

ORIGINAL ARTICLE

The Relationship Between Gensini Score and In-Hospital Mortality in Patients with ST-Segment Elevation Myocardial Infarction

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Abstract

Background: To date, several validated patient-based risk scores have been established to predict mortality and morbidity in patients presenting with ST-segment elevation myocardial infarction (STEMI). The Gensini score was originally developed to quantify the severity of coronary artery disease (CAD).

Objectives: We intend to assess the association between severity of CAD assessed by Gensini score and in-hospital mortality in patients with STEMI undergoing primary percutaneous coronary intervention (P-PCI).

Methods: A total of 539 patients presenting with acute STEMI, who underwent P-PCI within the first 12 hours from the onset of symptoms, were included. The severity of CAD was expressed as the sum of the Gensini scores for each lesion. Patients' demographic variables, medical histories and clinical features, as well as in hospital major adverse events were obtained from the medical reports.

Results: Of these 539 patients, 416 (77.2%) were male and mean age was 59.14 ± 12.68 years. In-hospital mortality rate was 5.4% (29 patients; 16 men). Mortality rate was 10.5% in female patients and 3.8% in males ($P = 0.004$). Mean Gensini scores were significantly different in the comparison between patients who survived (54.54 ± 26.34) and those who died (80.17 ± 26.51) ($P = 0.001$). The multivariable Cox proportional hazards regression analysis model revealed that the Gensini score ($P = 0.037$), female gender ($P = 0.039$), serum urea levels ($P = 0.041$), uric acid levels ($P = 0.008$) and LVEF ($P = 0.001$) were independently associated with in-hospital mortality in patients with STEMI undergoing P-PCI.

Conclusion: The Gensini score is independently associated with in-hospital mortality in STEMI patients treated with P-PCI. Therefore, it might play an important role in risk stratification of STEMI patients. (Int J Cardiovasc Sci. 2017;30(1):32-41)

Keywords: Myocardial Infarction; Hospital Mortality; Data Interpretation, Statistical; Percutaneous Coronary Intervention.

Introduction

Although primary percutaneous coronary intervention (P-PCI) has been contributing to a decrease in mortality in recent years, ST-segment elevation myocardial infarction (STEMI) is still one of the leading cause of mortality and morbidity all over the world.¹ In-hospital mortality rates were reported as 7-10% in some registries.² Currently, several validated risk factors and scoring systems are used to predict mortality in STEMI patients. In the fibrinolytic era,

thrombolysis in myocardial infarction (TIMI) risk score was developed as a clinical risk score to predict 30-day mortality in patients with STEMI.³ TIMI score was derived and validated among fibrinolytic-eligible patients enrolled in clinical trials, so it can not be easily applied in STEMI patients undergoing P-PCI. Recently, the Global Registry of Acute Coronary Events (GRACE) score has been defined for predicting mortality at 6 months in patients with acute coronary syndromes (ACS), but critically ill patients such as those who died early may be underrepresented.⁴ In addition

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to these clinical scores, some coronary angiography based scoring systems such as Gensini, SYNTAX (*synergy between percutaneous coronary intervention with Taxus and cardiac surgery*) and ACC/AHA have been established to assess the severity of lesions and provide some prognostic information for patients with coronary artery disease (CAD). Although these scoring systems provide quantitative evaluation, the valuable detailed information derived from angiography is not sufficiently used. In clinical practice, there is a need for an initial stratification of STEMI patients, which aims to identify those at higher risk and decrease the incidence of major adverse cardiovascular events through more appropriate targeting of preventive measures.

The Gensini scoring system is an objective method to determine the severity of CAD according to angiographic findings.⁵ It was originally developed to quantify the severity of CAD; however, subsequent studies have demonstrated its ability to identify patients who are at high risk of adverse events who are treated with PCI.⁶ However, little is known about the association between the severity of CAD assessed by the Gensini score and in-hospital mortality in patients with STEMI undergoing P-PCI.

Objective

The aim of the present study was to evaluate the predictive role of Gensini score to detect in-hospital mortality in STEMI patients treated with P-PCI.

Methods

Our single-center study was retrospective and non-randomized (prospective researching the information, retrospectively). A total of 539 consecutive patients presenting with first acute STEMI who underwent P-PCI within the 12 hours from the onset of symptoms, between 2004 and 2013, were included in our study. Patients' demographic variables, medical histories and clinical features, as well as in hospital major adverse events were obtained from medical reports. Since our institute is a tertiary center, P-PCI was conducted as the preferred reperfusion strategy for most STEMI cases. Briefly, the diagnosis of STEMI was made through the criteria of classical symptoms of coronary ischemia (chest pain lasting > 30 minutes), detection of > 1 mm ST-segment elevation in at least two contiguous leads and elevation in cardiac biomarkers, and defined by

the guidelines of the American College of Cardiology and the European Society of Cardiology.⁷ All STEMI patients were admitted and followed up in intensive coronary care unit and hospital stay was defined as this first admission period of STEMI patients. Previous CABG (coronary artery bypass graft) or PCI, previous STEMI history, reperfusion with thrombolytic drug, known malignancy and severe liver diseases, insufficient data from the clinical recordings and angiographic recordings were all defined as exclusion criteria.

The severity of CAD was calculated using the Gensini score, in which the calculation is based on the evaluation of the number of stenotic segments along with their respective degrees of luminal narrowing and localization within the coronary tree.⁵ The severity of the disease was expressed as the sum of the scores for each lesion. Two investigators blinded to the patient's clinical data analyzed the results of the coronary angiography. The study protocol was approved by the local ethics committee (2013-157).

Statistical analysis

Data was processed through SPSS 16.0 statistical package (SPSS Inc, Chicago, IL, USA). All data are expressed as numbers and percentages and continuous variables were tested for normal distribution using the Kolmogorov-Smirnov test. Continuous data with normal distribution are presented as mean and standard deviation and compared by the unpaired T-test, and non-normally distributed data are presented as median and interquartile range and compared through the Mann-Whitney U test. Categorical data are presented as counts and percentages and compared using the chi-square test. Logistic regression analysis was performed to identify independent predictors of in-hospital mortality. For the multivariate analysis, a forward stepwise logistic regression was performed using the variables which were significant at the univariate analysis, together with risk factors. P values < 0.05 were considered statistically significant.

Results

The study population consisted of 539 patients with first STEMI that underwent P-PCI. Of these 539 patients, 416 (77.2%) were male and 123 (22.8%) were female. Mean age of the study population was 59.14 ± 12.68 years. The baseline characteristics are presented in Table 1 and

Table 1 – Baseline demographical and clinical features of the groups

	Survival (n = 510)	Death (n = 29)	p value
Age (years)	58.58 ± 12.52	68.96 ± 11.52	0.001*
Sex (men), n (%)	400 (%78.4)	16 (%55.2)	0.004
Smoking, n (%)	233 (%45.7)	13 (%44.8)	0.928
Heart rate (beats/minute)	79.90 ± 16.99	86.51 ± 24.64	0.004
Systolic blood pressure, (mmHg)	132.23 ± 24.96	116.96 ± 24.67	0.756
Diastolic blood pressure, (mmHg)	77.73 ± 14.60	69.29 ± 17.43	0.119
Diabetes mellitus n (%)	116 (%22.7)	10 (%34.5)	0.146
Hypertension, n (%)	218 (%42.8)	19 (%65.5)	0.017
Hyperlipidemia, n (%)	96 (%18.8)	5 (%17.29)	0.832
Chronic renal disease, n (%)	18 (%3.5)	10 (%34.5)	0.001
Coronary artery disease, n (%)	84 (%16.5)	6 (%20.7)	0.553
Left ventricular ejection fraction, (%)	50.98 ± 8.50	34.72 ± 5.66	0.028
Left ventricular end diastolic diameter, (mm)	48.52 ± 5.58	29.38 ± 4.17	0.436*

*Data without normal distribution compared through Mann-Whitney U test.

Table 2. In-hospital mortality rate was 5.4% (29 patients; 16 men). Twenty-nine patients (5.3%) died during the hospital stay. Causes of death for these 29 patients were: malignant cardiac arrhythmias such as VT/VF in 8 patients (27.5%), cardiogenic shock in 8 patients (27.5%), acute pulmonary edema in 4 patients (13.7%), right heart failure in 3 patients (10.3%), bleeding complications in 2 patients (6.8%), septic shock in 1 patient (3%), acute mitral regurgitation in 1 patient (3%), ventricular septal rupture in 1 patient (3%), and ventricular free wall rupture in 1 patient (3%). Mortality rate was 10.5% for female patients and 3.8% for males ($P = 0.004$). Of these 539 patients who underwent P-PCI, 454 (84%) were treated successfully with BMS. From the remaining 85 patients, 18 (4%) were treated with DES, 26 (5%) with plain PTCA, in 18 (3%) patients the procedure failed, and 23 (5%) patients underwent CABG. In-hospital mortality did not differ between the groups on different therapies during P-PCI ($P > 0.05$).

In the initial statistical analysis, we found that some variables significantly differed between patients who survived and those who died. Female gender, history of hypertension, chronic renal disease, age, admission blood glucose, urea, creatinine and uric

acid levels, heart rate, leukocytes, hemoglobin, platelet and neutrophil count, and LVEF were found to be statistically significantly different between the two groups. ($P < 0.05$ for all). Angiographic data is shown in Table 3. Mean Gensini scores were significantly different in the comparison between patients who survived (54.54 ± 26.34) and those who died (80.17 ± 26.51) ($P = 0.001$) (Figure 1). The infarction-related vessel was the left anterior descending coronary artery (LAD) in 224 patients (41.5%), the circumflex coronary artery (CFX) in 104 patients (19.2%), and the right coronary artery (RCA) in 196 patients (36.3%). In-hospital mortality did not differ between the groups of different infarction-related vessels ($P > 0.05$).

We applied a logistic regression analysis to identify independent risk factors for in-hospital mortality in patients with STEMI undergoing P-PCI. The results of the univariable logistic regression analysis are shown in Table 4. For the multivariate analysis, a forward stepwise logistic regression was performed using the variables which were significant at the univariate analysis, together with risk factors. The multivariable Cox proportional hazards regression analysis model revealed that the Gensini score ($P = 0.037$), female

Table 2 – Laboratory findings of the groups

	Survival (n = 510)	Death (n = 29)	p value
Glucose (mg/dL)	149.37 ± 68.17	199.42 ± 103.91	0.048*
Urea (mg/dL)	38.09 ± 17.82	59.03 ± 35.34	0.001*
Creatinine (mg/dL)	1.05 ± 0.49	1.41 ± 0.66	0.001*
Uric acid (mg/dL)	5.52 ± 2.01	7.59 ± 2.97	0.002*
High density lipoprotein, (mg/dL)	42.13 ± 23.01	40.00 ± 7.82	0.670
Low density lipoprotein, (mg/dL)	113.74 ± 36.70	112.95 ± 46.49	0.881*
Triglycerides (mg/dL)	140.06 ± 100.43	128.20 ± 76.43	0.569*
Albumin (g/dL)	3.40 ± 0.54	3.15 ± 0.57	0.085*
Leukocytes (n/μL)	11.695.39 ± 4.031.71	14.646.42 ± 7.062.39	0.017*
Hemoglobin (g/dL)	13.77 ± 1.97	12.55 ± 2.07	0.006*
Hematocrit (%)	41.19 ± 5.18	37.68 ± 5.60	0.202
Platelet (x10 ³ /μL)	248.37 ± 70.35	253.25 ± 100.67	0.010
Neutrophil (n/μL)	7.953.01 ± 3.384.94	10.045.93 ± 6.286.28	0.032*
Lymphocyte (n/μL)	2531.72 ± 2362.84	2407.87 ± 2173.31	0.279*

*Data without normal distribution is compared by Mann-Whitney U test.

gender (P = 0.039), urea levels (P = 0.041), uric acid levels (P = 0.008) and LVEF (P = 0.001) were independently associated to in-hospital mortality in patients with STEMI undergoing P-PCI (Table 5).

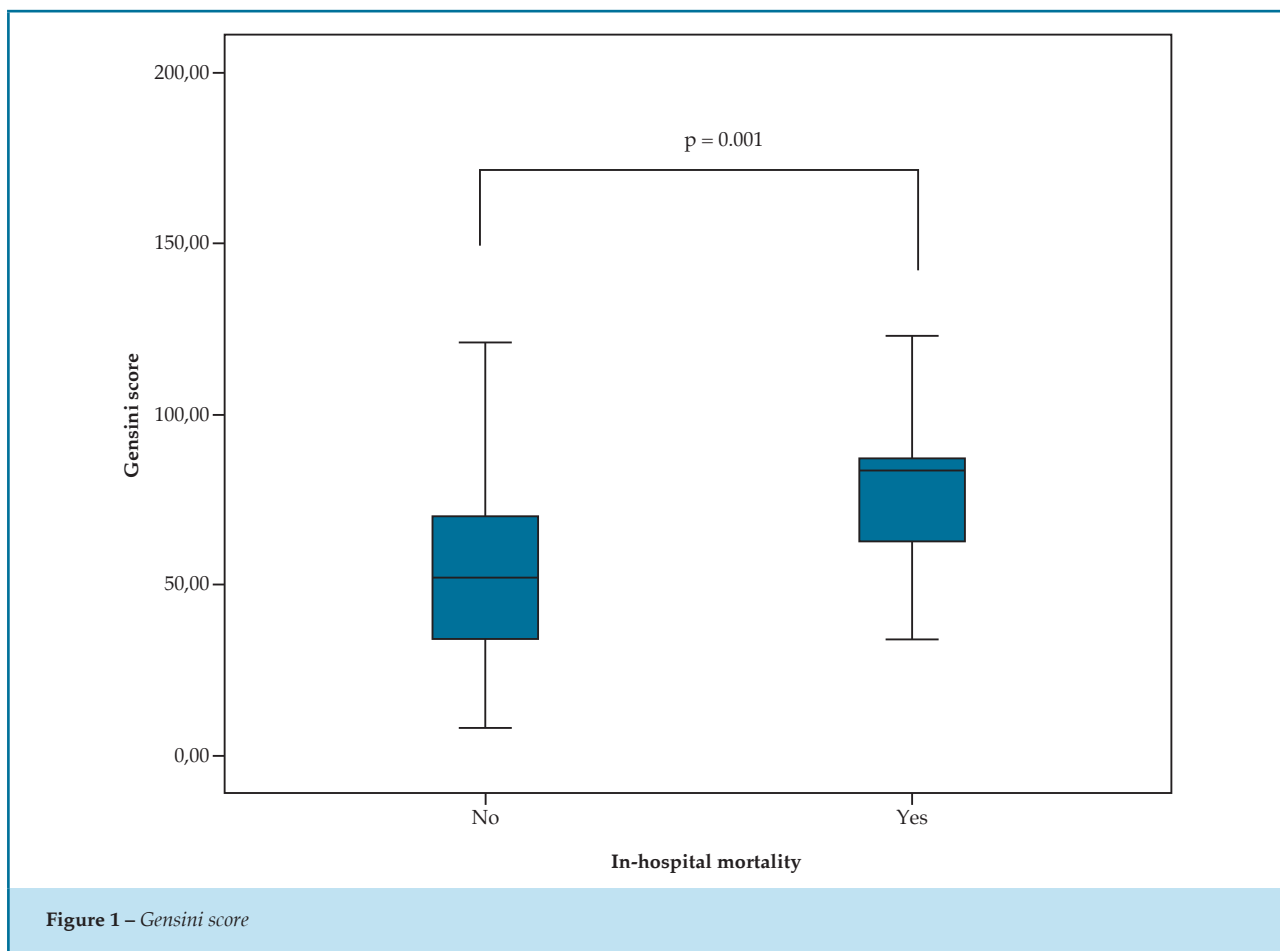
We independently examined 25 randomly chosen angiograms, visually estimated lesion scores, and calculated Gensini scores. The intra-observer and inter-observer correlation coefficient was 0.96 and 0.95 for the Gensini score, indicating good reproducibility and reliability.

Discussion

The main finding of this study was that the Gensini score is independently associated to in-hospital mortality in STEMI patients treated with P-PCI. Nonetheless, the female gender, higher serum urea and uric acid levels, and lower LVEF were also associated to in-hospital mortality in this group of patients.

STEMI is the most important part of ACS. Consistently with our data, in-hospital mortality rates ranged between 6% and 14%.⁸ Many factors such as previous MI, door to balloon time, presence

of diabetes, anemia, chronic renal failure, and ejection fraction on admission are known to be predictors of mortality in this era.⁹ To date, several validated patient-based risk scores such as TIMI, GRACE, ZWOLLE, CADILLAC and PAMI have been established for predicting mortality and morbidity in patients presenting with STEMI.¹⁰⁻¹³ Most of these scores were based on clinical parameters such as age, gender, Killip class, serum creatinine levels, and degree of ST-segment change. This is not surprising, as these scores were developed before the widespread adoption of P-PCI for STEMI. TIMI and GRACE scores are valuable tools for initial risk stratification of STEMI patients. TIMI is widely accepted due to its ease of use. Despite its good predictive power, the GRACE score has limited bedside use because of the necessity to use specialized computer software and graphs. These scores were not specifically optimized for patients with STEMI undergoing P-PCI. In the P-PCI era, some of the scoring systems such as CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications),¹² Stent-PAMI

**Table 3 – Angiographic data**

	Survival (n = 510)	Death (n = 29)	p value
Coronary artery involvement			
LAD, n (%)	210 (41.1)	14 (48.2)	
CFX, n (%)	104 (20.3)	5 (17.2)	0.148
RCA, n (%)	196 (38.4)	10 (34.4)	
Gensini score	54.54 ± 26.34	80.17 ± 26.51	0.001

LAD: left anterior descending coronary artery; CFX: circumflex coronary artery; RCA: right coronary artery

(Stent-Primary Angioplasty in Myocardial Infarction),¹⁰ and MCRS (The Mayo Clinic Risk Score)¹⁴ included angiographic variables in the scoring algorithm. The CADILLAC risk score was able to accurately predict 30-day and 1-year mortalities after P-PCI in STEMI patients. Baptista et al.¹⁵ applied the PAMI

risk score to a small population of STEMI patients and revealed that this method was able to predict in-hospital, 30-day and 6-month mortality. The MCRS is also a validated risk model for pre-procedure risk stratification and has been showing a good capacity for the prediction of in-hospital mortality.¹¹

Table 4 – Results of univariable logistic regression analysis

Variable	OR	p value
Female gender	2.955	0.005
Gensini score	1.029	0.001
Urea	1.026	0.001
Uric acid	1.363	0.001
LVEF	0.797	0.001
History of hypertension	1.007	0.020
History of chronic renal disease	14.36	0.001
Age	1.076	0.001
Admission blood glucose	1.007	0.001
Creatinine	1.811	0.001
Uric acid	1.363	0.001
Heart rate	1.022	0.048
Systolic blood pressure	0.974	0.002
Diastolic blood pressure	0.962	0.004
Leucocytes count	1.000	0.004
Neutrophil count	1.156	0.001
Hemoglobin	0.733	0.002
Hematocrit	0.879	0.001
Albumin	0.424	0.044

Table 5 – Effects of several variables on in-hospital mortality by the multivariable regression analysis

Variable	Adjusted OR	95% CI	p value
Female gender	7.780	1.10-54.66	0.039
Gensini score	1.033	1.00-1.06	0.037
Urea	1.030	1.00-1.06	0.041
Uric acid	1.544	1.11-2.13	0.008
LVEF	0.761	0.65-0.88	0.001

**By entering gender, age, history of hypertension, chronic renal disease, admission blood glucose, urea, creatinine, uric acid, heart rate, SBP, DBP, leukocytes count, neutrophil count, hemoglobin, hematocrit, albumin, LVEF and the Gensini score*

In addition to those scores, which were established from combination of both clinical and angiographic variables, some scoring systems based solely on

angiographic data such as SYNTAX are associated to short and long-term follow-up in patients with STEMI undergoing P-PCI.¹⁶⁻¹⁸

The purpose of coronary scoring systems is to quantify the severity of coronary stenosis. Different coronary arteries carry different volumes of blood to the heart, and coronary scores take this into account. The degree of stenosis was also considered in these scoring systems. Overall, the individual ability of these angiography based scores to predict mortality is uncertain, and an important limitation is that these scores have been largely limited to elective patients.¹⁹ Although the SYNTAX score is frequently used for predicting mortality in patients with STEMI undergoing P-PCI, the percent diameter stenosis is not considered in scoring and a distinction is made only between occlusive (100%) and non-occlusive (50-99% stenosis) disease. Furthermore, stenosis is considered severe when it causes $\geq 50\%$ reduction in the luminal diameter by visual assessment in vessels ≥ 1.5 mm. However, in the Gensini score, lesions causing $< 50\%$ reduction in the luminal diameter in vessels < 1.5 mm diameter are considered in the scoring algorithm. The Gensini score was originally developed to quantify the severity of CAD. It has been widely used in clinical trials to assess the extent and severity of CAD. However, subsequent studies have demonstrated its ability to identify patients treated by PCI who are at high risk of adverse events. Nevertheless, little is known about the correlation between the Gensini score and short-term mortality in STEMI patients.²⁰⁻²³ There are few recently published studies that have evaluated the Gensini score in the context of P-PCI. In a recent report, the Gensini score was found to be associated with lower MACE during hospital stay and at 6 months after PCI in acute STEMI patients.²⁴ Thus, the authors concluded that it could be used to predict short-term MACE in STEMI patients during the post PCI period. Acet et al.²⁵ found that the TIMI risk index is significantly related to the Gensini score in predicting the extent and severity of CAD in patients with STEMI.

This study represents the analysis of the relationship between the Gensini score and in-hospital mortality in patients with STEMI undergoing P-PCI. The current study has demonstrated that STEMI patients with higher Gensini scores, regardless of other clinical variables, are at increased risk of in-hospital mortality. According to our study, a 1 point increase in the Gensini score is related to a 3% increase of in-hospital mortality risk in patients with STEMI undergoing P-PCI. Several factors could account for this finding: the Gensini score concentrates on the LMCA, proximal LAD, and mid-LAD arteries, which are assigned relatively higher weighting factors.

Occlusion of these coronary arteries causes large areas of infarction which may be related to higher mortality rates. One of the limitations of using the Gensini score for risk stratification is the absence of any clinical variables. This deficiency can be successfully addressed through its combination with clinical-based risk models. In our study, we also found that female gender, higher urea and uric acid levels and lower LVEF were associated to in-hospital mortality in STEMI patients undergoing P-PCI. These findings were consistent with previous studies in literature.²⁰⁻²³ In the univariate regression analysis, differently from other variables, hemoglobin, hematocrit, albumin and LVEF were found to be negatively correlated to in-hospital mortality, meaning that lower values in these variables were associated to a higher mortality. However, this association was no longer significant after the multivariate analysis, except for LVEF. Mortality rate was 10.5% (13/123) in women and 3.8% (16/416) in men. Higher in-hospital mortality in women is often attributed to a delayed hospital admission, a higher clustering of comorbidities, older age and more bleeding complications after interventions.²⁶⁻²⁸ Our study highlights the importance of adjusting mortality to these variables. We did not find a difference in the presence of diabetes, even though others have reported that this tends to be more common.

The result of our study was an improvement of existing conventional risk factors and scoring systems for STEMI patients. A particular strength of our study is that all patients admitted to hospital with a diagnosis of STEMI were included, unlike reports from some registries, in which only data from selected patients were analysed. Improving the prediction of mortality is a major challenge and selecting the proper therapy is difficult, but we think that the combination of established risk factors such as TIMI and GRACE with angiographic score assessment provides the best information to predict in-hospital mortality in STEMI patients undergoing P-PCI. Readily available risk factors such as hypertension, smoking, diabetes, LDL, family history of MI and clinical variables such as age, gender, door to balloon time and biomarkers should also be considered to improve the prediction of mortality.

Limitations

Our study has some important limitations. First and foremost, this study has a retrospective and single-center design. The results of this study may not be extrapolated

to all patients such as those who present with other form of ACS or those who were not treated with PCI. The relatively small sample size of the current study indicates the need to validate the findings with a larger patient cohort. Door to balloon time and onset of the infarction are important parameters which may also be associated to in hospital mortality. However, due to our retrospective design and insufficient medical reports, a considerable amount of patient data about the onset of the infarction or door to balloon time were lacking or unreliable. Therefore, these parameters could not be studied. In clinical practice, angiographic scores are calculated by visual lesion assessment (rather than laboratory determination), which would likely lead to greater interobserver variability. Also, we did not compare the Gensini score to other angiographic score systems such as the SYNTAX, which is frequently used to predict mortality in STEMI patients undergoing P-PCI. Further prospective randomized studies with a large sample and attendance of multicentre are required to confirm this hypothesis more effectively.

Conclusions

It is clear that there is a clinical necessity for an accurate and useful scoring system to identify patients at a higher risk for in-hospital mortality, who require more intensive care. The Gensini score may have a valuable role in the

risk stratification of STEMI patients undergoing P-PCI. However, the Gensini score should be improved through a combination that includes clinical, procedural and laboratory variables.

Author contributions

Conception and design of the research: Yildirim E, Iyisoy A, Yuksel UC. Acquisition of data: Yildirim E, Celik M, Yuksel UC, Bugan B, Gokoglan Y. Analysis and interpretation of the data: Yildirim E, Iyisoy A, Celik M, Yuksel UC, Bugan B, Gokoglan Y. Statistical analysis: Yildirim E, Celik M, Acikel C. Writing of the manuscript: Celik M, Bugan B. Critical revision of the manuscript for intellectual content: Yildirim E, Iyisoy A, Yuksel UC, Acikel C, Gokoglan Y. Supervision: Iyisoy A.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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