The Relationship between H2FPEF Score and Thrombus Burden in Patients with ST Elevation Myocardial Infarction

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Abstract

Background and Aim: The presence of intracoronary thrombus (ICT) is known to be associated with poor clinical outcomes, including death, in patients diagnosed with ST-segment elevated myocardial infarction (STEMI). Despite this, the predictors of ICT are still uncertain. The aim of our study was to investigate the relationship between thrombus burden (TB) and obesity (H), hypertension (H), atrial fibrillation (F), pulmonary hypertension (P), an age >60 years (E), and E/e' > 9 (F) (H2FPEF) score in STEMI patients. **Methods:** One hundred consecutive STEMI patients were included in the study. Patients were divided into two groups according to the low TB (grades 0–3) and high TB (HTB) (grades 4 and 5) in comparison with the TB grade before percutaneous coronary intervention in coronary angiographic imaging. H2FPEF score was calculated for all patients. **Results:** The H2FPEF score was higher in the HTB group (2.94 ± 1.68 vs. 1.62 ± 1.15, $P < 0.001$). In STEMI patients, the red cell distribution width (odds ratio [OR]: 2.443, 95% confidence interval [CI]: 1.382–4.316; $P = 0.002$) and H2FPEF score (OR: 2.360, 95% CI: 1.447–3.847; $P = 0.001$) were independent predictors of HTB. H2FPEF score above a cutoff level of two predicted HTB with a sensitivity of 78% and a specificity of 50%. **Conclusion:** H2FPEF score may be used as a useful score in predicting HTB in STEMI patients.

Keywords: H2FPEF score, ST-segment elevated myocardial infarction, thrombus burden

Introduction

Increased cardiac risk factors cause an increase in the incidence of ST-elevated myocardial infarction (STEMI).[1] Although primary percutaneous coronary intervention (PCI) is applied in most centers, STEMI is still a common cause of death worldwide.[2] Early risk classification of patients will have positive effects on risk reduction with appropriate therapeutic options in future.[3] The Synergy between Percutaneous Coronary Intervention (SYNTAX) score is useful in predicting the success of the revascularization (surgical or percutaneous invasive intervention) planned to be performed according to the angiographic anatomical results of the patients and the prognosis of the patients. Furthermore, it provides information about the prevalence and complexity of coronary artery disease (CAD).[4] Although there are plans for treatment strategies, the presence of an intracoronary thrombus (ICT) is a risk factor for stent thrombosis and recurrent infarctions in the short and long term, as well as complications such as spasm in the coronary arteries, lack of flow, and distal embolization in patients with an angiographic thrombus.[5]

While the H2FPEF score is current, it is useful in the etiological distinguishing of unexplained shortness of breath (preserved ejection fractionated heart failure or non-cardiac causes). The H2FPEF score consists of a combination of clinical and echocardiographic data (left ventricular (LV) filling and pulmonary artery systolic pressure indicators) such as obesity, hypertension (HT), age, and atrial fibrillation (AF).[6] Several

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studies conducted separately with these parameters have shown the severity and complexity of CAD and its association with adverse events.[7-9]

As far as we know, there is no study investigating the relationship between the thrombus burden (TB) and the H2FPEF score in STEMI patients. Therefore, in our study, we aimed to investigate the relationship between TB and H2FPEF scores in STEMI patients.

Methods

Patient population

One hundred consecutive patients who underwent coronary angiography with the diagnosis of STEMI were included in the study. The diagnosis of STEMI was made in patients consulting with chest pain in at least two adjacent derivations and patients with ST-segment elevation measured from the J point in 12-lead electrocardiography (ECG) (≥2.5 mm in males <40 years of age in V2-V3 derivations, ≥2 mm in males over 40 years of age, ≥1.5 mm in females over 40 years of age, and/or ≥1 mm in other derivations (in the absence of LV hypertrophy or left bundle branch block).[10]

Patients with a history of coronary artery bypass grafting (CABG), valve surgery, PCI, or diagnosed heart failure with reduced LV function (LV ejection fraction [LVEF] ≤40%), history of stroke, chronic kidney disease (estimated glomerular filtration rate <30 (ml/min/1.73 m^2), an active infection, known coagulopathy, malignancy, chronic pulmonary embolism, diagnosis of pulmonary HT, regular alcohol use (>20 g/day), chronic obstructive pulmonary disease, permanent heart pacemaker or mitral annular calcification, moderate heart valve disease, mitral valve repair or a prosthetic valve, thyroid dysfunction, pre-PCI resuscitation, upper segment elevation or depression in the aVR lead, and receiving thrombolytic therapy or under 18 years of age were not included in the study.

The hospital's electronic medical records were used to obtain the data on patients' laboratory values. This study received the ethical committee's approval (decision no: 2022-YÖNP-0019), and it was conducted according to the Declaration of Helsinki.

Blood analysis

Blood samples were taken from antecubital peripheral veins at the time of admission. All hematological parameters were studied using a Mindray BC-6000 (Mindray Co., Shenzhen, China) hematology device. Biochemical parameters were studied using a Roche COBAS c 701 (Roche Diagnostics, GmbH, Mannheim, Germany) device. The lipid profile was studied within the first 24 h following 12 h of fasting.

Echocardiographic imaging protocol

Blood pressure (BP) levels were measured just before starting echocardiographic imaging. Echocardiographic examinations were performed following the patients' BP measurements. All patients underwent echocardiographic examinations by connecting simultaneous ECG using a Vivid 7 Pro device (GE, Vingmed, Horten, Norway). Echocardiographic measurements were performed in the left lateral position. The LVEF was calculated using the modified Simpson formula. Systolic pulmonary artery pressure (sPAP) was calculated using the formula sPAP = 4 × (highest tricuspid regurgitation rate)^2 + right atrial pressure. LV filling pressures were obtained by the ratio of early mitral flow rate (E) to early diastolic mitral annular tissue rate (e ̀).[11]

H2FPEF score

When calculating the H2FPEF score, six parameters were used, and the calculation was made as in the literature (obesity 2 points, AF 3 points, and other parameters 1 point).[12]

1 – Obesity (body mass index >30 kg/m^2)
2 – Age >60
3 – AF
4 – Use of 2 or more antihypertensive drugs
5 – Pulmonary artery systolic pressure >35 mmHg
6 – E/e ̀>9.

Coronary angiography and thrombus burden classification

Coronary angiographies (GE Healthcare Innova 2100, New Jersey, USA) were performed by an experienced cardiologist using the standard Judkins technique and iobitridol (Xenetix-350, Guerbet BP, France) with the femoral or radial approach. Angiographic images were evaluated by two experienced cardiologists with the digital system for a quantitative analysis of images obtained from at least two different angles.

The angiographic TB was classified as in the literature:[13] grade 0: No thrombus, grade 1: A possible thrombus (turbidity, irregular lesion contour, and reduced contrast intensity), grade 2: The presence of a thrombus with a vessel diameter of <½ in multiple angiographic projections, grade 3: The presence of a thrombus with vessel diameter of >½ and <2 in multiple angiographic projections, grade 4: The presence of a thrombus with vessel diameter of >2 in multiple angiographic projections, and grade 5: Obstruction of the entire thrombus and vessel. The patients were divided into two groups according to low-TB (LTB) (grades 0–3) and high-TB (HTB) groups (grades 4 and 5).

Statistical analysis

An SPSS 19.0 (SPSS Inc., Chicago, IL, USA) application was used for statistical analysis. The distribution of continuous variables was evaluated using the Kolmogorov–Smirnov test. Data were presented as mean ± standard deviation or median (interquartile range). Categorical variables are expressed as percentages and numbers. A *t*-test and the Mann–Whitney U-test or Kruskal–Wallis tests were used to compare normal and nonnormally distributed parameters, respectively. The Chi-square or Fisher's exact tests were used to compare the probability ratios of categorical variables. Single and multiple logistic regression analyses were performed to predict HTB in STEMI patients. The Hosmer–Lemeshow test was used to evaluate the model fit. Receiver operating characteristic (ROC) curves were created for HTB of H2FPEF, and cutoff values were determined. *P* values were found statistically significant <0.05.

Ethical statement

The study approval was obtained from the Ethics Committee of Clinical Research of Canakkale Onsekiz Mart University (Date: 2022.04.27 and Decision no: 2022-YÖNP-0019). The study was performed in accordance with the Declaration of Helsinki.

Results

Our study consisted of a total of 100 patients diagnosed with STEMI, 76 males and 24 females. The mean age was 63.98 ± 9.18 years in the HTB group, the mean age was 62.20 ± 10.25 years in the LTB group. A high red cell distribution width (RDW) (14.69 ± 1.25 vs. 13.92 ± 0.99, $P = 0.001$) and a high H2FPEF score (2.94 ± 1.68 vs. 1.62 ± 1.15, $P < 0.001$) were found in the HTB group. Our study groups mostly had proximal left anterior descending coronary artery (LAD) lesions. The number of our patients with LAD bifurcation lesions was three patients and it was not statistically significant. As shown in Table 1, there were no statistical differences between the groups in terms of other routine serum biomarkers. The demographic and laboratory data of the patients are shown in Table 1.

As shown in Table 2, a statistically significant relationship was observed between the H2FPEF score and TB ($P < 0.001$). When the H2FPEF score was divided into three groups according to low (0–1), medium (2–5), and high (≥6) scores, it was seen that 35, 60, and five patients were distributed among the groups, respectively [Table 2].

As a result of the univariate analysis of the variables for predicting HTB, RDW (odds ratio [OR]: 1.989, 95% confidence interval [CI]: 1.1269–3.116; $P = 0.003$), Killip status (OR: 11.294, 95% CI: 2.435–52.379; $P = 0.002$), and the H2FPEF score were found as (OR: 1.937, 95% CI: 1.371–2.738; $P < 0.001$), whereas RDW (OR: 2.443, 95% CI: 1.382–4.316; $P = 0.002$) and the H2FPEF score (OR: 2.360, 95% CI: 1.447–3.847; $P = 0.001$) were found to be significant in multivariate analysis. In the Hosmer–Lemeshow test ($\chi^2 = 9.60$, $P = 0.294$), there was a good model fit [Table 3]. The H2FPEF score was significantly higher in patients with a HTB (2.94 ± 1.68 vs. 1.62 ± 1.15; $P < 0.001$) [Figure 1].

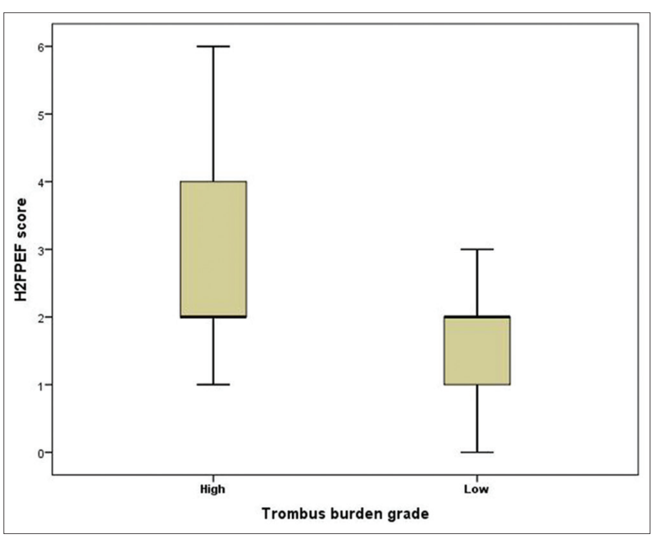

Figure 1: H2FPEF score values according to thrombus burden grade

ROC curve analysis was performed to evaluate the H2FPEF score in predicting HTB. The cutoff value of HTB ≥2 (area under the curve: 0.724, 95% CI 0.626–0.822, $P < 0.001$ with 78% sensitivity and 50% specificity) [Figure 2].

A significant increase in H2FPEF score was observed for the responsible lesion LAD or RCA ($P < 0.001$) and right coronary artery (RCA) or circumflex artery (CX) ($P = 0.037$) differentiation [Figure 3].

Discussion

The important findings of our study related to the TB of the H2FPEF score in STEMI patients were as follows: (1) higher H2FPEF score values were found in the HTB group; (2) the H2FPEF score and RDW were found to be independent predictors of HTB in STEMI patients; (3) the H2FPEF score had a sensitivity of 78%, a specificity of 50%, and an AUC of 0.72 for predicting a HTB.

Early PCI is the recommended revascularization method in STEMI patients.[14] Emergency revascularization plays a key role in the perfusion of myocardial tissue since inadequate perfusion can be presented with various clinical outcomes ranging from an increase in infarction sizes to heart failure.[15,16] STEMI is a process that continues with the formation of a thrombus following the rupture or erosion of the atherosclerotic plaque in the epicardial coronary arteries.[17] An ICT burden is associated with poor clinical outcomes including decreased ventricular functions, increased infarction dimensions, stent

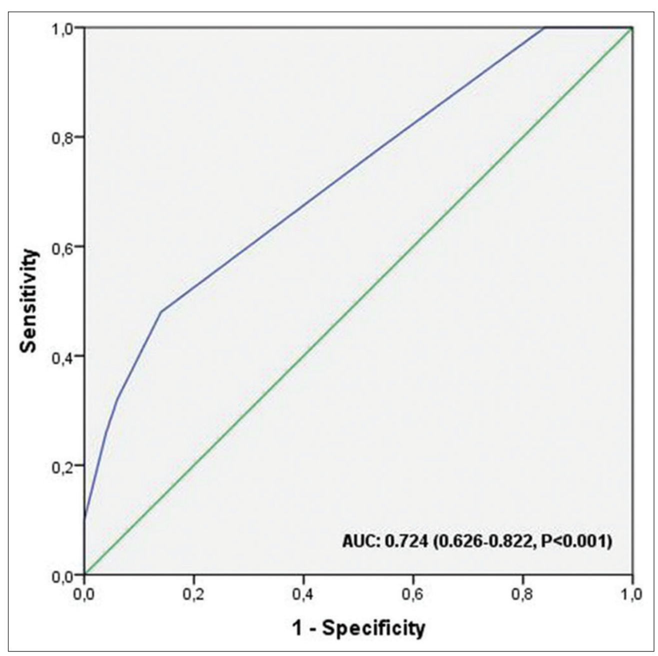

Figure 2: Receiver operating characteristic curves for H2FPEF score values for the prediction of thrombus burden grade

Table 1: Demographic, clinical, laboratory, and angiographic features of patients

	HTB (n=50), n (%)	LTB (n=50), n (%)	P
H2FPEF score	2.94±1.68	1.62±1.15	<0.001
Age (years)	63.98±9.18	62.20±10.25	0.363
Gender (male/female)	39/11	37/13	0.640
BMI (kg/m^2)	24.88±1.46	25.14±1.52	0.387
Smoking	18 (36)	20 (40)	0.680
Hypertension	27 (54)	29 (58)	0.687
Diabetes mellitus	15 (30)	14 (28)	0.826
Family history of CAD	8 (16)	3 (6)	0.110
SBP (mmHg)	104.58±19.42	107.44±20.71	0.478
DBP (mmHg)	81.66±7.71	80.60±7.80	0.521
Laboratory data			
Glucose (mg/dl)	113 (922.25-172)	105.5 (91-125.2)	0.387
Creatinine (mg/dl)	0.86±0.15	0.81±0.14	0.091
Hemoglobin (g/dl)	12.69±2.29	13.17±1.89	0.252
WBC count (10^9/L)	8.03±2.15	8.31±2.15	0.522
Platelet count (10^9/L)	259.12±93.33	252.82±56.68	0.685
Red cell distribution width (%)	14.69±1.25	13.92±0.99	0.001
LDL-cholesterol (mg/dl)	113.4 (77.9-160)	114.3 (83.7-142.9)	0.962
HDL-cholesterol (mg/dl)	41.80±13.10	41.67±10.50	0.956
Triglyceride (mg/dl)	106.15 (84.1-136.9)	118.5 (99.1-149.7)	0.152
Cardiac Tn (ng/L)	43.5 (22-63)	39.2 (23.5-73.3)	0.588
Angiographic data			
IRA			
LAD	33 (66)	38 (76)	0.403
LCX	5 (10)	2 (4)	
RCA	12 (24)	10 (20)	
Killip II-IV	11 (22)	7 (14)	0.298
Pain to balloon time (min)	275 (133.75-354.75)	200 (120-320)	0.141
Echocardiographic data			
LVEF (%)	48.3±4.88	49.9±6.84	0.187
LVEDD (mm)	39.9±9.3	40.3±9.2	0.830
LVESD (mm)	27.6±6.2	28±6.1	0.710
LA (mm)	28.8±5.4	29.9±5.49	0.327
RA (mm)	24±7.51	22.6±6.08	0.310
IVS (mm)	11.8±1.1	11.4±1.3	0.211
PW (mm)	8.3±0.8	8.5±0.9	0.441
Medical therapy before admission			
Aspirin	28 (56)	25 (50)	0.548
Antiplatelet	3 (6)	2 (4)	0.646
Beta-blocker	4 (8)	9 (18)	0.137
Statin	6 (12)	4 (8)	0.505
ACEI/ARB	10 (20)	4 (8)	0.084

BMI: Body mass index, CAD: Coronary artery disease, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, WBC: White blood cell, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, Tn: Troponin, IRA: Infarct-related artery, LAD: Left anterior descending artery, LCx: Left circumflex artery, RCA: Right coronary artery, LVEF: Left ventricular ejection fraction, LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, LA: Left atrium, RA: Right atrium, IVS: Interventricular septum, PW: Posterior wall, ACEI: Angiotensinogen converting enzyme inhibitor, ARB: Angiotensin receptor blocker, LTB: Low thrombus burden, HTB: High thrombus burden, H2FPEF: Obesity (H), hypertension (H), atrial fibrillation (F), pulmonary hypertension (P), an age >60 years (E), and E/e' > 9 (F)

thrombosis, and increased mortality. In addition, a HTB is associated with increased 30-day mortality in STEMI patients.[18,19] The pathogenesis of ICT development has not been fully understood. It is known that inflammation, in particular, triggers plaque rupture and thrombus formation.[20] HTB may cause distal embolization as well as undesirable complications due to decreased epicardial blood flow and lead to a decrease in the success of the procedure. In addition to all these, RDW, which was simply obtained from hemogram values, was shown to be associated with TB in STEMI patients, and similar results were obtained in our study results.[21] In a study of STEMI and non-ST-segment elevation myocardial infarction (NSTEMI) patients, basal troponin values were shown to be predictive of TB,[22] and similar results could not be obtained in our study.

We consider that the most important reason why similar results could not be obtained in our study may be that only STEMI patients were included in our study. Although LVEF decreases are less common in acute coronary syndrome (ACS) patients after primary PCI, as seen in our study, we think that the higher decrease in H2FPEF score LVEF values in STEMI patients will be a stimulant for the clinician in terms of TB.

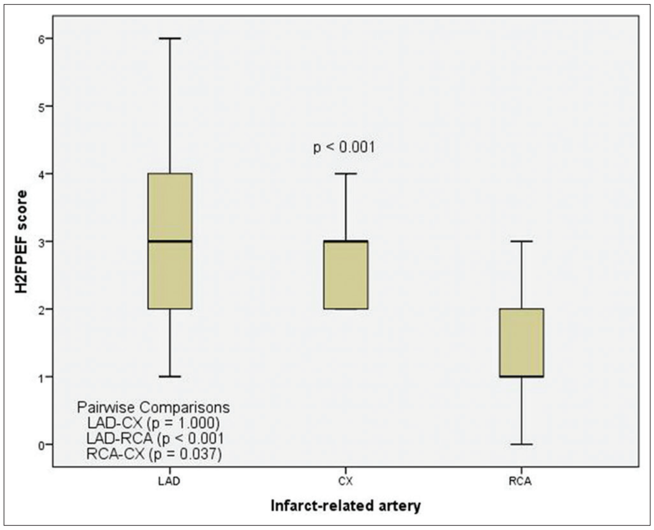

Figure 3: Relationship between culprit vessels and H2FPEF score

Table 2: Association of the total H2FPEF score and high and low thrombus burden result

H2FPEF score (n=100)	HTB (n=50), n (%)	LTB (n=50), n (%)	P
Low 0-1 (n=35)			
0	0	8 (16)	<0.001
1	11 (22)	15 (30)	
Intermediate 2-5 (n=60)			
2	15 (30)	20 (40)	
3	8 (16)	4 (8)	
4	3 (6)	1 (2)	
5	8 (16)	2 (4)	
High ≥6 (n=5)			
6	5 (10)	0	

LTB: Low thrombus burden, HTB: High thrombus burden, H2FPEF: Obesity (H), hypertension (H), atrial fibrillation (F), pulmonary hypertension (P), an age >60 years (E), and E/e' > 9 (F)

Studies have shown that those with HTB are older compared to those with a LTB, and the frequency of HT is more common in HTB patients.[23,24] The lack of similar results in our study supports the position that the pathogenesis of ICT development is not clear.

It has been shown that there may be significant differences in age values in patients with a diagnosis of STEMI, depending on the infarct-related artery (IRA).[25] As seen in our study, the H2FPEF score, including the age component, was found to be associated with the IRA.

The H2FPEF score is the current score used to distinguish unexplained shortness of breath from preserved ejection fractional heart failure or non-cardiac causes. However, the H2FPEF score has been shown to predict nephropathy after revascularization in patients diagnosed with ACS.[26] In another current study, its relationship between H2FPEF and SYNTAX scores was shown in patients with NSTEMI.[27] As can be understood from the examples in the literature, the H2FPEF score helps the clinician with various issues besides its main purpose. In addition, as seen in our study, the H2FPEF score was associated with HTB in STEMI patients.

Study limitations

One of the limitations of our study was the relatively low number of cases and the fact that it was a single center after the wide exclusion criteria. In our study, TB was decided by evaluating angiographic images, and since STEMI patients needed urgent revascularization, specific imaging methods such as intravascular ultrasound and optical coherence tomography were not used. In addition, data obtained in our study evaluating the H2FPEF score in newly diagnosed STEMI patients were short-term follow-up data; the long-term usability of such data has not been investigated, and multicenter studies are needed to confirm the H2FPEF score results and cutoff values in STEMI patients.

Conclusions

TB can be easily predicted in STEMI patients with an H2FPEF score. The H2FPEF score may be helpful in TB management

Table 3: Univariate and multivariate analysis for prediction of high thrombus burden

Variables	Univariate OR (95% CI)	P	Multivariate OR (95% CI)	P
Family history of CAD	1.194 (0.371-3.841)	0.766	0.595 (0.126-2.814)	0.512
Smoking	0.844 (0.376-1.894)	0.680	0.540 (0.184-1.583)	0.261
Previous statin use	1.568 (0.414-5.935)	0.508	0.723 (0.114-4.597)	0.731
Triglyceride	0.997 (0.987-1.006)	0.520	0.993 (0.981-1.005)	0.278
Cardiac Tn	0.196 (0.980-1.004)	0.196	0.986 (0.971-1.002)	0.085
Red cell distribution width	1.989 (1.269-3.116)	0.003	2.443 (1.382-4.316)	0.002
Killip status, ≥II	11.294 (2.435-52.379)	0.002	2.970 (0.682-12.937)	0.147
Pain to balloon time	1.001 (0.998-1.003)	0.617	1.003 (1.000-1.007)	0.060
H2FPEF score	1.937 (1.371-2.738)	<0.001	2.360 (1.447-3.847)	0.001

CAD: Coronary artery disease, Tn: Troponin, OR: Odds ratio, CI: Confidence interval, H2FPEF: Obesity (H), hypertension (H), atrial fibrillation (F), pulmonary hypertension (P), an age >60 years (E), and E/e' > 9 (F) for high-risk patients and to avoid undesirable clinical outcomes that may occur due to TB. According to the current guidelines, additional medical treatments such as glycoprotein IIb/IIIa inhibitors are recommended in STEMI patients in the presence of a massive thrombus or in cases where a sufficient flow degree cannot be achieved during revascularization. The H2FPEF score can be helpful in medical treatment management such as the use of a glycoprotein IIb/IIIa inhibitor and thus can be used in the treatment management of high-risk individuals.

Declaration of patient consent

Both verbal and written informed consents were obtained from the participants.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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