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The impact of preoperative fibrinogen-albumin ratio on mortality in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

Lei Xiao[1], Yu Jia[1], Xueli Wang, He Huang*

Department of Cardiology, West China Hospital, Sichuan University, Chengdu, China

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ABSTRACT

Background: We investigated the prognostic value of fibrinogen-albumin ratio (FAR) in patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI) based on inflammation and hemorheology alterations and to determine whether FAR can supplement incremental predictive information to the Global Registry of Acute Coronary Events (GRACE) score.

Methods: We retrospectively analyzed 475 STEMI patients undergoing pPCI. Kaplan-Meier curve, Cox proportional hazards regression model, and Hosmer-Lemeshow test were used to evaluate the prognostic value of FAR in the patients.

Results: Patients were assigned to groups of high FAR ($\geq$0.080) vs low FAR ($<$ 0.080) based on the optimal cutoff value of 0.080. In all, 59 patients (12.4%) died; the mortality rate was higher in high FAR patients than in low FAR patients (20.5% vs. 8.6%, $p < .001$). FAR positively correlated with C-reactive protein, GRACE score, and Gensini score ($p < .001$). On multivariate analysis, FAR was an independent prognostic factor in STEMI patients undergoing pPCI. Accordingly, adding FAR to the GRACE score improved the C-index, net reclassification index, and integrated discrimination improvement.

Conclusions: Preoperative FAR is an independent prognostic factor in STEMI patients undergoing pPCI and might improve risk stratification in STEMI.

1. Introduction

Coronary atherosclerotic heart disease is the leading cause of morbidity and mortality worldwide. Acute ST-segment elevation myocardial infarction (STEMI) is the most serious type of coronary heart disease (CHD). Despite tremendous advances in revascularization strategies, including percutaneous coronary intervention (PCI), coronary artery bypass graft, and coronary intensive care, the first-year mortality rate for STEMI patients remains approximately 10% [1]. Researchers have been trying to identify more effective predictors to improve prognosis of acute myocardial infarction (AMI)-related mortality. The Global Registry of Acute Coronary Events (GRACE) [2] score is currently one of the most widely used risk stratification tools and predictors of mortality in STEMI patients. However, the GRACE score still needs to be improved because it does not include some disease dimensions concerning STEMI outcomes such as inflammation, hemorheology, and coronary artery lesion. Separate biomarkers addressing such aspects of STEMI pathophysiology may provide additional information [3].

CHD is a chronic inflammatory state and the inflammatory reaction is involved throughout the pathological process of atherosclerosis, from fatty streak formation during coronary atherosclerosis development to plaque rupture during AMI [4,5]. Simultaneously, high plasma viscosity and thrombus tendency are considered primary risk factors for acute coronary syndrome and thrombotic events [6,7]. However, evaluating inflammatory status and hemorheological alteration is useful in inflammatory and thrombotic diseases but is complex and expensive, so the clinical application is limited.

Fibrinogen (FIB) and albumin (ALB) are widely used and important factors in response to systemic inflammatory and hemorheological alterations. Previous studies have shown that increased concentration of FIB, a positive acute-phase inflammatory protein that increases thrombosis risk, is an independent predictor of CHD and MI [8,9]. Increased FIB concentration is an independent factor in myocardial injury

* Corresponding author at: Department of Cardiology, West China Hospital, Sichuan University, 37 Guoxue Road, Chengdu 610041, Sichuan, China.
E-mail address: xhehuang@yahoo.com (H. Huang).

[1] These authors contributed equally to this work.

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prognosis [8]. In contrast, studies have shown that decreased concentration of ALB, a negative inflammatory protein and major factor affecting plasma viscosity, is a risk factor for incident AMI in patients with CHD and is associated with increased cardiovascular morbidity and long-term mortality [10,11]. Furthermore, hypoalbuminemia can predict the no-flow phenomenon in STEMI patients after PCI [12].

Fibrinogen-albumin ratio (FAR), comprising these two indicators, is a valuable serological marker [13] that may reflect information on hemorheology and inflammation as well as some possible additional disease conditions in STEMI patients. Increased FAR concentration have been reported in patients with cardiovascular events [14,15] and are significantly associated with the severity of coronary stenosis in STEMI patients [15], suggesting that FAR may play an important role in vascular thrombotic diseases. Therefore, FAR may aid in STEMI prognosis, which has not been studied so far. We aimed to investigate the prognostic value of FAR for all-cause mortality in STEMI patients undergoing primary PCI (pPCI) and to determine whether FAR knowledge adds predictive information to the GRACE score.

2. Materials and methods

2.1. Study population

The present investigation was a single-center, observational, retrospective cohort study among consecutive STEMI patients who underwent pPCI at Department of Cardiology, West China Hospital, Sichuan University, Chengdu, China, from May 2016 to September 2017. The diagnosis of STEMI was based on the criteria determined by the American College of Cardiology [16] and the European Society of Cardiology [17], which was defined as > 30 min of continuous typical chest pain and ST-segment elevation by ≥2 mm in 2 contiguous electrocardiography leads or new left bundle-branch block or increased cardiac troponin T (cTnT), with or without evidence of continuing ischemia or hemodynamic instability within 12 h of symptom onset. Twenty-three patients who refused pPCI and six patients diagnosed with non-spontaneous STEMI after pPCI were excluded. A total of 21 patients with a history of severe valvular disease (n = 3), severe liver disease (n = 2), neoplasm (n = 5), end-stage renal disease with dialysis treatment (n = 7), autoimmune disease (n = 3), or systemic inflammatory disease (n = 1) were also excluded. Finally, a total of 475 patients were selected and included consecutively into this study. The study protocol was approved by the Human Ethical Committee of West China Hospital of Sichuan University in accordance with the Declaration of Helsinki [18]. All participants gave informed written consent.

2.2. Data collection

Comprehensive information on medical history, cardiovascular risk factors, vital signs at admission, medications at discharge, and final diagnosis was obtained from hospital records or via interview. Blood samples were collected before pPCI; complete blood count was analyzed using an automated hematology analysis system (LH750, Beckman Coulter Inc.). The FIB concentration was measured using a Sysmex CA-7000 analyzer (Siemens Healthcare Diagnostics); concentration of alanine aminotransferase, lactate dehydrogenase, albumin, blood urea nitrogen, creatinine, uric acid, high-density lipoprotein, low-density lipoprotein, and total cholesterol were analyzed using an Architect c16000 analyzer (Abbott Diagnostics); the C-reactive protein (CRP) concentration was determined using a Cobas S6000 Hitachi analyzer (Roche Diagnostics); and the concentration of cTnT and N-terminal pro-brain natriuretic peptide (NT-proBNP) were analyzed using an immunology analyzer (Cobas E601, Roche Diagnostics) with the electrochemiluminescence method. The left ventricular ejection fraction (LVEF) was calculated using the biplane Simpson's method with the Philips iE33 ultrasound system (Philips Medical Systems). The GRACE score was calculated from age, heart rate, Killip class, systolic blood pressure, creatinine concentration, cardiac arrest, ST-segment deviation, and increased cardiac enzyme concentration at admission as previously reported [2]. Further, the Gensini score was calculated according to the geometrical severity of lesions, the cumulative effects of multiple obstructions, the significance of their locations, and the modifying influence of the collaterals of the coronary artery after coronary arteriography [19].

2.3. Primary endpoint and follow-up

The primary endpoint was all-cause death. In-hospital and post-discharge outcomes were collected from medical records and during patient follow-up visits to the hospital. Participants were followed up via telephone interview, clinical attendance, or letter correspondence.

2.4. Statistical analysis

Data were calculated as mean ± standard deviation or median with interquartile interval (25th–75th percentile) for continuous variables and as frequencies and percentages for categorical variables. Patient characteristics and their association with FAR were compared using analysis of variance for continuous variables and χ^2 test for categorical variables. The receiver operating characteristic (ROC) curve was applied to determine an optimal cutoff value for FAR according to the Youden index. Spearman's correlation coefficient was used to examine the association between FAR and CRP, GRACE score, and Gensini score. Cumulative survival rates between the low FAR and high FAR groups were compared by using the Kaplan-Meier curve and the log-rank test. Cox proportional hazards model was employed to investigate whether FAR was related to time-to-mortality during the study period. To build the Cox model, a univariate model for each predictor variable was employed, with mortality as the outcome variable. Meanwhile, the variables that were significant in the univariate model were included in the multivariable Cox model. Results are reported as hazard ratios (HRs) with 95% confidence intervals (CIs). To assess whether the accuracy of predicting all-cause mortality would improve after adding FAR to the GRACE score, the C-index, net reclassification improvement (NRI), and integrated discrimination improvement (IDI) were calculated by Hosmer-Lemeshow test. Data analysis was performed using SPSS Statistics for Windows version 21.0 (Chicago, IL: SPSS, Inc.) and R for Windows version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria). A 2-sided $p < .05$ was considered statistically significant in all analyses.

3. Results

3.1. Baseline patient characteristics

In total, 475 consecutive STEMI patients undergoing pPCI were included in the study. The average age was 64.07 ± 13.47 y, and 363 (76.4%) were males. The median interval between the appearance of symptoms before pPCI and blood sampling was 5.2 (2.3–10.5) h. Of these patients, 23 (4.8%) died while they were hospitalized and 36 (7.6%) died during the follow-up period (median follow-up duration, 14.4 [9.3–17.6] months). The median preoperative FAR value among patients was 0.067 (0.054–0.087). The optimal cutoff value for FAR determined by the ROC curve was 0.080 (the area under the ROC curve: 0.659, 95% CI: 0.578–0.735, $p < .001$) with a sensitivity of 56.9% and specificity of 72.4% (Fig. 1). The patients were assigned to groups based on a high (≥0.080) or low (< 0.080) FAR.

3.2. Association between preoperative FAR and clinical characteristics

There were significant differences in terms of age ($p < .001$), diabetes status ($p = .021$), diastolic blood pressure on admission ($p = .040$), proportion of patients with Killip class ≥2 ($p = .017$),

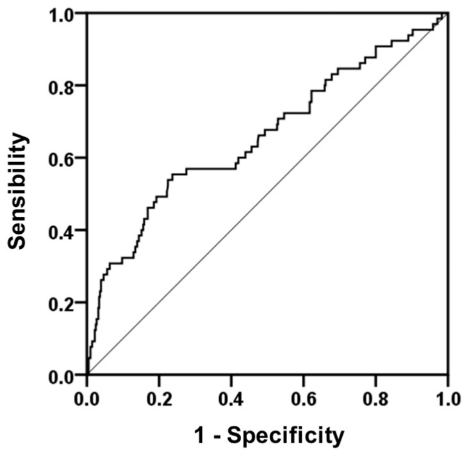

Fig. 1. Determination of the cutoff value for the FAR in STEMI patients undergoing pPCI by ROC analysis. FAR, Fibrinogen-Albumin Ratio; STEMI, ST-segment elevation myocardial infarction; pPCI, primary percutaneous coronary intervention; ROC, receiver operating characteristic.

hemoglobin concentration ($p < .001$), creatinine concentration ($p < .001$), CRP ($p < .001$), total cholesterol ($p = .004$), NT-proBNP ($p < .001$), cTnT ($p = .001$), LVEF ($p < .001$), GRACE score ($p < .001$), and Gensini score ($p = .002$) between the two groups, as shown in Table 1. FAR positively correlated with CRP concentration ($r = 0.527$, $p < .001$) (Fig. 2), GRACE score ($r = 0.285$, $p < .001$), and Gensini score ($r = 0.403$, $p < .001$) (Fig. 3).

3.3. FAR and all-cause mortality

All-cause mortality in our cohort was 12.4% (59 patients). Death included heart failure ($n = 17$), cardiogenic shock ($n = 7$), recurrent myocardial infarction ($n = 6$), pulmonary infection ($n = 5$), malignant arrhythmia ($n = 5$), sudden death ($n = 4$), multiple organ failure ($n = 3$), massive gastrointestinal hemorrhage ($n = 3$), acute renal failure ($n = 2$), cerebral hemorrhage ($n = 1$), and death of unknown origin at other hospitals ($n = 6$). The mortality rate was higher in high FAR group than in the low FAR group (20.5% vs. 8.6%, $p < .001$). Kaplan-Meier survival analysis showed that the cumulative survival rate of the high FAR group was lower than that of the low FAR group during the follow-up period of > 1 y (log-rank = 19.41, $p < .001$) (Fig. 4). Univariate analysis showed that age, heart rate, Killip class, hemoglobin, creatinine concentration, NT-proBNP, LVEF, and FAR were prognostic factors. Multivariate analysis indicated age, Killip class, creatinine concentration, LVEF, and FAR as independent prognostic factors in STEMI patients undergoing pPCI (Table 2).

3.4. Discrimination and reclassification of FAR

Adding FAR to the GRACE score improved the prediction of mortality, as shown by the significant increase in the C-index for FAR with GRACE score (C-index: 0.797, 95% CI 0.741–0.819) compared with that for GRACE score alone (C-index: 0.755, 95% CI 0.723–0.790) ($p = .001$). IDI also improved significantly after adding FAR (IDI: 0.014, 95% CI 0.005–0.026; $p = .006$). Furthermore, the addition of FAR significantly improved the reclassification of patients beyond the GRACE score (NRI: 0.278, 95% CI 0.014–0.543; $p = .039$) (Table 3).

4. Discussion

Our study showed that FAR may be associated with cardiovascular risk factors and underlying cardiovascular disease burden; accordingly, the patients with high FAR had older age and higher total cholesterol, creatinine, cTnT, and NT-proBNP concentration in addition to worse cardiac function (Killip class and LVEF) than patients with low FAR. FAR had a significantly positive correlation with the Gensini score, which is an effective and relatively simple means of quantifying angiographic atherosclerosis that has been clinically widely used [20], similar to a previous study concerning the association between FAR and Syntax score [15]; wherein information about the severity and extent of coronary arteriosclerosis lesions could be obtained before operation with the help of the calculated FAR of STEMI patients admitted to the hospital. In addition, a positive correlation was also found between FAR and CRP, a widely used inflammation indicator. Both FIB and CRP are hepatic acute phase proteins produced in response to circulating proinflammatory cytokines, which might help assess the inflammatory state [21]. After adjusting for confounding factors, FAR was an independent predictor of all-cause mortality. Thus, FAR successfully

Table 1
Relationship between clinical characteristics and the FAR in patients with STEMI undergoing pPCI.

Characteristic	High FAR ($n = 151$)	Low FAR ($n = 324$)	p
Age, years	67.96 ± 12.90	62.26 ± 13.37	< 0.001
Males, n (%)	107 (70.9%)	256 (79.0%)	NS
BMI, kg/m^2	24.38 ± 9.42	27.43 ± 61.76	NS
Smoking, n (%)	67 (44.4%)	142 (43.8%)	NS
Drinking, n (%)	86 (56.9%)	171 (52.8%)	NS
Hypertension, n (%)	75 (50.0%)	169 (52.2%)	NS
Diabetes, n (%)	115 (76.2%)	275 (84.9%)	0.021
SBP, mmHg	121.85 ± 23.72	125.10 ± 22.94	NS
DBP, mmHg	76.05 ± 16.26	79.34 ± 16.10	0.040
Heart rate, /min	81.43 ± 17.70	77.97 ± 15.99	NS
Killip class ≥2, n (%)	104 (68.9%)	186 (57.4%)	0.017
GRACE Score, n	176.52 ± 40.59	153.65 ± 39.65	< 0.001
Laboratory findings			
WBC, $*10^9$/l	12.35 ± 17.04	13.82 ± 55.31	NS
Neutrophil count, $*10^9$/l	10.34 ± 11.51	10.52 ± 12.23	NS
Hemoglobin, g/l	128.29 ± 25.471	138.07 ± 21.143	< 0.001
Platelet count, $*10^{12}$/l	177.162 ± 68.75	172.71 ± 77.11	NS
ALT, IU/l	49.36 ± 123.03	45.61 ± 92.74	NS
LDH, IU/l	369.29 ± 356.98	369.12 ± 474.74	NS
Creatinine, μmol/l	106.34 ± 112.70	81.99 ± 36.52	< 0.001
Blood urea nitrogen, mmol/l	7.55 ± 5.71	7.43 ± 20.26	NS
Uric acid, mmol/l	381.68 ± 193.08	381.18 ± 106.00	NS
Total cholesterol, mmol/l	4.65 ± 1.10	4.34 ± 1.13	0.004
HDL, mmol/l	1.16 ± 0.34	1.17 ± 0.32	NS
LDL, mmol/l	2.77 ± 0.98	2.74 ± 0.94	NS
CRP, mg/l	18.0 (5.7–70.9)	3.6 (2.2–6.5)	< 0.001
NT-proBNP, pg/ml	1741 (580–4450)	233 (73–967)	< 0.001
Cardiac Troponin T, pg/ml	965.3 (184.6–2633.0)	179.3 (36.5–1020.5)	0.001
LVEF, (%)	49.05 ± 11.55	54.20 ± 10.22	< 0.001
Discharge medication			
Dual antiplatelet therapy, n (%)	140 (92.7%)	304 (93.8%)	NS
β-blockers, n (%)	86 (57.0%)	179 (55.2%)	NS
Statins, n (%)	143 (95.3%)	296 (94.3%)	NS
Affected coronary artery			
Left main, n (%)	21 (13.9%)	41 (12.7%)	NS
Left anterior descending, n (%)	123 (81.4%)	274 (84.6%)	NS
Left circumflex, n (%)	80 (53.0%)	212 (65.4%)	0.009
Right coronary artery, n (%)	108 (71.5%)	237 (73.1%)	NS
Gensini score, n	66.32 ± 41.98	56.99 ± 40.64	0.002
Outcome			
All-cause mortality	31 (20.5%)	28 (8.6%)	< 0.001

FAR, Fibrinogen-Albumin Ratio; STEMI, ST-segment elevation myocardial infarction; pPCI, primary percutaneous coronary intervention; BMI, Body Mass Index; SBP, systolic blood pressure; DBP, diastolic blood pressure; GRACE, Global Registry of Acute Coronary Events; NT-proBNP, N-terminal pro-brain natriuretic peptide; LVEF, left ventricular ejection fraction.

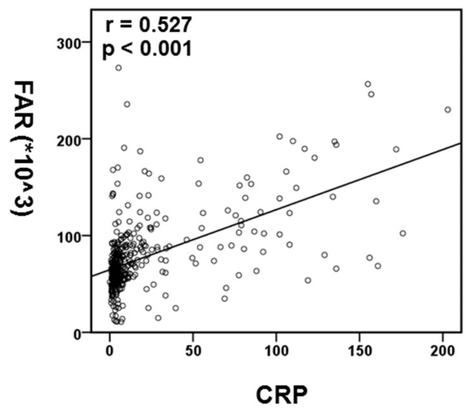

Fig. 2. Correlations of FAR with the CRP. FAR, Fibrinogen-Albumin Ratio; CRP, C-reactive protein.

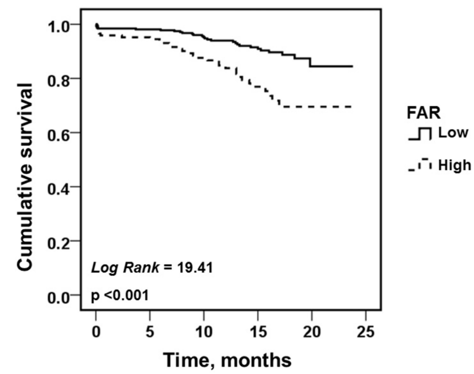

Fig. 4. Kaplan-Meier analysis survival curve stratified by FAR in patients with STEMI undergoing pPCI. FAR, Fibrinogen-Albumin Ratio; STEMI, ST-segment elevation myocardial infarction; pPCI, primary percutaneous coronary intervention.

predicted poor prognosis in STEMI patients undergoing pPCI, possibly based on underlying inflammatory mechanisms and hemorheological alterations during AMI.

FIB, the numerator in FAR, is a reaction protein of acute phase inflammation with positive proinflammatory effects [22]. FIB upregulates the synthesis of the proinflammatory cytokines such as interleukin-1 and tumor necrosis factor [23,24], which could inhibit the formation of stable fibrous caps, attack collagen in the cap, and mediate enhanced expression of adhesion molecules, resulting in endothelial dysfunction and thrombus formation. All these reactions could further conceivably induce the activation and rupture of plaque, thrombosis, and ischemia [25]. FIB also acts as a precursor of fibrin that binds to platelet FIB receptors and promotes platelet aggregation [26]. In addition, increased FIB concentration is associated with increased plasma viscosity by increasing convection and diffusion resistance of large particles, which further lead to decreased blood flow velocity and increased erythrocyte aggregation by binding of adjacent erythrocytes leading to rouleaux by protein ridges, ultimately increasing the affinity for thromboxane and the risk of thrombosis [27].

Serum ALB, the main component that maintains plasma oncotic pressure, is also involved in acute inflammatory reactions, but acts as a negative inflammatory protein that has been shown to have protective anti-inflammation properties [28]. Thus, hypoalbuminemia may result in worsening oxidative damage and inflammation [29] because of the effect of cytokines, such as interleukin-6 and tumor necrosis factor-α, and reduced potential for oxygen radical scavenging [30], which would further promote endothelial damage, plaque erosion, and rupture [28,31]. In contrast, ALB is one of the main factors affecting plasma viscosity, which might negatively correlate with erythrocyte aggregation and play an important role in inhibiting platelet activation and

Table 2
Cox regression of all-cause mortality for patients with STEMI undergoing pPCI.

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	*p*	HR	95% CI	*p*
FAR	1.011	1.006–1.016	< 0.001	1.007	1.001–1.013	0.017
Age	1.052	1.030–1.075	< 0.001	1.030	1.004–1.057	0.026
Heart rate	1.053	1.015–1.092	0.006	1.009	0.994–1.015	NS
Killip class	2.814	2.254–3.514	< 0.001	2.649	1.865–3.267	< 0.001
Hemoglobin	0.984	0.977–0.990	< 0.001	1.010	0.999–1.022	NS
Creatinine	1.004	1.003–1.006	< 0.001	1.004	1.002–1.006	< 0.001
NT-proBNP	1.012	1.007–1.016	< 0.001	1.004	0.994–1.015	NS
LVEF	0.901	0.874–0.929	< 0.001	0.923	0.898–0.940	< 0.001

STEMI, ST-segment elevation myocardial infarction; pPCI, primary percutaneous coronary intervention; FAR, Fibrinogen-Albumin Ratio; NT-proBNP, N-terminal pro-brain natriuretic peptide; LVEF, left ventricular ejection fraction.

aggregation [32]. Hypoproteinemia stimulates the synthesis of lipids and coagulation factors, leading to hyperlipidemia and hypercoagulability, which results in the formation of atherosclerotic plaques and thrombosis [32]. Moreover, serum ALB is the most sensitive indicator of one's nutritional status, which has a significant impact on the prognosis of AMI [33].

The inflammatory response to AMI is significant with acute exacerbation [34]. In AMI, the ruptured atherosclerotic plaques can lead to microcirculation disorders, which further stimulate systemic inflammation [35]. Inflammation plays a key role in the instability of atherosclerotic plaques and the adhesion of thrombi to the damaged plaque surface [35,36]. In addition, inflammation is positively associated with myocardial ischemia-reperfusion injury, suggesting that a

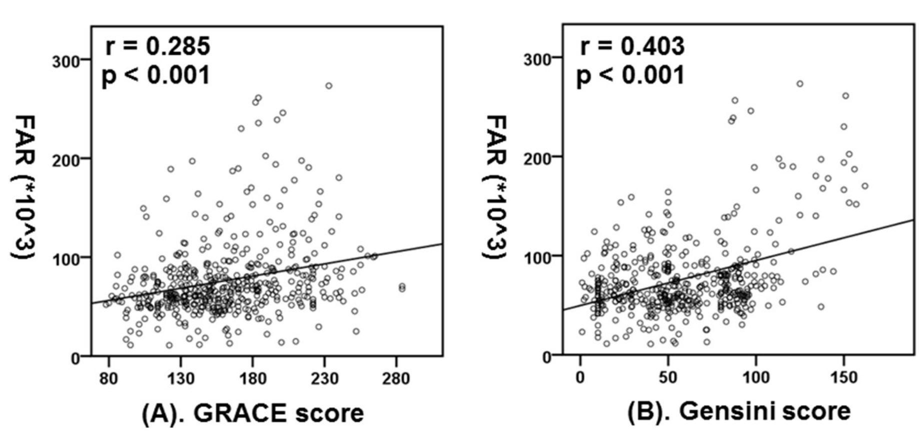

Fig. 3. Correlations of FAR with the (A) GRACE score and (B) Gensini score. FAR, Fibrinogen-Albumin Ratio; GRACE, Global Registry of Acute Coronary Events.

Table 3
Evaluation of predictive value for All-cause mortality.

	C-index (95% CI)	p	NRI (95% CI)	p	IDI (95% CI)	p
All-cause mortality						
GRACE score	0.755 (0.723–0.790)	Ref.		Ref.		Ref.
GRACE scores + FAR	0.797 (0.741–0.819)	0.001	0.278(0.014–0.543)	0.039	0.014(0.005–0.026)	0.006

GRACE, Global Registry of Acute Coronary Events; FAR, Fibrinogen-Albumin Ratio; NRI, net reclassification improvement; IDI, integrated discrimination improvement.

higher degree of inflammation leads to a larger infarct size [37]. In contrast, the tendency toward ischemia and thrombosis in vascular stenosis is because of the hemorheological alteration of slower blood flow and increased viscosity, which could have direct mechanical effects on either the vascular endothelium or an existing atheromatous plaque [38]. The magnitude of plasma viscosity is of major importance in determining blood flow in microcirculation and tissue perfusion. Increased plasma viscosity has been shown to adversely affect oxygen transport in ischemic myocardium, and adverse blood flow may also lead to increased blood cell aggregation and thrombus development [39]. Therefore, as FAR derived from the ratio of FIB to ALB, patients with high FAR who are accompanied by high FIB concentration and/or low ALB concentration may have more severe inflammation and greater tendency to thrombosis compared with the patients with low FAR, as well the more severe coronary artery lesions. Finally, FAR predicts mortality in STEMI patients, possibly with the pathophysiological mechanisms of the status of inflammation and hemorheological alterations.

On the other hand, addition of the FAR to the GRACE model results in significantly increased C-index and improved NRI and IDI. Adding FAR to the GRACE score led to the additional benefits including improvement in discrimination and reclassification into a higher or lower risk cohort, as indicated by NRI. The combination of FAR and the GRACE score improved the probability of the model prediction results being consistent with the actual observational outcomes and the probability of individual predicted outcomes, as described by C-index and IDI. Therefore, the integrated predictive power of the GRACE scoring model improved. Usually, the purpose of risk stratification is safety and avoid underestimating the possibility of adverse consequences. Thus, risk prediction focuses on sensitivity and often lacks specificity. So, whether to recommend the inclusion of new markers in the acute coronary syndrome (ACS) evaluation model depends on the level of specific improvement that can be achieved, because the sensitivity is already good. In our study, the improvement in prognostic accuracy of GRACE score was mediated by increased specificity, which led to a better positive predictive value. Nevertheless, STEMI is the most serious type of ACS and requires urgent intervention. The additional predictive value of FAR might be blunted by the actual severity of the disease and its critical complications. Therefore, the net increase in C-index in previous studies about biomarker's additional predictive value on improving the GRACE score [40,41] is similar to ours, although the net increase in C-index in our study was not much.

Indeed, FAR was significantly correlated with the GRACE score with a relatively weak correlation coefficient in our study, indicating that it was related to the disease pathways not fully represented by the GRACE variables. The GRACE score risk stratification, a multivariable task that needs to account for clinical characteristics and electrocardiographic and biochemical variables, can provide important prognostic information in STEMI; however, the ability of the scoring systems to discriminate between outcome groups leaves room for improvement [2]. This may be related to the randomicity of cardiovascular events and the difficulty of predicting outcomes based on risk assessment with limited information at a single point in time. Furthermore, disease dimensions such as inflammation or hemorheological alterations that are related to outcomes in ST-segment elevation acute coronary syndrome are not fully captured by the variables included in scoring systems [3]. In addition, the stenotic severity of coronary artery lesions is a strong prognostic factor for mortality in STEMI [17] but is not included in the GRACE score because it is very difficult to be obtained before operation. Our study showed that increased FAR was significantly associated with more severe coronary artery lesions. Therefore, FAR could be added to the GRACE score for information concerning coronary lesions as well as inflammation and hemorheology to enhance the risk stratification and prognostic evaluation ability of GRACE score.

Although, there is no literature data on the association between FAR and coronary events. We infer that FAR is related to STEMI and our research indicated that FAR successfully predicted outcomes in STEMI patients undergoing pPCI. In the earliest literature on FAR, researchers compared FARs between patients with cerebrovascular events and healthy people, and concluded that FAR could be used as a predictor of hemorheological abnormalities [13]. Sapmaz et al. found a significantly increased FAR in patients with cardiovascular events and speculated that FIB and ALB may affect plasma viscosity and play an important role in the development of vascular thrombosis. They also pointed out that FIB concentration may be more significant compared with ALB concentration in the study of cardiovascular events [14]. Karahan et al. reported a significant correlation between FAR and Syntax score in predicting the severity of coronary artery disease in STEMI patients [15]. FAR has successfully predicted outcomes in some cancers and has been reported in some studies as an inflammatory marker and hemorheological index [42–44]. In summary, FAR has been considered to be related to thrombotic events. Furthermore, the practicability, availability, and low cost of FAR make it a promising serum biomarker, which has an important role in evaluating inflammation and hemorheology.

There are several limitations to this investigation. First, this was a single-center, retrospective study with a small sample size. Second, we measured only the initial preoperative FAR, and its changes over time may provide additional prognostic value. Third, we have not measured blood viscosity with the established physical methods. Fourth, complications in STEMI patients were not evaluated. Accordingly, future prospective and larger sample size studies are warranted to clarify the role of FAR over the course of STEMI.

In conclusion, our study suggests that preoperative FAR is useful in reflecting a patient's inflammatory status and hemorheological alteration and is a useful predictor of mortality in STEMI patients undergoing pPCI. FAR may be a promising serum biomarker that enables a further moderate improvement in risk stratification and prognostic evaluation in STEMI in addition to the GRACE score, which needs further prospective evaluation in clinical practice.

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