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Predictive values of D-dimer for the long-term prognosis of acute ST-segment elevation infarction

A retrospective study in southwestern China

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Abstract

D-dimer is a primary degradation product of cross-linked fibrin, and can be an effective diagnostic factor of venous thromboembolism. However, its prognostic role in patients with acute ST-segment elevation myocardial infarction (STEMI) remains controversial. This study aimed to investigate whether D-dimer has a predictive value for long-term prognosis in patients with STEMI.

We retrospectively enrolled 872 STEMI patients treated with primary percutaneous coronary intervention. Patients were divided into quartiles according to their admission D-dimer increased multiple, with the highest quartile (G4) (n = 219) defined as increased multiple ≧1.33, and the lowest quartile (G1) (n = 215) as increased multiple ≦0.33.

Compared with G1, higher in-hospital heart failure (40.2% vs 10.2%, $P < .0001$), malignant arrhythmia (14.2% vs 2.3%, $P < .0001$), and all-cause mortality (5.9% vs 0%, $P < .0001$) rates were observed in G4. After a follow-up period of 29 months, 84 patients had died. In the Cox multivariate analysis, a high admission D-dimer increased multiple (≧1.33) was found to be an independent predictor of all-cause mortality (hazards ratio: 2.53, 95% confidence interval: 1.02–6.26, $P = .045$).

Thus, there was an association between a high D-dimer level and the increase in in-hospital major adverse cardiovascular events, such as heart failure, malignant arrhythmias, and death. High D-dimer level was also an independent predictor of long-term all-cause mortality.

Abbreviations: AMI = acute myocardial infarction, CI = confidence interval, DM = diabetes mellitus, HR = hazards ratio, IRA = infarction-related artery, MACE = major adverse cardiac events, p-PCI = primary percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction.

Keywords: clinical outcomes, D-dimer, long-term prognosis, ST-segment elevation myocardial infarction

1. Introduction

China is one of the most populous countries in the world, and also has a marked increasing burden of coronary heart disease. The World Bank estimates that there will be 23 million cases of acute myocardial infarction (AMI) in China annually by the year 2030.[1] As a subtype of AMI, STEMI is the most critical condition because of its high mortality and poor outcome. For these patients, identification of a biomarker that can help determine patients with poor prognosis in an early stage is urgently needed. D-dimer, which is one of the final products of cross-linked fibrin, is a highly sensitive marker for thrombosis. It has been wildly used in the exclusion of deep vein thrombosis and pulmonary embolism in clinical settings.[2,3] Moreover, several researchers have shown that D-dimer can also predict future cardiovascular events among healthy individuals.[4] Recently, some studies have suggested that D-dimer levels had a connection with unstable coronary thrombus, and it significantly increased in patients with acute MI.[5] However, the relationship between the D-dimer levels and prognostic value in patients with STEMI has been controversial. In this study, we aimed to investigate whether D-dimer has a long-term prognostic value in STEMI patients in southwestern China.

2. Methods

Ethics Committee approval was obtained from the Institutional Ethics Committee of the First Affiliated Hospital of Chongqing Medical University to the commencement of the study (censorship number: 2019-148).

2.1. Patient population

We conducted a retrospective study of 943 consecutive patients treated with primary percutaneous coronary intervention (p-PCI) for acute STEMI within 48 hours of the onset of symptoms,

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between January 2015 and December 2017 in the First Affiliated Hospital of Chongqing Medical University. The inclusion criteria were as follows: electrocardiography revealing STEMI, which was defined as a typical chest pain lasting for > 30 minutes and ST-segment elevation ≥2 mm in 2 contiguous electrocardiography leads within 48 hours of symptom onset. The exclusion criteria included:

1. patients diagnosed with deep vein thrombosis (n = 10) and pulmonary embolism (n = 4);
2. patients with tumors (n = 3);
3. patients with missing or unavailable D-dimer data (n = 54).

Therefore, the final study population consisted of 872 patients.

2.2. Data collection

All clinical, laboratory, and angiographic data, as well as in-hospital adverse events (death, heart failure, and malignant arrhythmia), were recorded from hospital files and computer records. Peripheral venous blood samples were obtained from all patients immediately after admission, and tested within 24 hours. D-dimer levels were measured using an immunoturbidimetric test (STA-Liatest D-dimer). We utilized 1 analyzer: CS200i/CS5100 automatic analyzer (Sysmex, Japan) with the normal D-dimer value set between 0 and 0.55 μg/mL, and the CA92121 analyzer (San Diego, CA) with the normal value set at 0 to 600 ng/mL. To unify the 2 sets of data, the D-dimer levels were instead by increased multiple, which was defined as the levels of D-dimer divided by the upper limit of the normal range of D-dimer. The population was divided into 4 groups based on quartiles of D-dimer increased multiple (G1≦0.33, G2 0.33–0.64, G3 0.64–1.33, G4≧1.33), the flow diagram is shown in Figure 1.

2.3. Coronary angiography and PCI

All patients were administered loading doses of antiplatelet medications (300 mg aspirin and 180 mg ticagrelor) before coronary angiography. The right radial artery or femoral artery of patients who underwent PCI, and 3000I U heparin was administered when the coronary anatomy was first defined. The assessments for infarction-related artery (IRA) judgment, IRA thrombolysis in myocardial infarction (TIMI) flows before and after intervention,[6] thrombus loads, and the number of culprit vessels were evaluated by 2 senior cardiac doctors. Nitroglycerine with a dose of 150 μg was selectively injected into the IRA to rule out a possible coronary spasm. The use of glycoprotein IIb/IIIa receptor blocker was left to the primary operator's discretion. Stent implantation depends on the stenosis degree of IRA. For lesions that were not suitable for stenting, only balloon dilatation was performed. After the intervention, all patients were received a dual-antiplatelet therapy (100 mg asprin combined with 75 mg clopidogrel or 180 mg ticagrelor) for 12 months. The usage of statins, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and β-blockers was determined by the clinician after assessment of patients' conditions.

2.4. Definition

Patients were evaluated according to the Killip clinical examination classification.[7] Patients with diabetes mellitus (DM) were determined to be those with documented DM currently using either oral hypoglycemic agents or insulin treatment at admission. Triple vessel coronary artery disease was defined as the stenosis degree ≧50% of all 3 coronary systems (left main stenosis ≧50% was counted as 2 systems: the left anterior descending and circumflex; for example, the left main and right

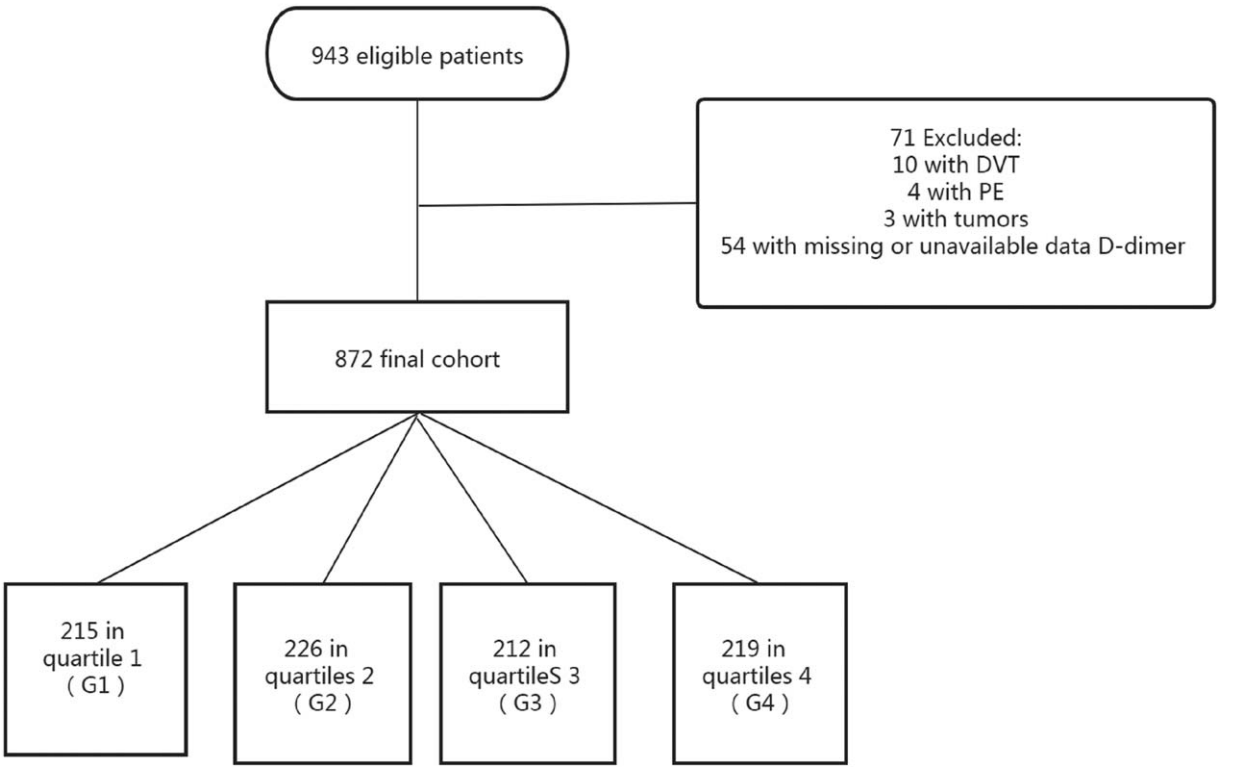

Figure 1. Flow diagram showing patient inclusion and exclusion in the study. DVT = deep vein thrombosis, PE = pulmonary embolism.

coronary disease was considered as triple vessel disease). Revascularization was defined as repeated PCI or bypass grafting not only of the IRA but also of the non-infarct related artery, driven by ischemic symptoms (stable/unstable angina or re-infarction) or detection of ischemia by non-invasive tests. Malignant arrhythmias were defined as arrhythmias causing hemodynamic disorders, such as ventricular tachycardia, ventricular fibrillation, cardiac arrest, high atrioventricular block, and so on.

2.5. Follow-up

Follow-up data were obtained via telephone interviews. All interviews were performed with informed consent. The major adverse cardiac events (MACE) included all-cause mortality, rehospitalization for all causes, and revascularization. All-cause mortality was regarded as the primary endpoint. The mean follow-up duration was 29 months.

2.6. Statistical analysis

Continuous variables are expressed as mean ± standard deviation or median (interquartile range) depending on normality, as assessed using the Kolmogorov–Smirnov test. Categorical variables are shown as a percentage and number of patients. The parametric tests will be applied when normality (and homogeneity of variance) assumptions are satisfied; otherwise, the equivalent non-parametric test was used. The one-way analysis of variance (ANOVA) tests will be applied when normality assumptions of continuous variables were satisfied; otherwise, the Kruskal–Wallis test would be used. Categorical variables were compared using the Chi-Squared test or the Fisher exact test. Pearson or Spearman correlation tests were used for the correlation analysis. Survival curves were calculated using the Kaplan–Meier method, with the significance evaluated using the long-rank tests. A forward LR stepwise Cox multivariate analysis was used to identify independent predictors of all-cause mortality; all variables with P value $< .1$ at univariate analysis and some factors previously shown to be associated with mortality (sex, previous myocardial infarction, hypertension, DM, smoking) were included in the model. A P value $< .05$ was considered statistically significant. The Statistical Package for Social Sciences (SPSS Inc, Chicago, IL) version 20.0 was used for the statistical analysis.

3. Results

3.1. Baseline characteristics

The baseline characteristics of the study populations are shown in Table 1. The patients in the highest quartile (G4) were older (mean age 68.7 ± 12.9 years, $P < .001$) than those in the other quartiles. Body mass index in G4 was significantly lower than that in G1 (23.6 ± 3.6 vs 24.8 ± 3.7, $P = .002$), and the reperfusion time in G4 was the longest than those of the other quartiles (median time 6.0 (7.0), $P = .027$). Compared with the lowest quartile (G1), female sex (28.8% vs 8.8%, $P < .001$), and the Killip class≥2 (38.4% vs 11.6%, $P < .001$) were significantly more frequent in G4. However, smoking was less frequently observed in G4 (55.7% vs 78.1%, $P < .001$). Hyperlipidemia in the Fisher exact test showed a statistical difference in the whole cohort, but after adjusting the P value, there was no statistical difference observed between the groups. Hypertension, DM, previous myocardial infraction history, and previous PCI history were not statistically different among the groups.

3.2. Laboratory findings

The laboratory data of the patients are presented in Table 2. Hemoglobin level ($P < .001$) was significantly lower in G4 than in other quartiles. Cardiac troponin I, creatine kinase–MB, white blood cell, platelet, total-cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and left ventricular ejection fraction were not statistically different between the groups.

3.3. Angiographic characteristics and antiplatelet therapy

The angiographic characteristics and antiplatelet therapy during hospitalization are shown in Table 3. The frequency of IRA, triple-vessel disease, and the percentage of Tirofiban usage were similar among the 4 groups. But aspirin and ticagrelor combined treatment in G4 was significantly more common than in G1 (68.5% vs 58.6%, $P < .001$).

Table 1

Baseline clinical characteristics of patients.

Variable	All patients N = 872	G1 N = 215	G2 N = 226	G3 N = 212	G4 N = 219	*P* value
Age, yr (mean ± SD)	63.7 ± 12.7	57.4 ± 10.6[†,‡,§]	62.0 ± 12.1[*,‡,§]	66.6 ± 12.3[*,†]	68.7 ± 12.8[*,†]	<.001
Female gender, % (n)	19.8 (173)	8.8 (19)[‡,§]	15.5 (35)[‡,§]	26.4 (56)[*,†]	28.8 (63)[*,†]	<.001
Hypertension, % (n)	50.8 (443)	45.6 (98)	49.6 (112)	51.9 (110)	56.2 (123)	.196
Diabetes mellitus, % (n)	18.7 (163)	17.7 (38)	16.4 (37)	20.8 (44)	20.1 (44)	.610
Hyperlipidemia, % (n)	3.6 (31)	5.1 (11)[§]	5.3 (12)[§]	2.8 (6)[§]	0.9 (2)[*,†,‡]	.039
Previous MI, % (n)	3.4 (30)	2.3 (5)	3.5 (8)	5.7 (12)	2.3 (5)	.184
Previous PCI, % (n)	2.5 (22)	2.3 (5)	2.7 (6)	2.4 (5)	2.7 (6)	.990
Smoking, % (n)	67.9 (592)	78.1 (168)[‡,§]	71.7 (162)[§]	66.0 (140)[*]	55.7 (122)[*,†]	<.001
Killip class≥2, % (n)	24.0 (209)	11.6 (25)[‡,§]	19.9 (45)[§]	25.9 (55)[*,§]	38.4 (84)[*,†,‡]	<.001
BMI, kg/m^2 (mean ± SD)	24.3 ± 3.5	24.8 ± 3.7[‡,§]	24.7 ± 3.4[‡,§]	23.8 ± 3.2[*,†]	23.6 ± 3.6[*,†]	.002

BMI = body mass index, MI = myocardial infarction, PCI = percutaneous coronary intervention, SD = standard deviation.

[*] Compared with G1, P value < .05.

[†] Compared with G2, P value < .05.

[‡] Compared with G3, P value < .05.

[§] Compared with G4, P value < .05.

Table 2

Laboratory data of patients.

Variable	All patients N = 872	G1 N = 215	G2 N = 226	G3 N = 212	G4 N = 219	*P* value
cTNI (ng/mL) Median (IQR)	3.38 (13.18)	2.46 (9.75)	3.08 (9.49)	5.49 (15.71)	3.43 (14.24)	.14
CK-MB (ng/mL) Median (IQR)	26.6 (56.1)	19.9 (52.0)	30.0 (60.3)	30.1 (57.2)	23.8 (57.5)	.177
WBC ($^{\wedge}10^9$/L) Median (IQR)	10.9 (4.6)	10.4 (4.5)	11.1 (4.6)	11.4 (4.8)	11.0 (5.3)	.27
Platelet ($^{\wedge}10^9$/L) Median (IQR)	192.5 (83.0)	198.0 (85.0)	189.5 (77.0)	192.5 (77.0)	191.0 (96.0)	.645
Hb (g/L) Median (IQR)	139.0 (24.0)	143.0 (21.0)[‡,§]	140.0 (23.0)[§]	136.0 (24.0)[*]	133.0 (25.0)[*,†]	<.001
Total-cholesterol (mg/dL) Median (IQR)	4.33 (1.33)	4.27 (1.35)	4.38 (1.30)	4.36 (1.19)	4.14 (1.43)	.092
HDL-C (mg/dL) Median (IQR)	1.09 (0.39)	1.06 (0.37)	1.09 (0.40)	1.10 (0.38)	1.09 (0.40)	.33
LDL-C (mg/dl) Median (IQR)	2.78 (1.19)	2.69 (1.27)	2.84 (1.22)	2.90 (0.98)	2.75 (1.19)	.167
LVEF (%) Median (IQR)	57.0 (9.0)	56.0 (8.0)	59.0 (7.0)	56.5 (12.00)	55.5 (10.0)	.122

CK-MB = creatine kinase–MB, cTNI = cardiac troponin I, Hb = hemoglobin, HDL = high-density lipoprotein cholesterol, IQR = interquartile range, LDL-C = low-density lipoprotein cholesterol, LVEF = left ventricular ejection fraction, SD = standard deviation, WBC = white blood cell.

[*] Compared with G1, *P* value < .05.

[†] Compared with G2, *P* value < .05.

[‡] Compared with G3, *P* value < .05.

[§] Compared with G4, *P* value < .05.

Table 3

Angiographic characteristics and antiplatelet therapy during hospitalization of patients.

Variable	All patients N = 872	G1 N = 215	G2 N = 226	G3 N = 212	G4 N = 219	*P* value
IRA						
LAD % (n)	49.3 (430)	54.9 (118)	47.3 (107)	50.0 (106)	45.2 (99)	.209
LCX % (n)	8.6 (75)	12.1 (26)	9.7 (22)	5.7 (12)	6.8 (15)	.075
RCA % (n)	39.3 (343)	32.1 (69)	39.4 (89)	42.0 (89)	43.8 (96)	.066
Triple-vessel % (n) Disease % (n)	35.7 (311)	33.0 (71)	34.1 (77)	35. 8 (76)	39.7 (87)	.479
Tirofiban usage % (n)	55.3 (482)	52.6 (113)	56.2 (127)	61.3 (130)[§]	51.1 (112)[‡]	.147
Asprin + ticagrelor % (n)	64.2 (560)	58.6 (126)[§]	65.0 (147)	64.6 (137)	68.5 (150)[*]	<.001

Asprin + ticagrelor, dual-antiplatelet therapy during hospitalization which included 100 mg asprin and 180 mg ticagrelor.

IRA = infarction-related artery, LAD = left anterior descending coronary artery, RCA = right coronary artery.

[*] Compared with G1, *P* value < .05.

[†] Compared with G2, *P* value < .05.

[‡] Compared with G3, *P* value < .05.

[§] Compared with G4, *P* value < .05.

3.4. In-hospital outcomes

Table 4 summarizes the in-hospital outcomes after p-PCI. Both heart failure (42.2% vs 10.2%, $P < .001$) and malignant arrhythmias (14.2% vs 2.3%, $P < .001$) were significantly more frequent in G4 than in G1. During the in-hospital duration, 21 patients (2.3%) had died. Mortality significantly differed between G1 and G4 (5.9% vs 0%, $P < .001$).

3.5. Long-term follow-up outcomes

No patient was lost to follow-up, excluding the 21 deaths during hospitalization. The total of 851 patients completed the telephone interview. The outcomes are depicted in Table 5. Patients in G4 had a significantly higher rehospitalization rate than those in G1 (33.5% vs 22.8%, $P < .05$). There was no difference in revascularization among the groups. After a follow-up period of 29 months, 84 patients (9.7%) had died; of these, 11 (5.1%) deaths occurred in G1, 10 (4.5%) in G2, 24 (11.5%) in G3, and 39 (18.9%) in G4. Kaplan–Meier survival analysis showed significantly lower long-term survival rates for the patients with D-dimer levels in G4 (log-rank *P* value < .001) (Fig. 2).

In the univariate analysis, high D-dimer increased multiple on admission (quartile 4) was found to be predictive of long-term all-cause mortality (hazards ratio (HR) 4.10, 95% confidence interval (CI) 2.05–8.22, $P < .0001$). In the multivariate analysis,

Table 4

In-hospital outcomes according to D-dimer increased multiple quartiles.

Variable	All patients N = 872	G1 N = 215	G2 N = 226	G3 N = 212	G4 N = 219	*P* value
Heart failure % (n)	23.9 (208)	10.2 (22)[†,‡,§]	20.8 (47)[*,§]	24.1 (51)[*,§]	40.2 (88)[*,†,‡]	<.001
Malignant arrhythmias % (n)	6.2 (54)	2.3 (5)[§]	4.4 (10)[§]	3.8 (8)[§]	14.2 (31)[*,†,‡]	<.001
Death % (n)	2.4 (21)	0 (0)[‡,§]	1.8 (4)[§]	1.9 (4)[*,§]	5.9 (13)[*,†,‡]	.002

Malignant arrhythmias include ventricular tachycardia, ventricular fibrillation, cardiac arrest, and high atrioventricular block.

[*] Compared with G1, *P* value < .05.

[†] Compared with G2, *P* value < .05.

[‡] Compared with G3, *P* value < .05.

[§] Compared with G4, *P* value < .05.

Table 5

Long-term outcomes according to D-dimer increased multiple quartiles.

Variable	All patients N = 851	G1 N = 215	G2 N = 226	G3 N = 212	G4 N = 219	*P* value
Rehospitalization for all causes % (n)	28.0 (241)	22.8 (49)[§]	25.1 (56)	30.8 (65)	33.5 (71)[*]	.05
Revascularization % (n)	7.5 (45)	8.1 (12)	8.1 (14)	6.0 (9)	7.5 (10)	.881
All-cause death % (n)	9.9 (84)	5.1 (11)[‡,§]	4.5 (10)[‡,§]	11.5 (24)[*,†,§]	18.9 (39)[*,†,‡]	<.001

[*] Compared with G1, *P* value < .05.
[†] Compared with G2, *P* value < .05.
[‡] Compared with G3, *P* value < .05.
[§] Compared with G4, *P* value < .05.

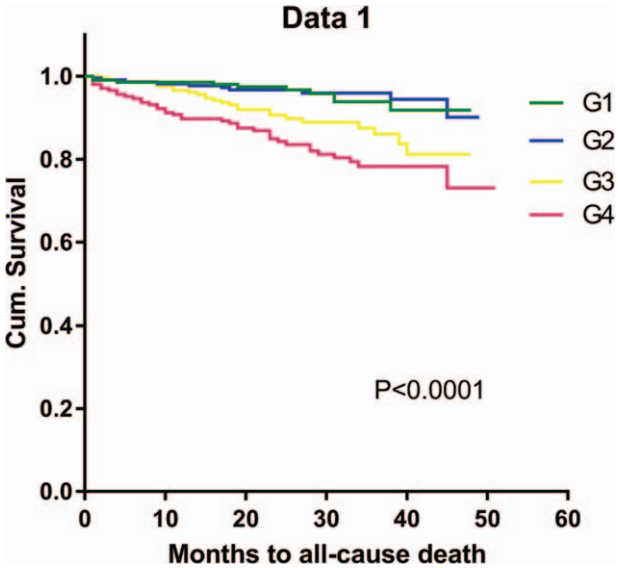

Figure 2. ???.

high D-dimer maintained its significance (HR 2.53, 95% CI 1.02–6.26, *P* = .045). The univariate and multivariate predictors of all-cause death are shown in Table 6. In this study, age (HR 1.04, 95% CI 1.01–1.07, *P* = .01) and the Killip class≥2 (HR 2.20, 95% CI 1.23–3.92, *P* = .008) were also found to be independent predictors of 29-month all-cause mortality.

4. Discussion

This study demonstrates that plasma D-dimer increased multiple was associated with a remarkable increase in in-hospital MACE (heart failure, malignant arrhythmia, death) and rehospitalization in the long-term follow-up. However, there was no significant difference in terms of the incidence of revascularization. After adjusting for potential confounders, high D-dimer level (increased multiple≧1.33) was one of the independent predictors of long-term all-cause mortality. The other independent predictors of long-term all-cause mortality were age and Killip class≥2. It was speculated that the high D-dimer level in patients with STMEI indicates poor outcomes regardless of whether it is during the in-hospital or long-term period.

AMI, especially STEMI, is the most severe form of coronary vascular disease. Its acute onset and poor prognosis have become a worldwide problem. Be different from western countries, China faces a higher increasing burden in the incidence of MACE after STEMI, which may be due to the regional income diversity, uneven investment in healthcare capacity and insufficient treatment strategies.[8] Thus, it is of great significance to find a biomarker that has a prognostic value for patients with STEMI, which could help doctors identify high-risk patients who may

Table 6

Independent predictors of long-term mortality.

	Univariate analysis			Stepwise multivariate		
Variable	HR	95% CI	*P* value	HR	95% CI	*P* value
D-dimer quartile 2	0.90	0.37–2.16	.813			
D-dimer quartile 3	2.50	1.19–5.22	.015			
D-dimer quartile 4	4.10	2.05–8.22	<.0001	2.53	1.02–6.26	.045
Age	1.05	1.03–1.07	<.0001	1.04	1.01–1.07	.01
gender	0.81	0.48–1.35	.413			
Previous MI	1.30	0.41–4.12	.658			
Hypertension	0.85	0.55–1.32	.473			
Hyperlipidemia	0.29	0.04–2.10	.221			
Diabetes mellitus	1.27	0.75–2.13	.378			
Smoking,	0.85	0.54–1.33	.473			
Killip class≥2	3.14	2.04–4.85	<.0001	2.20	1.23–3.92	.008
BMI	0.91	0.84–0.99	.025			
Hb	0.99	0.98–1.10	.02			
Asprin + ticagrelor	0.755	0.479–1.192	.228			

Asprin + ticagrelor, dual-antiplatelet therapy during hospitalization which included 100 mg asprin and 180 mg ticagrelor.
BMI = body mass index, CI = confidence interval, Hb = hemoglobin, HR = hazards ratio, MI = myocardial infarction.

have poor prognosis on an early phase and establish standard diagnostic, therapeutic, and follow-up schedules for them.

D-dimer, which is the end product generated from fibrin degradation by plasmin, was discovered in the late 1980s.[9] Its blood concentration depends on the clotting activation with fibrin generation, stabilization by factor XIIIa, and subsequent degradation by the endogenous fibrinolytic system.[10] It can be obviously increased in thrombus formation. Some previous researches indicated that higher D-dimer levels indicate a higher number of obstructed pulmonary segmental arteries than lower D-dimer levels, and a higher clot burden within the vasculature.[10,11] D-dimer is already widely used in the diagnosis of venous thromboembolism. Earlier studies have already shown that AMI is the result of unstable atherosclerotic plaque rupture or erosion, and secondary thrombosis subsequently limits or completely blocks coronary blood flow.[12–15] During the pathological process of AMI, high D-dimer levels have a connection with larger vulnerable plaque and greater necrotic cores. Elevated D-dimer levels may be a sign of subclinical plaque rupture or erosion, which contributes to the diagnosis and prognosis of acute chest pain, unstable angina, and non-STEMI patients.[16,17]

In our study, patients with high D-dimer levels had higher risks of heart failure and malignant arrhythmia. We speculate that the strong relation of high D-dimer levels on admission to the development of no-reflow may partially explain its association with worse prognoses. No-reflow is defined as the thrombolysis in myocardial infarction flow grade$\leq$2 without mechanical obstruction of the vessel after recanalization. It is an indication of reperfusion failure, which may lead to extensive damage to the myocardial collagen matrix and decrease myocardial strength and stiffness.[18] Patients with no-reflow are more frequently observed the left ventricular expansion and regional wall motion depression.[19,20] Although the pathological mechanisms of no-reflow have not been fully elucidated, but a large quantity of researches have shown that distal microembolization is one of the main pathophysiological mechanisms.[21–23] Sarli et al found that thrombus burden, which can be reflected by high D-dimer levels, is an independent predictor of distal microembolization, eventually leading to no-reflow and in-hospital MACE in patients with STEMI.[24] Erkol et al reported similar conclusions that high D-dimer level on admission predicted a higher risk of no-reflow after p-PCI and an increased mortality at long-term follow-up in patients with STEMI, but it could not be independently predictive of long-term mortality and MACE after adjusting for potential confounders, such as sex, age, and complications.[25] Nevertheless, Akgül et al reported a 6-month observation of patients with STEMI, finally demonstrated that a high level of D-dimer was an independent predictor of in-hospital and 6-month all-cause mortality.[26] In contrast to the majority of previous studies, our study is the first one to investigate the association between D-dimer and STEMI in southwestern China. In the present study, high D-dimer level on admission was found to be related to poor outcomes, and D-dimer increased multiple was independently predictive of long-term all-cause mortality. Accordingly, more active clinical interventions need to be carried on.

4.1. Limitations

First, this study is a single-center retrospective study. Second, it is non-randomized; thus, a selection bias may exist. However, to reduce bias, all data were collected by different researchers and 2 individuals verified data concurrently. All of the researchers were blinded to the content of the study as well. Third, we found that a subset of patients with normal D-dimer levels had severe multivessel disease and heavy thrombotic burden. It is probably because the D-dimer in plasma will change depending on the time the blood samples were collected, and onset of coronary thrombotic events. Fourth, the lack of imaging and pathological data prevented us from identifying the size and composition of the thrombus. Finally, despite adjustment for multiple risk factors, it is possible that residual confounding factors from unmeasured variables were still present.

5. Conclusions

A high D-dimer level on admission is associated with increased adverse events and mortality during both the hospitalization and subsequent long-term follow-up periods. This may be explained by its relation to a higher thrombotic burden in coronary arteries. We think that more multi-center, multi-ethnic studies are needed to confirm our conclusions.

Author contributions

Guarantor of integrity of entire study: Suxin Luo, Jian Shen, Qi Zhou.
Study concepts: Suxin Luo, Jian Shen, Qi Zhou.
Study design: Qi Zhou.
Literature research: Qi Zhou, Yuzhou Xue.
Clinical studies: Qi Zhou.
Experimental studies: Qi Zhou.
Data acquisition: Qi Zhou, Yuzhou Xue, Jian Shen, Yi Wen, Wei Zhou.
Data analysis/interpretation: Qi Zhou.
Statistical analysis: Qi Zhou.
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