrombotic risk assessment.

In the current study, higher incidence of MACE in patients with high TB highlights its role in predicting adverse outcomes. This may be attributed to an increased risk of stent thrombosis, impaired coronary perfusion, and persistent inflammation, which contribute to worse clinical prognosis. A finding consistent with Scarparo *et al*.[14] who demonstrated that high TB was associated with worse long-term outcomes, including higher 10-year mortality (aHR 2.27, 95% CI: 1.42–3.63; p = 0.001) and 10-year MACE (aHR 1.46, 95% CI: 1.03–2.08; p = 0.033). Additionally, HTB was linked to increased 30-day mortality (aHR 5.60, 95% CI: 2.49–12.61; $p < 0.001$) and 30-day MACE (aHR 2.72, 95% CI: 1.45–5.08; p = 0.002) in STEMI patients undergoing PCI. Also, Jin *et al*. [15] found that a higher H_2FPEF score was substantially related with an elevated incidence of HF-related events (33.8%) and acute coronary syndromes (ACS, 19.5%) over a 40-month follow-up. The H_2FPEF score predicted HF-related events (AUC: 0.723) and ACS (AUC: 0.670), with a cut-off score of 6.5 identified as a threshold for adverse cardiovascular events.

Patients with high TB who developed MACE during follow up had significantly higher H_2FPEF score. ROC curve identified H_2FPEF score cut-off value of >4 to predict MACE in patients with high TB. Therefore, we can use this simple, non-invasive score in risk stratification and predicting MACE in this group of patients. To date, no comprehensive or widely acknowledged study has directly explored the link between the H2FPEF score and major adverse cardiovascular events among individuals with STEMI.

Limitations

This study is limited by its small sample size, single ethnic population, and short follow-up period, which may affect generalizability of data. Further validation through large-scale, multicenter studies is warranted.

Table 1: General characteristics according to thrombus burden

Characteristics	Total	Thrombus burden		P-value
		Low (n = 40)	High (n = 60)	
Age (years)	57 ±12	58 ±11	57 ±12	0.744
Gender				
Males	80 (80)	32 (80)	48 (80)	1.0
Females	20 (20)	8 (20)	12 (20)	
Hypertension	80 (80)	27 (67.5)	53 (88.3)	0.011*
Diabetes mellitus	59 (59)	24 (60)	35 (58.3)	0.868
Dyslipidemia	55 (55)	25 (62.5)	30 (50)	0.218
Smoking	75 (75)	30 (75)	45 (75)	1.0
Family history	35 (35)	14 (35)	21 (35)	1.0
Heart rate, bpm	79±11	80±12	79±11	0.729
Systolic blood pressure, mmHg	129±19	129±20	129±18	0.864
Diastolic blood pressure,mmHg	76±7	76±7	76±6	0.671
Body mass index, Kg/m^2	27 ±2	26 ±2	27 ±3	0.181

Data were presented as mean ±SD or n (%), *Significant P-value; SD: Standard deviation; n: Number; %: Percentage.

Table 2: Echocardiographic and angiographic findings according to thrombus burden

Characteristics	Total	Thrombus burden		P-value
		Low (n = 40)	High (n = 60)	
LVEF, %	0.5877 ±0.0667	0.594 ±0.069	0.5835 ±0.0654	0.444
PASP, mmHg	31 ±5	30 ±4	32 ±6	0.105
E/e	7 ±2	7 ±2	7 ±2	0.408
Wall Motion abnormality	59 (59)	24 (60)	35 (58.3)	0.868
H2FPEF	2 (0 - 6)	2 (0 - 5)	2 (0 - 6)	
Low (0 – 1)	32 (32.0)	18 (45.0)	14 (23.3)	0.03*
Intermediate (2 – 5)	64 (64.0)	22 (55.0)	42 (70.0)	
High (≥ 6)	4 (4.0)	0 (0.0)	4 (6.7)	
No of stent deployed				
No stent	12 (12)	6 (15)	6 (10)	0.918
One	66 (66)	26 (65)	40 (66.7)	
Two	19 (19)	7 (17.5)	12 (20)	
Three	3 (3)	1 (2.5)	2 (3.3)	
Type of stent				
DES	88 (100)	34 (100)	54 (100)	-
Result of PCI				
TIMI 0	2 (2)	0 (0)	2 (3.3)	0.6
TIMI I	1 (1)	0 (0)	1 (1.7)	
TIMI II	10 (10)	3 (7.5)	7 (11.7)	
TIMI III	87 (87)	37 (92.5)	50 (83.3)	

Data were presented as mean ±SD, median (range) or n (%), *Significant P-value; LVEF: Left ventricular ejection fraction; PASP: Pulmonary artery systolic pressure; E/e: Ratio of early diastolic mitral inflow velocity to early diastolic mitral annular velocity; DES: Drug-eluting stent; PCI: percutaneous coronary intervention; TIMI: Thrombolysis in Myocardial Infarction.

Table 3: In-hospital and long-term outcomes according to thrombus burden

Characteristics	Total	Thrombus burden		P-value
		Low (n = 40)	High (n = 60)	
In-hospital outcome				
Heart failure	0 (0)	0 (0)	0 (0)	-
Shock	5 (5)	1 (2.5)	4 (6.7)	0.645
Malignant arrhythmia	4 (4)	0 (0)	4 (6.7)	0.148
Stroke	1 (1)	0 (0)	1 (1.7)	1.0
Re-infarction	1 (1)	0 (0)	1 (1.7)	1.0
mortality	5 (5)	2 (5)	3 (5)	1.0
long-term outcome				
Heart failure	3 (3)	0 (0)	3 (5)	0.273
Shock	1 (1)	0 (0)	1 (1.7)	1
Malignant arrhythmias	0 (0)	0 (0)	0 (0)	-
Stroke	4 (4)	1 (2.5)	3 (5)	0.648
Re-infarction	9 (9)	2 (5)	7 (11.7)	0.309
mortality	2 (2)	0 (0)	2 (3.3)	0.515
MACE	18 (18)	3 (7.5)	15 (25)	0.026*

Data were presented as n (%) *Significant P-value; MACE: Major adverse cardiac events

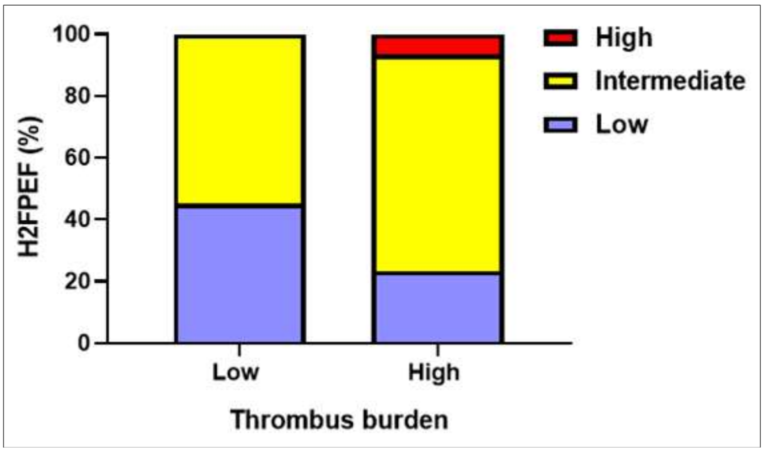

Fig 1: H_2FPEF according to thrombus grading in the studied patients

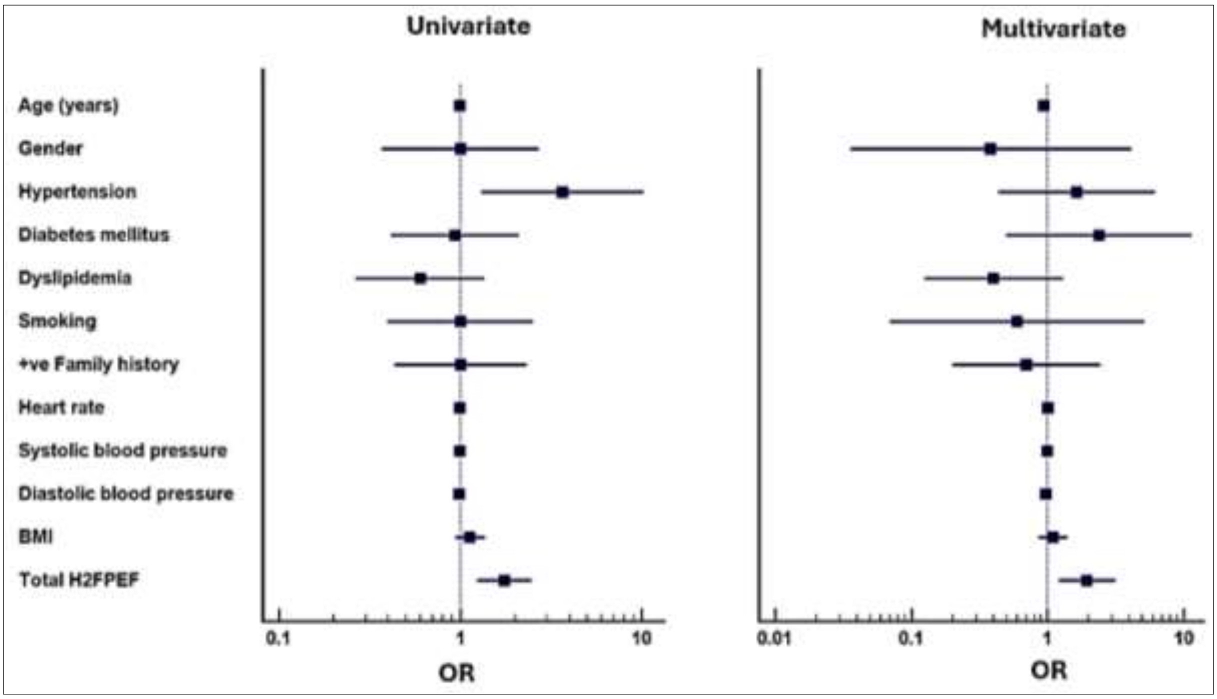

Fig 2: Univariate and multivariate logistic regression analysis to predict high thrombus grade.

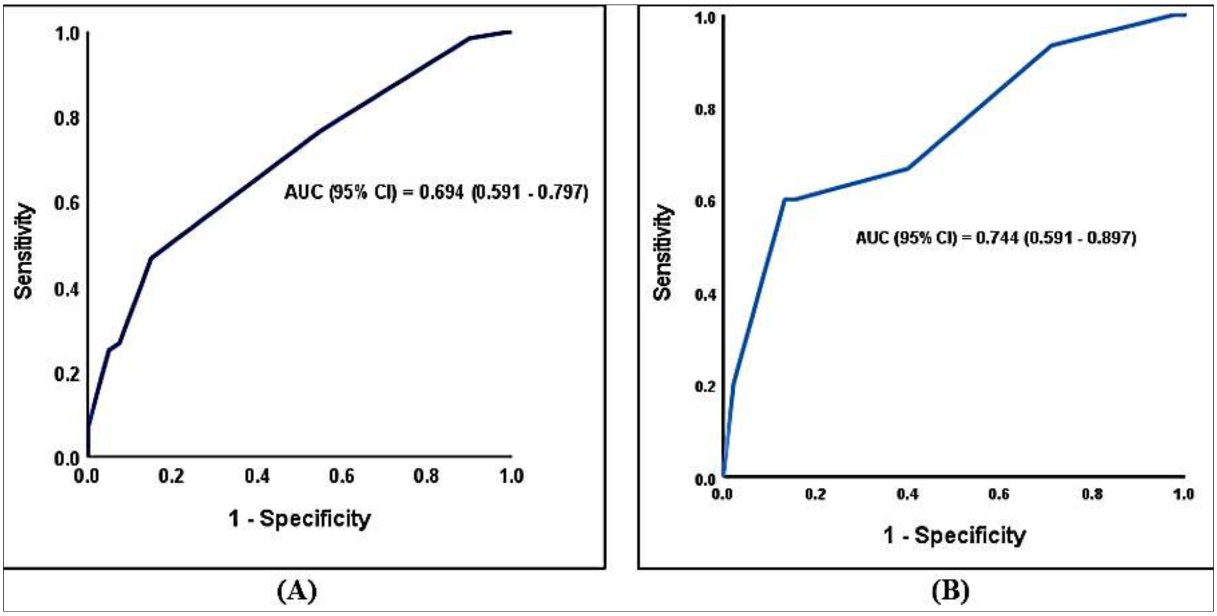

Fig 3: ROC analysis of (A) H2FPEF to predict high thrombus grade and (B) to predict MACE in patients with high thrombus burden.

Conclusions

The H_2FPEF score is a significant predictor of TB and MACE in STEMI patients, with a score >2 effectively identifying high-risk individuals. Integrating H2FPEF score evaluation into the management of STEMI may facilitate more precise risk stratification and guide therapeutic strategies aimed at optimizing patient outcomes.

Ethical statement

The study was approved by the institutional Ethics Committee of Benha Faculty of Medicine, Approval No. MS 29-7-2023

Financial support and sponsorship

Nil.

Conflict of interest

None.

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How to Cite This Article
Sabry ASM, Abo-Elazm TH, Lebda NMA, Abd Al-Naby MS. The correlation and clinical outcome between H2FPEF score and thrombus burden in STEMI patient. International Journal of Cardiology Sciences 2025; 7(1): 98-103.