ARCHIVES OF THE TURKISH SOCIETY OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Use of TIMI Risk Index as a Simple and Valuable Prognostic Tool in Patients with ST-Segment Elevation Myocardial Infarction Who Underwent Primary Percutaneous Coronary Intervention

Primer Perkütan Koroner Girişim Uygulanan ST-Segment Yükselmeli Miyokart Enfarktüslü Hastalarda Basit ve Değerli Bir Prognostik Araç Olarak TIMI Risk İndeksinin Kullanımı

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

ABSTRACT

Objective: Thrombolysis in Myocardial Infarction Risk Index is a risk stratification model developed to determine the prognosis in ST-segment elevation myocardial infarction patients who underwent fibrinolytic therapy. The information on the effectiveness of Thrombolysis in Myocardial Infarction Risk Index in patients who underwent primary percutaneous coronary intervention is limited. This study aimed to demonstrate the predictive value of Thrombolysis in Myocardial Infarction Risk Index on clinical outcomes in patients presenting with ST-segment elevation myocardial infarction and subsequently undergoing primary percutaneous coronary intervention.

Methods: A total of 963 patients who presented with ST-segment elevation myocardial infarction and subsequently underwent primary percutaneous coronary intervention were reviewed retrospectively. The discriminative power of Thrombolysis in Myocardial Infarction Risk Index for each outcome of congestive heart failure, death, stroke, and myocardial infarction within 1 month and 1 year after admission was assessed.

Results: Congestive heart failure, death, stroke, and myocardial infarction, and the major adverse cardiac events, which is the composite outcome thereof, were higher in the patient groups with high Thrombolysis in Myocardial Infarction Risk Index values ($P < .05$). Thrombolysis in Myocardial Infarction Risk Index was an independent predictor of the following outcomes: 1-month survival rate [odds ratio:1.054 (1.036-1.073)], 1-year survival rate [odds ratio:1.048 (1.031-1.065)], hospitalization rate due to congestive heart failure within 1 month [odds ratio:1.041(1.026-1.057)], and within 1 year [odds ratio:1.040 (1.024-1.055)]. The Thrombolysis in Myocardial Infarction Risk Index level was found to have good discriminative power for 1-month mortality and 1-year mortality rates (Thrombolysis in Myocardial Infarction Risk Index: 22.76, C-statistic: 0.71-0.68, respectively).

Conclusion: The results of this study indicated that Thrombolysis in Myocardial Infarction Risk Index value is an independent predictor of clinical outcomes such as death and heart failure but not subsequent myocardial infarction in ST-segment elevation myocardial infarction patients. The use of Thrombolysis in Myocardial Infarction Risk Index can be considered in ST-segment elevation myocardial infarction patients who underwent primary percutaneous coronary intervention as it is an easily applicable and important indicator of prognosis.

Keywords: TIMI risk index, ST-elevation myocardial infarction, prognosis

ÖZET

Amaç: Miyokart Enfarktüsünde Tromboliz (TIMI) Risk Endeksi (TRI), fibrinolitik tedavi uygulanan ST-segment yükselmeli miyokart enfarktüsü (STEMI) hastalarında prognozu belirlemek için geliştirilmiş bir risk sınıflandırma modelidir. Primer perkütan koroner girişim (PPKG) uygulanan hastalarda TRI'nin etkinliğine ilişkin bilgiler sınırlıdır. Bu çalışma STEMI ile başvuran ve daha sonra PPCI uygulanan hastalarda TRI'nin klinik sonuçlar üzerindeki prediktif değerini göstermeyi amaçlamıştır.

Yöntemler: STEMI ile başvuran ve ardından PPKG uygulanan 963 hasta geriye dönük olarak incelendi. TRI'nin konjestif kalp yetmezliği (KKY), ölüm, inme ve miyokart enfarktüsü (MI) için bir ay ve bir yıllık ayırt edici gücü değerlendirildi.

İdris Buğra Çerik, M.D.[1]
Ahmet Kaya, M.D.[2]
Seçkin Dereli, M.D.[2]
Fatih Akkaya, M.D.[2]
Mustafa Yenerçağ, M.D.[2]
Osman Bektaş, M.D.[2]

[1]*Department of Cardiology, Cumhuriyet University School of Medicine, Sivas, Turkey*
[2]*Department of Cardiology, Ordu University Training and Research Hospital, Ordu, Turkey*

Corresponding author:
İdris Buğra Çerik
✉ cerikbugra@gmail.com

Received: June 9, 2021
Accepted: November 4, 2021

Cite this article as: Çerik İB, Kaya A, Dereli S, Akkaya F, Yenerçağ M, Bektaş O. Use of TIMI risk index as a simple and valuable prognostic tool in patients with ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention. Turk Kardiyol Dern Ars 2022;50(3):192-201.

DOI: 10.5543/tkda.2022.21143

Bulgular: KKY, ölüm, inme ve MI ve bunların bileşik sonucu olan majör advers kardiyak olaylar (MACE), TRI değerleri yüksek olan hasta gruplarında daha yüksekti (P < ,05). TRI, aşağıdaki sonuçların bağımsız bir öngördücüsü idi; bir aylık sağkalım oranı [Odds oranı (OR): 1,054 (1,036-1,073)], bir yıllık sağkalım oranı [OR: 1,048 (1,031-1,065)], bir ay içinde KKY nedeniyle hastaneye yatış oranı [OR: 1,041(1,026-1,057)] ve bir yıl içinde [OR: 1,040 (1,024-1,055)]. TRI düzeyinin bir aylık mortalite ve bir yıllık mortalite oranlarında iyi bir ayırt edici güce sahip olduğu saptandı (sırasıyla TRI: 22,76, C-istatistik: 0,71-0,68).

Sonuç: Bu çalışmanın sonuçları, TRI değerinin PPKG uygulanan STEMI hastalarında ölüm ve kalp yetmezliği gibi klinik sonlanımların bağımsız bir öngörücüsü olduğunu ancak tekrarlayan MI için olmadığını göstermiştir. Kolay uygulanabilen ve önemli bir prognoz göstergesi olduğu için TRI'nin kullanımı PPKG uygulanan STEMI hastalarında da düşünülmelidir.

Anahtar Kelimeler: TIMI risk indeksi, ST yükselmeli miyokart enfarktüsü, prognoz

The mortality rates tend to decrease in patients who underwent primary percutaneous intervention (PPCI) for ST-segment elevation myocardial infarction (STEMI) through the significant progress made in invasive treatment methods, yet STEMI remains to be one of the most important causes of death worldwide, accounting for approximately 10% of the mortalities.[1,2]

The main objective in the treatment of STEMI is to reperfuse the infarct-related coronary artery as soon as possible; however, the management of patients based on their risk profiles is also of great importance in terms of short and long-term mortality and morbidity.[3] Because clinical outcomes in STEMI patients were found to be related to many parameters,[4] most of the scoring systems proposed for the risk stratification are complex and include many clinical, laboratory, and angiographic parameters.[5] The continuation of the improvements to the currently used treatments and the changing mortality and morbidity rates necessitate re-validation of the risk scores.

Thrombolysis in Myocardial Infarction (TIMI) Risk Index (TRI) is a simple index that was created and validated in order to carry out the risk stratification of the STEMI patients treated with fibrinolytic therapy, using the parameters of age, heart rate, and systolic blood pressure (SBP) measured at the time of admission, without the need for any laboratory parameters.[6-8] Thrombolysis in Myocardial Infarction Risk Index, which is calculated using the formula of "heart rate × [age/10]^2)/systolic blood pressure," aims to provide information about the clinical outcomes of patients.[6] Thrombolysis in Myocardial Infarction Risk Index has been shown to predict stent thrombosis in the elderly patient population and the risk of the development of a no-reflow phenomenon in patients who have undergone percutaneous coronary intervention.[9-11] Additionally, TRI has been shown to be a strong parameter in terms of predicting short and long-term survival and heart failure in the period when PPCI is not routinely used.[8] Today, PPCI has become the standard treatment approach; hence, the results of the previously conducted studies on heterogeneous patients in terms of treatment methods may not reflect the outcomes that we would achieve with the current patient management.

In view of the foregoing, this study aimed to assess the predictive role of TRI, which was shown to be effective in patients that received fibrinolytic therapy in previous studies, regarding the development of short and long-term death, heart failure, stroke, and recurrent myocardial infarction in patients who underwent PPCI due to the diagnosis of STEMI.

ABBREVIATIONS

ANOVA	Analysis of variance
ASA	Acetylsalicylic acid
BNP	Brain natriuretic peptide
CABG	Coronary artery bypass grafting
CHF	Congestive heart failure
CRP	C-reactive protein
CS	Cardiogenic shock
DM	Diabetes mellitus
EF	Ejection fraction
GRACE	Global Registry of Acute Coronary Events
GS	Gensini score
HF	Heart failure
HPL	Hyperlipidemia
HT	Hypertension
MACE	Major adverse cardiac event
MI	Myocardial infarctions
TRI	Modified TRI value
PPCI	Primary percutaneous intervention
ROC	Receiver operating characteristic
SBP	Systolic blood pressure
STEMI	ST-segment elevation myocardial infarction
SYNTAX	Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery
TIMI	Thrombolysis in Myocardial Infarction

Methods

Study Group

A total of 963 consecutive STEMI patients who were admitted to the emergency department of a tertiary hospital between January 2015 and January 2020 were reviewed retrospectively.

The ethics committee approval of the study (OUTF: 2019-10/08) was obtained from the ethics committee of the university, where the study was conducted.

All patients diagnosed with STEMI based on the current European Society of Cardiology Fourth Universal Definition of Myocardial Infarction Guideline were included in the study. Diagnostic criteria were as follows: new ST elevation at the J-point in 2 contiguous leads with the cut-point: ≥1 mm in all leads other than leads V2-V3, V7-V9, V3R-V4R where the following cut-points apply for V2-V3: ≥2 mm in men ≥ 40 years; ≥ 2.5 mm in men < 40 years, or ≥1.5 mm in women regardless of age, for V7-V9: ≥1 mm in men < 40 years, ≥0.5 mm in others, for V3R-V4R: ≥1 mm in men <30 years, ≥0.5 mm in others or a definite/probable new left bundle branch block and typical chest pain.[12]

All patient data were obtained from the electronic medical records. Patients' previous coronary artery bypass grafting (CABG) operation, previous myocardial infarctions (MI), diabetes mellitus (DM), hypertension (HT), and hyperlipidemia (HPL) histories were recorded. The results of the basic blood tests administered at the time of

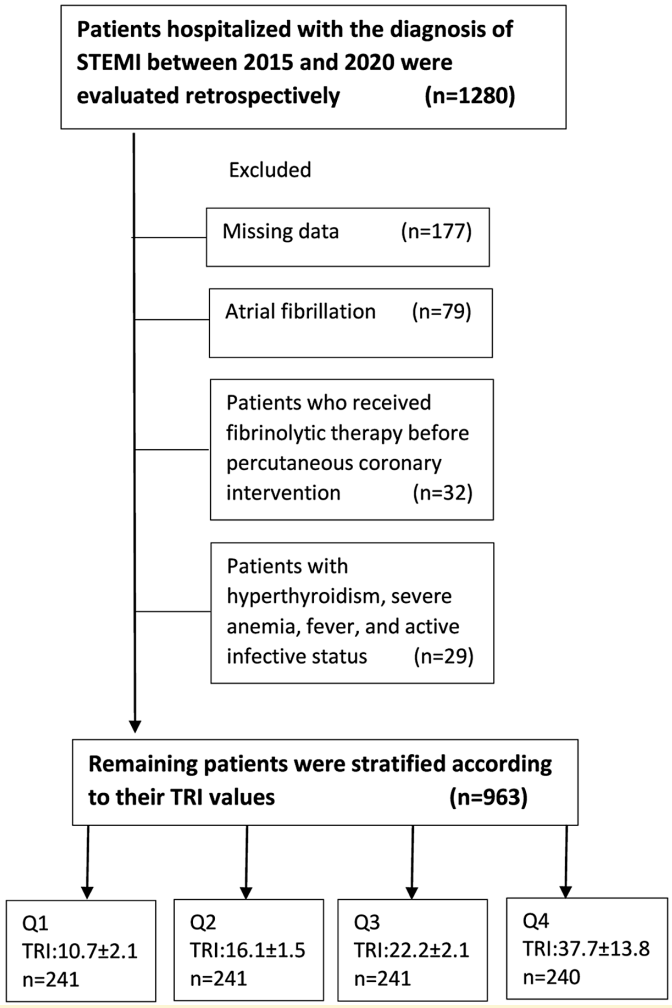

Figure 1. Patient flowchart.

admission and of the echocardiography test performed before the patients were discharged were reviewed.

All patients included in the study are those who underwent PPCI; hence, patients who underwent fibrinolytic at the referral from another hospital or at admission were not included in the study. Patients with hyperthyroidism, severe anemia, fever, and active infective status were excluded from the study because they can change the TRI value regardless of cardiac status. Atrial fibrillation patients were excluded from the study due to possible inaccuracy in basal TRI calculation and treatment heterogeneity. In addition, patients with missing data for TRI calculation were excluded from the study.

A total of 317 patients, whose data were missing and/or who have met the exclusion criteria, were excluded from the study, and data in respect to the remaining 963 patients were analyzed. The flow chart according to patient selection is presented in Figure 1.

All patients included in the study were administered 300 mg acetylsalicylic acid (ASA), 600 mg clopidogrel, and 70 IU/kg unfractionated heparin before PPCI was administered, in accordance with the current treatment guidelines. Following the completion of the PPCI procedure, patients were continued to be treated with 100 mg/day ASA and 75 mg/day clopidogrel.[13]

Long-term outcome information of the patients was obtained through hospital records and telephone contact.

Echocardiographic imaging of the patients was performed by experienced cardiologists using the Vivid 7 ultrasound device (GE Vingmed Ultrasound AS, Horten, Norway). Basic echocardiographic evaluations of all patients were performed before they were discharged in line with the current echocardiography recommendations and their ejection fractions were calculated using the Simpson method.[14]

The blood samples of all patients taken at the time of their admission to the emergency department were analyzed using standard biochemical methods (Beckman Coulter Inc., Brea, CA, USA).

Descriptions/Diagnostic Criteria

Cardiogenic Shock: Patients who were determined to have a persistent SBP of <80 mm Hg for more than 30 minutes and/or who need long-term positive inotropic therapy were considered to have developed cardiogenic shock (CS). Patients who were determined to have an SBP of <90 mm Hg yet did not meet the criteria for CS were considered to be hypotensive.

Thrombolysis in Myocardial Infarction Risk Index: TRI value was calculated using the following formula as previously defined[6];

TRI = (heart rate × [age/10]2)/systolic blood pressure

Thrombolysis in Myocardial Infarction Risk Index values was calculated using the patients' data (heart rate, age, and SBP) obtained at the time of their admission to the emergency department and then recorded. Patients, who were stratified in ascending order based on their TRI values, were reviewed in 4 groups (Q1 [n = 241], Q2 [n = 241], Q3 [n = 241], and Q4 [n = 240]).

One-month Mortality: 1-month mortality was defined as any death from any cause within a period of 1 month.

One-year Mortality: 1-year mortality was defined as any death from any cause within a period of 1 year.

Stroke: Patients who, within 1 year, had transient ischemic attacks proven with magnetic resonance or computed tomography and/or strokes that have resulted in the loss of strength, were considered to have had a stroke.

Myocardial Infarction: Patients, who were diagnosed with MI within the specified period according to the diagnostic criteria outlined in the "Fourth Universal Definition of Myocardial Infarction" guidelines, were considered to have had MI.[12]

Heart Failure: Patients, who were hospitalized due to volume congestion or with signs of low cardiac output and heart failure (HF) within the first month or within 1 year, were considered to have had HF.

Major Adverse Cardiac Event: Patients with congestive heart failure (CHF), death, stroke, and MI at the end of 1 year, were considered to have had a major adverse cardiac event (MACE), which is the composite outcome thereof.

Statistical Analysis

The collected data were analyzed using the Statistical Package for the Social Sciences Version 22.0 (IBM Corp., Armonk, NY, USA) software package. Categorical variables were expressed as numbers and percentages (n, %), whereas the continuous variables were expressed as mean ± standard deviation or median, interquartile range (median, 25th-75th percentiles) based on the data distribution. Kolmogorov–Smirnov test was used to check whether the data conformed to the normal distribution. A one-way analysis of variance (ANOVA) test was used for the comparisons of more than 2 independent groups. Following the ANOVA test, Tukey's test or Games–Howell post hoc test was used for post hoc analysis based on the assumption of homogeneity. A chi-squared test was used to assess the categorically obtained data. Logistic regression analysis was performed to assess the correlation of clinical outcomes with TRI. All significant parameters in univariate analysis were assessed individually using a multivariate model with possible confounding factors (DM, HT, smoking, anterior MI, dyslipidemia, and hemoglobin). C-statistic values were obtained based on the receiver operating characteristic (ROC) analysis to evaluate the diagnostic test performance of TRI in the determination of the clinical outcomes. Spearman's correlation analysis was used for the correlation analysis of TRI and other clinical outcome indicators. The probability (*P*) values obtained as ≤.05 as a result of the performed tests were considered to indicate statistical significance.

Results

A total of 963 patients with a mean age of 57.9 ± 11.3 years and of whom 23.7% were female were included in the study. During the study period, death occurred in 69(7.2%) of these patients, 128(13.3%) of them were hospitalized due to HF, 44(4.6%) of them had a recurrent MI, 10(1%) of them had a stroke, and MACE took place in a total of 190(19.7%) patients.

Patients, who were stratified in ascending order based on their TRI values, were reviewed in 4 groups. The mean TRI values of these groups were as follows; Q1=10.7 ± 2.1, Q2=16.1 ± 1.5, Q3=22.2 ± 2.18, and Q4=37.7 ± 13.8. The difference between the mean TRI values of these groups was found to be statistically significant ($P < .001$). The difference between the mean age values of these groups was also found to be statistically significant ($P < .001$), since age is one of the variables in the formula used to calculate the TRI values. On the other hand, no significant difference was found between the groups in terms of comorbidities, such as previous MI, CABG operation, or stent implantation histories, or in terms of the types of cardiac medical treatment administered. Interestingly, an inverse relationship was observed between smoking and TRI values. Accordingly, smoking was found to be less common among the patients with high TRI values ($P < .001$). Insulin use was significantly higher in the diabetic patients of the Q4 group compared to the diabetic patients in other groups ($P < .001$). The demographic characteristics of the patient groups are shown in Table 1.

Comparison of the patient groups in terms of basic laboratory parameters revealed that the plasma glucose levels were higher

Table 1. Comparison of the Demographic Characteristics of the Groups

Variables	Q1 (n=241)	Q2 (n=241)	Q3 (n=241)	Q4 (n=240)	*P*
Female, n (%)	29 (12)	46 (19.1)	59 (24.5)	85 (35.4)	<.001
Age	46 ± 7.9	54 ± 6.9	61.4 ± 7.2	70.9 ± 8.6	<.001
DM, n (%)	47 (19.5)	41(17)	58 (24.1)	80 (33.3)	<.001
Hypertension, n (%)	75 (31.1)	108 (44.8)	115 (47.7)	100 (41.7)	<.001
Smoking, n (%)	170 (70.5)	149 (61.8)	121 (50.2)	88 (36.7)	<.001
Dyslipidemia, n (%)	95 (39.4)	112 (46.5)	79 (32.8)	89 (37.1)	.019
History of MI, n (%)	30 (12.4)	23 (9.5)	23 (9.5)	25 (10.4)	.695
History of PCI, n (%)	25 (10.4)	20 (8.3)	22 (9.1)	24 (10)	.867
History of CABG, n (%)	7 (2.9)	10 (4.1)	5 (2.1)	8 (3.3)	.617
PAD, n (%)	14 (5.8)	21 (8.7)	18 (7.5)	18 (7.5)	.681
ASA, n (%)	41 (17)	27 (11.2)	26 (10.8)	33 (13.8)	.159
Clopidogrel, n (%)	0	3 (1.2)	3 (1.2)	2 (0.8)	.389
Insulin, n (%)	13 (5.4)	13 (5.4)	12 (5)	37 (15.4)	<.001
OAD, n (%)	27 (11.2)	31 (12.9)	52 (21.6)	43 (17.9)	.007
Beta-blocker, n (%)	24 (10)	29 (12)	24 (10)	16 (6.7)	.254
Statin, n (%)	43 (17.8)	48 (19.9)	42 (17.4)	44 (18.3)	.903
ACE, n (%)	45 (18.7)	54 (22.4)	45 (18.7)	52 (21.7)	.632
CCB, n (%)	12 (5)	15 (6.2)	12 (5)	9 (3.8)	.670

ACE, angiotensin-converting enzyme; ASA, acetylsalicylic acid; CABG, coronary artery bypass greft; CCB, calcium chanel blocker; DBP, diastolic blood pressure; DM, diabetes mellitus; MI, myocardial infarction; OAD, oral antidiabetic usage; PAD, peripheral artery disease; PCI, Percutan coronary intervention; SBP, systolic blood pressure.

Table 2. Comparison of Laboratory Parameters Between Groups

Variables	Q1 (n=241)	Q2 (n=241)	Q3 (n=241)	Q4 (n=240)	*P*
WBC (10^3/μL)	12.7 (10.1-15.1)	11.5 (9.8-13.7)	11.8 (9.6-13.7)	11.7 (9.3-14.5)	0.06
Hemoglobin (g/dL)	14.1 ± 1.7	13.8 ± 1.7	13.6 ± 1.7	12.6 ± 2	<.001
Platelet (10^3/μL)	274 ± 69	272 ± 65	260 ± 63	261 ± 65	.074
Plasma glucose (mg/dL)	122 (102-147)[a]	120 (99-147)[a]	136 (113-177)[a,b]	145 (112-189)[b]	<.001
Creatinin (mg/dL)	0.87 (0.77-0.97)[a]	0.82 (0.72-0.95)[a]	0.91 (0.8-1)[a,b]	0.92 (0.8-1.1)[b]	<.001
CRP (mg/dL)	9.3 (5.1-15.3)[a]	9.5 (5.4-15.4)[a]	9.8 (6.5-15.5)[a]	12.3 (7.4-20.6)[b]	<.001
Troponin (ng/mL)	1.6 (0.5-3.9)[a]	1.4 (0.6-3.9)[a,b,c]	1.8 (0.7-4.4)[a,b]	2.6 (1.1-6.3)[c]	.009
Peak troponin (ng/mL)	80 (37-151)[a,b]	68 (38-133)[a]	71 (41-144)[a]	86 (43-194)[b]	.011
LDL (mg/dL)	119.5 ± 37.8[a]	117.9 ± 35.5[a,b]	113.8 ± 31.5[a,b]	110 ± 33.9[b]	.035
Trigliseride (mg/dL)	133 (94-178)[a]	123 (84-181)[a]	116 (84-157)[b]	113 (82-159)[b]	.006
D-dimer (μg/L)	0.34 (0.16-0.62)[a]	0.33 (0.18-0.51)[a]	0.38 (0.21-0.62)[a,b]	0.62 (0.4-1.2)[b]	<.001
BNP (ng/L)	49.7 (26.9-86.4)[a]	51.7 (29.7-89.7)[a]	58 (34-97.4)[a]	73.9 (44-174.5)[b]	<.001
TRI	10.7 ± 2.1[a]	16.1 ± 1.5[b]	22.2 ± 2.18[c]	37.7 ± 13.8[d]	<.001

BNP, brain natriuretic peptid; CRP, C-reactive protein; EF, ejection fraction; LDL, low-density lipoprotein; TRI, Thrombolysis in Myocardial Infarction Risk Index; WBC, white blood cell. [a,b,c,d]Similar superscript letters indicate no statistical difference, different superscript letters indicate a statistically significant difference.

in the patients included in Q3 and Q4 groups, in line with the frequency of DM among the patients of these groups ($P < .001$). Creatinine, C-reactive protein (CRP), D-dimer, and brain natriuretic peptide (BNP) parameters were found to be higher in TRI high tertiles than in TRI low tertiles ($P < .001$). Interestingly, triglyceride and low-density lipoprotein levels were found to be lower in high TRI quartiles compared to other groups ($P = .006$ and $P = .035$, respectively). Detailed information on the distribution of the biochemical parameters by the TRI quartiles and the post hoc analyses thereof is given in Table 2.

Comparison of the patient groups in terms of their clinical conditions did not reveal any significant difference between the groups in terms of infarct pattern (anterior MI), stent length, or localization of the lesion in the epicardial coronary artery ($P > .05$). However, observation of no-reflow following the procedure and low ejection fraction (EF) was found to be significantly higher in the Q4 group compared to the other groups ($P < .001$). Cardiogenic shock, HT, and high Killip class were found to be more common in quartiles with high TRI values ($P < .001$). The comparison of the clinical conditions of the patients by the groups is detailed in Table 3.

Table 3. Comparison of the Clinical and Angiographic Characteristics of the Groups

Variables		Q1 (n=241)	Q2 (n=241)	Q3 (n=241)	Q4 (n=240)	*P*
Killip class 1		90.9	93.8	82.2	73.3	<.001
2		5.8	5	11.2	13.3	
3		2.1	0.8	4.1	9.6	
4		1.2	0.4	2.5	3.8	
Cardiogenic shock, n (%)		6 (2.5)	2 (0.8)	10 (4.1)	29 (12.1)	<.001
Hypotension, n (%)		11 (4.6)	8 (3.3)	14 (5.8)	49 (20.4)	<.001
SBP, mm Hg		134 ± 26.5	135 ± 25.5	133 ± 26.9	118.2 ± 30.1	<.001
DBP, mm Hg		78.5 ± 15.4	79 ± 15.3	78 ± 17.7	69.4 ± 19.3	<.001
Heart rate (beat/min)		68.9 ± 16.1	75 ± 13.4	79 ± 14.1	84 ± 15.3	<.001
Stent diameter		21.7 ± 8.7	22 ± 9.7	22.7 ± 9.8	22.1 ± 7.9	.288
Anterior MI, n(%)		98 (40.7)	116 (48.1)	115 (47.7)	125 (52.1)	.099
Localization of the occlusion	*Prox*	57.7	54.4	58.1	56.7	.914
	Mid	37.3	42.3	37.3	40.4	
	Distal	5	3.3	4.6	2.9	
No-reflow		15 (6.2)[a]	16 (6.6)[a]	16 (6.6)[a]	41 (17.1)[b]	<.001
EF (%)		47.4 ± 8.1[a]	47.5 ± 7.1[a]	46.5 ± 6.8[a]	44.2 ± 9.1[b]	<.001

DBP, diastolic blood pressure; EF, ejection fraction; MI, myocardial infarction; SBP, systolic blood pressure. [a,b]Similar superscript letters indicate no statistical difference, different superscript letters indicate a statistically significant difference.

Table 4. Comparison of Clinical Outcomes According to TRI Tertiles

Variables	Q1 (n=241)	Q2 (n=241)	Q3 (n=241)	Q4 (n=240)	*P*
Stroke	4 (1.7)[a]	3 (1.3)[a]	2 (0.8)[a]	7 (2.9)[b]	.003
Death first month	6 (2.5)[a]	9 (3.7)[a]	7 (2.9)[a]	28 (11.7)[b]	<.001
Death first year	11 (4.6)[a]	9 (3.7)[a]	11 (4.6)[a]	38 (15.8)[b]	<.001
CHF first month	23 (9.6)[a]	23 (9.5)[a]	17 (7.1)[a]	54 (22.5)[b]	<.001
CHF first year	26 (10.9)[a]	25 (10.4)[a,b]	19 (7.9)[b]	58 (24.2)[c]	<.001
MI first month	6 (2.5)	1 (0.4)	11 (4.6)	3 (1.3)	.015
MI first year	15 (6.3)	3 (1.3)	16 (6.6)	10 (4.2)	.022
TVR	16 (6.7)	17 (7)	20 (8.2)	18 (7.5)	.659
MACE[a]	40 (16.6)[a]	31 (12.9)[a]	38 (15.8)[a]	81 (33.8)[b]	<.001

CHF, congestive heart failure; MACE, major advers cardiac events; MI, myocardial infarction; TRI, Thrombolysis in Myocardial Infarction Risk Index; TVR, target vessel revascularization. [a]MACE, the sum of death, MI, CHF, and stroke at the end of one year. [a,b,c]Similar superscript letters indicate no statistical difference, different superscript letters indicate a statistically significant difference.

Comparison of the groups in terms of clinical outcomes revealed that stroke (P = .003), 1-month and 1-year mortality rates (P < .001), hospitalization rates due to HF within 1 month and 1 year (P < .001), and MACE (P < .001) were more in the Q4 group compared to the other groups. Target vessel revascularization was not found to have differed significantly between the groups, whereas the significant difference found between the groups in terms of MI was not found to be related to TRI quartiles. The results in terms of clinical outcomes are detailed in Table 4, whereas the distribution of clinical outcomes by the patient groups is given in Figure 2.

The univariate logistic regression analysis, which was conducted to assess the predictivity of TRI in the determination of the clinical outcomes of all patients, revealed that TRI was predictive in respect of the death rates within 1 month and 1 year (P < .001), hospitalization rates due to HF within 1 month and 1 year (P <.001), and MACE (P < .001). Additionally, multivariate logistic regression analysis adjusted with DM, HT, smoking, anterior MI, dyslipidemia, and hemoglobin coefficients also indicated TRI value as a significant indicator, in respect to each parameter for which TRI was determined to be predictive as a result of the univariate analysis (P < .001)(Table 5).

Correlation analysis of the TRI values with EF, CRP, BNP, peak troponin, and basal creatinine levels, which were previously determined to be associated with clinical outcomes, revealed a weak but significant correlation between TRI values and EF (r: –0.186, P < .001), peak troponin (r: 0.148, P < .001), CRP (r: 0.205, P < .001), and creatinine (r: 0.219) levels and a moderate and significant correlation with the BNP (r: 0.515, P < .001) levels (Figure 3).

The cutoff value was determined as 22.76 with the highest sensitivity and specificity in the ROC curves analyses, which were performed to determine the predictive value of TRI in the determination of the negative clinical outcomes. High sensitivity and specificity values were determined for death rates within 1 month (area under the curve (AUC): 0.71[0.62-0.78], P < .001, sensitivity 64%, specificity 63%) and for death rates

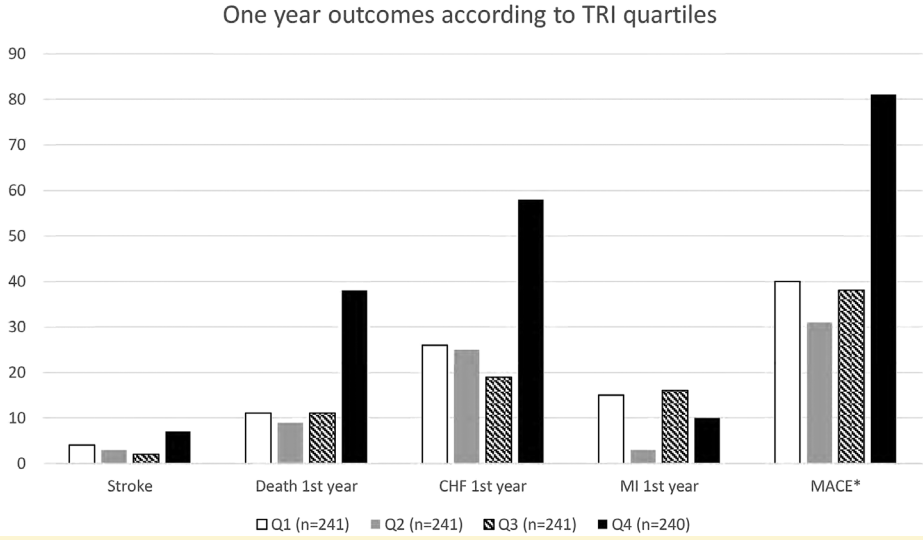

Figure 2. One-year outcome according to TRI quartiles. TRI, Thrombolysis in Myocardial Infarction Risk Index.

Table 5. Predictability of TRI in Clinical Outcomes in Multivariate Regression Analysis

Variables	Unadjusted OR (CI)	*P*	Adjusted* OR (CI)	*P*
Death first month	1.06 (1.044-1.078)	<.001	1.054 (1.036-1.073)	<.001
Death first year	1.055 (1.039-1.071)	<.001	1.048 (1.031-1.065)	<.001
CHF first month	1.043 (1.029-1.057)	<.001	1.041 (1.026-1.057)	<.001
CHF first year	1.042 (1.028-1.056)	<.001	1.040 (1.024-1.055)	<.001
MI first month	1.010 (0.976-1.041)	.572		
MI first year	1.006 (0.982-1.032)	.612		
MACE†	1.040 (1.028-1.053)	<.001	1.036 (1.022-1.050)	<.001

CHF, congestive heart failure; MACE, major adverse cardiac events; MI, myocardial infarction; OR, odds ratio; TRI, Thrombolysis in Myocardial Infarction Risk Index.
*Adjustment coefficients: diabetes mellitus, hypertension, smoking, anterior myocardial infarction, dyslipidemia, and hemoglobin; †MACE, the sum of death, MI, CHF, and stroke at the end of 1 year.

within 1 year (AUC: 0.68[0.61-0.76], sensitivity 65%, specificity 67%, $P < .001$); yet, lower sensitivity and specificity values could be achieved for hospitalization rates due to CHF within 1 month (AUC: 0.63), hospitalization rates due to CHF within 1 year (AUC: 0.62), and for MACE (AUC: 0.63). The ROC curve graph of TRI in relation to the predictive value of TRI in the determination of death rates within 1 month and 1 year is given in Figure 4.

Discussion

The result of this study demonstrated, in which 963 patients treated with PPCI were reviewed retrospectively in order to assess the predictive value of TRI on prognosis, that TRI high levels are a significant and independent predictor of short and long-term survival, hospitalization for HF, stroke, and MACE, which is composite thereof. In addition, it has been shown that TRI is significantly correlated with BNP with proven prognostic value. Furthermore, it has been shown that TRI performed well prognostically, in STEMI patients treated with current treatment approaches and in terms of determination of 1-month and 1-year survival rates in particular.

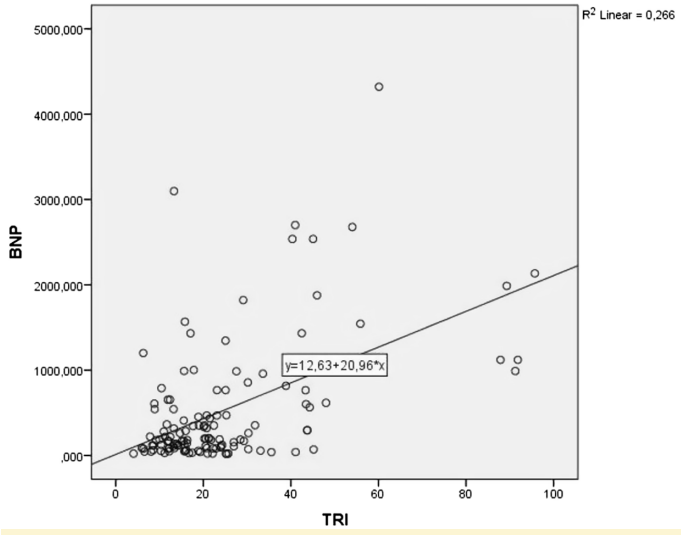

Figure 3. Correlation graph between BNP and TRI. TRI, Thrombolysis in Myocardial Infarction Risk Index; BNP, brain natriuretic peptide.

Thrombolysis in Myocardial Infarction Risk Index formula was derived from the findings of a substudy of the intravenous lanoteplase for the treatment of infarcted myocardium early (In TIME-II) randomized trial conducted on 13 253 STEMI patients, which revealed that advanced age, increased heart rate, and SBP are the parameters that have the strongest relationship with mortality and that TRI, which is derived from these parameters, is a strong predictor of 30-day mortality.[6] Additionally, in another study, in which a total of 11 510 patients were evaluated in order to validate the predictive role of TRI using the data from the Enhanced Feedback for Effective Cardiac Treatment study, TRI was shown to be a strong predictor of 30-day mortality in both STEMI patients and non-ST-segment elevation myocardial infarction patients.[7,15] The largest-scale study, in which the predictive efficacy of TRI was investigated, was the registry study conducted by Wiviot et al. on 153,486 STEMI patients. It was shown as a result of the said study that TRI had a strong diagnostic performance in predicting the in-hospital mortality outcome (C-statistic: 0.79). Nearly half of the patients included in the subgroups of the mentioned study did not undergo reperfusion strategy, and the discriminative capacity was high in these patients (C-statistic: 0.71), as well as in patients who underwent reperfusion strategy (C-statistic:0.81). The mentioned study was conducted in a very heterogeneous group, as pointed out by its authors, in terms of the treatments administered and the characteristics of the patient population.[8] The mortality rates found in the said study in relation to both patient groups that did and did not undergo reperfusion strategy are higher (12.3% and 5.2%, respectively) compared to the mortality rates found in this study. This difference, which necessitates the re-assessment of the efficacy of TRI on clinical outcomes in today's conditions, may be attributed to the improvements in reperfusion therapy, access to PPCI, and shortening of treatment time. Hence, it was demonstrated as a result of this study that the TRI performed well prognostically in terms of determination of 1-month mortality (C-statistic: 0.71 for 1-month mortality) and 1-year mortality (C-statistic: 0.68 for 1-year mortality) despite the decreasing mortality rates.

Many models have been defined for risk stratification in STEMI patients based on coronary angiography, clinical conditions of patients, and laboratory parameters. To give a few examples, Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score was used for

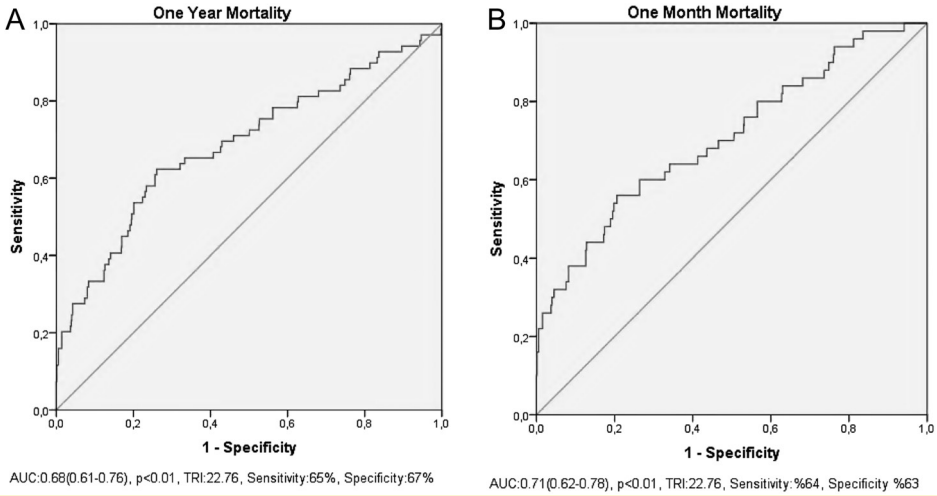

Figure 4. ROC curve chart of TRI to predict mortality within (A) 1 year and (B) 1 month. TRI, Thrombolysis in Myocardial Infarction Risk Index; ROC, receiver operating characteristic.

the assessment of the complexity of coronary artery disease in MI, TIMI risk score was used to predict the mortality during the fibrinolytic treatment period, the Global Registry of Acute Coronary Events (GRACE) risk score, and Gensini score (GS) risk score.[16-19] The aforementioned scoring models need a comprehensive evaluation of patients, and even data of patients after percutaneous procedures are necessary for use of these models. However, time is life in the management of STEMI patients. Therefore, a simple scoring method that will be calculated at the first evaluation of a patient without any need for additional parameters such as TRI may be the best risk assessment method. Moreover, in a study, TRI was compared with other prognostic risk stratification methods and was found to have correlated with SYNTAX score, TIMI risk score, GRACE risk score, and the Gensini risk score.[5] Nonetheless, the limitations of the risk stratification models used in the aforementioned relatively small study were that they were not validated in terms of the modern treatment methods and that they were used in patients. In comparison, the results of this study are similar to the said relatively small study in terms of the relationship between TRI and mortality, notwithstanding that this study does not provide information about the risk stratification models that were assessed in the said study. In conclusion, it was necessary to reassess whether TRI is a good method of risk stratification in patients with STEMI.

The current treatment approach in STEMI patients is revascularization of infarct-related arteries as soon as possible with PPCI. However, adequate myocardial perfusion may not develop even in cases when epicardial coronary artery patency is achieved in patients with successful stent implantation. This situation is referred to as the no-reflow phenomenon,[20] and the fact it may occur in patients who underwent PPCI and in whom epicardial coronary artery patency was achieved is reported to be associated with increased in-hospital and long-term mortality.[21] Additionally, in a study conducted by Acet et al[10] on 371 STEMI patients, TRI levels, as well as in-hospital mortality rates, were found to be significantly higher in patients who have developed no-reflow compared to those who have not developed no-reflow.[10] In parallel with the mentioned study, in this study, the number of patients who have developed no-reflow was determined to be more in the patient group with higher TRI values. The pathophysiology of the no-reflow phenomenon has not been fully explained and it has a multifactorial nature.[10] In summary, TRI was a very strong predictor in terms of its ability to assess the multifactorial nature of mortality in STEMI patients as a single parameter.

The development of CS remains as one of the most important predictors of mortality due to MI, despite the developments in revascularization and modern treatments.[22] The relationship between TRI value and CS seems to be inevitable, as the SBP and heart rate, which are among the parameters used in the calculation of TRI, are the parameters that are directly affected in CS. Furthermore, it is of the opinion of the authors of this study that brings the age variable into the equation and serves as a correction to the SBP and heart rate parameters, which renders TRI a better predictor of mortality. It was observed in this study that the development of CS was significantly higher in patients with higher TRI values. This result suggests that TRIs that are calculated as high at the time of admission to the hospital may serve as a warning in terms of the development of CS and may provide clinical benefit in terms of early diagnosis and taking the corresponding treatment measures.

Biochemical and echocardiographic markers such as EF, BNP, CRP, and troponin levels, which are established markers in acute MI patients in relation to short and long-term outcomes, guide cardiologists in terms of the prognosis of the patients.[23-25] All of the aforementioned parameters, which vary at different stages of the treatment of STEMI patients, were found to have correlated with the TRI value, which is an index based on the initial clinical evaluation of the patients and does not contain any laboratory parameters. From among the aforementioned parameters, it was BNP that was determined to have the highest correlation with TRI in this study.

In a recently published study conducted on approximately 5000 STEMI patients, Kaya et al[26] investigated the prognostic efficacy of a modified TRI value (mTRI), which was obtained by including the blood urea nitrogen as another variable in the formula to

calculate the TRI.[26] The authors of the said study argued that the discriminative power of TRI in assessing the in-hospital mortality was high (C-statistic:0.70) but that the discriminative power of mTRI was even higher (C-statistic:0.81). In comparison, 1-month and 1-year mortality rates found as a result of this study support the results of the said study in respect to the discriminative power of TRI in assessing the in-hospital mortality but not in respect tp the discriminative power of mTRI in assessing the in-hospital mortality, which was argued to be superior to TRI. It may be that the diagnostic criteria used for the clinical outcomes in the 2 studies were different and might have given rise to the said difference between the results of the 2 studies. It is of the opinion of the authors of this study that TRI is a simpler and easier to use and more useful prognostic tool compared to mTRI for both types of outcomes, that is 1-month mortality and 1-year mortality.

Limitations

This study was conducted as a single-center and retrospective study and with a relatively low number of patients compared to large-scale registry studies. Thus, it is possible that there were some confounding factors that may not be identified due to the retrospective nature of the study. As such, the study could not provide information on prolonged door to balloon or wire time, inappropriate stent implantation, inappropriate stent size or length selection, inadequate anticoagulation, and non-compliance with medical therapy. Additionally, the STEMI patients reviewed within the scope of this study were treated with the modern angiographic approach, yet not with new generation P2Y12 inhibitors. The prognostic role of TRI was found to have correlated with biomarkers; however, this correlation could not be evaluated, since the study data were not sufficient to measure other clinical risk scores.

Conclusion

High TRI levels were determined to be a significant and independent predictor of short and long-term survival, hospitalization due to HF, stroke, and MACE, which is a composite thereof. A cutoff value of 22.76 indicated that TRI has good discriminative power in respect to 1-month mortality and 1-year mortality. In addition, BNP, which has proven prognostic value, was found to be significantly correlated with TRI. Furthermore, it was observed that TRI performed well prognostically in STEMI patients treated with current treatment approaches. In parallel with the continuously advancing treatment approaches, there will also be a need to validate the existing methods used for risk stratification and to develop new risk stratification methods.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Ordu University (Approval No: 2018-19).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-Review: Externally peer-reviewed.

Author Contributions: Concept – A.K., İ.B.Ç.; Design – A.K., İ.B.Ç.; Supervision – S.D., M.Y., O.B.; Materials – A.K., O.B.; Data Collection and/or Processing – S.D., F.A., M.Y.; Analysis and/or Interpretation – İ.B.Ç., A.K.; Literature Review – İ.B.Ç., F.A.; Writing – İ.B.Ç.; Critical Review – A.K., M.Y.

Declaration of Interests: None declared.

Funding: None.

References

1. Townsend N, Wilson L, Bhatnagar P, Wickramasinghe K, Rayner M, Nichols M. Cardiovascular disease in Europe: epidemiological update 2016. *Eur Heart J*. 2016;37(42):3232-3245. [CrossRef]
2. Pedersen F, Butrymovich V, Kelbæk H, et al. Short- and long-term cause of death in patients treated with primary PCI for STEMI. *J Am Coll Cardiol*. 2014;64(20):2101-2108. [CrossRef]
3. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39(2):119-177. [CrossRef]
4. Velibey Y, Parsova EC, Ceylan US, et al. Outcomes of survivors of ST-segment elevation myocardial infarction complicated by out-of-hospital cardiac arrest: a single-center surveillance study. *Turk Kardiyol Dern Ars*. 2019;47(1):10-20. [CrossRef]
5. Acet H, Ertaş F, Bilik MZ, et al. The relationship of TIMI risk index with SYNTAX and Gensini risk scores in predicting the extent and severity of coronary artery disease in patients with STEMI undergoing primary percutaneous coronary intervention. *Ther Adv Cardiovasc Dis*. 2015;9(5):257-266. [CrossRef]
6. Morrow DA, Antman EM, Giugliano RP, et al. A simple risk index for rapid initial triage of patients with ST-elevation myocardial infarction: an InTIME II substudy. *Lancet*. 2001;358(9293):1571-1575. [CrossRef]
7. Bradshaw PJ, Ko DT, Newman AM, Donovan LR, Tu JV. Validation of the Thrombolysis In Myocardial Infarction (TIMI) risk index for predicting early mortality in a population-based cohort of STEMI and non-STEMI patients. *Can J Cardiol*. 2007;23(1):51-56. [CrossRef]
8. Wiviott SD, Morrow DA, Frederick PD, et al. Performance of the thrombolysis in myocardial infarction risk index in the National Registry of myocardial Infarction-3 and -4: a simple index that predicts mortality in ST-segment elevation myocardial infarction. *J Am Coll Cardiol*. 2004;44(4):783-789. [CrossRef]
9. Furnaz S, Karim M, Ashraf T, et al. Performance of the TIMI risk score in predicting mortality after primary percutaneous coronary intervention in elderly women: results from a developing country. *PLoS ONE*. 2019;14(7):e0220289. [CrossRef]
10. Acet H, Ertaş F, Akil MA, et al. The utility of the TIMI risk index on admission for predicting angiographic no-reflow after primary percutaneous coronary intervention in patients with STEMI. *Turk J Med Sci*. 2016;46(3):604-613. [CrossRef]
11. Çınar T, Karabağ Y, Burak C, et al. A simple score for the prediction of stent thrombosis in patients with ST elevation myocardial infarction: TIMI risk index. *J Cardiovasc Thorac Res*. 2019;11(3):182-188. [CrossRef]
12. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *Glob Heart*. 2018;13(4):305-338. [CrossRef]
13. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2012;33(20):2569-2619. [CrossRef]
14. Spencer KT, Kimura BJ, Korcarz CE, Pellikka PA, Rahko PS, Siegel RJ. Focused cardiac ultrasound: recommendations from the American Society of echocardiography. *J Am Soc Echocardiogr*. 2013;26(6):567-581. [CrossRef]
15. Tu JV, Donovan LR, Lee DS, et al. Effectiveness of public report cards for improving the quality of cardiac care: the EFFECT study: a randomized trial. *JAMA*. 2009;302(21):2330-2337. [CrossRef]
16. Serruys PW, Onuma Y, Garg S, et al. Assessment of the SYNTAX score in the Syntax study. *EuroIntervention*. 2009;5(1):50-56. [CrossRef]
17. de Araújo Gonçalves P, Ferreira J, Aguiar C, Seabra-Gomes R. TIMI, PURSUIT, and GRACE risk scores: sustained prognostic value and interaction with revascularization in NSTE-ACS. *Eur Heart J*. 2005;26(9):865-872. [CrossRef]
18. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. *Am J Cardiol*. 1983;51(3):606. [CrossRef]

19. Granger CB, Goldberg RJ, Dabbous O, et al. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med*. 2003;163(19):2345-2353. [CrossRef]
20. Harrison RW, Aggarwal A, Ou FS, et al. Incidence and outcomes of no-reflow phenomenon during percutaneous coronary intervention among patients with acute myocardial infarction. *Am J Cardiol*. 2013;111(2):178-184. [CrossRef]
21. Ndrepepa G, Tiroch K, Fusaro M, et al. 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. *J Am Coll Cardiol*. 2010;55(21):2383-2389. [CrossRef]
22. Scholz KH, Maier SK, Jung J, et al. Reduction in treatment times through formalized data feedback: results from a prospective multicenter study of ST-segment elevation myocardial infarction. *JACC Cardiovasc Interv*. 2012;5(8):848-857. [CrossRef]
23. Grabowski M, Filipiak KJ, Karpinski G, et al. Prognostic value of B-type natriuretic peptide levels on admission in patients with acute ST elevation myocardial infarction. *Acta Cardiol*. 2005;60(5):537-542. [CrossRef]
24. Zairis MN, Manousakis SJ, Stefanidis AS, et al. C-reactive protein levels on admission are associated with response to thrombolysis and prognosis after ST-segment elevation acute myocardial infarction. *Am Heart J*. 2002;144(5):782-789. [CrossRef]
25. Kontos MC, Shah R, Fritz LM, et al. Implication of different cardiac troponin I levels for clinical outcomes and prognosis of acute chest pain patients. *J Am Coll Cardiol*. 2004;43(6):958-965. [CrossRef]
26. Kaya A, Keskin M, Güvenç TS, Tatlısu MA, Kayapınar O. The predictive role of modified TIMI risk index in patients with ST-segment elevation myocardial infarction. *Acta Cardiol*. 2019;74(1):29-36. [CrossRef]