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The Value of D-Dimer Level in Predicting Contrast-Induced Acute Kidney Injury in Patients With Acute ST-Segment Elevation Myocardial Infarction After PCI

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Abstract

Contrast-induced acute kidney injury (CI-AKI) is a serious complication of percutaneous coronary intervention (PCI) in patients with acute ST-segment elevation myocardial infarction (STEMI). Early identification of high-risk patients has an essential role in preventing CI-AKI. This study was designed to evaluate the predictive value of D-dimer, a marker of thrombosis and hypercoagulable state, for CI-AKI and prognosis in patients with STEMI. We included 400 patients with STEMI who underwent PCI. The patients were subdivided into 4 groups according to D-dimer level using the 4-quantile method. Contrast-induced acute kidney injury occurred in 66 (16.5%) patients. The incidence of CI-AKI in the highest quartile of the D-dimer groups (29.0%) was higher than that in the other 3 groups. Multivariable logistic regression showed that a low D-dimer level was significantly associated with a decreased risk of CI-AKI independent of confounding factors, with an odds ratio (OR) of 0.487 (95% CI: 0.178-0.931, $P = 0.041$) for those in the first quartile compared with those in the highest quartile. Age (OR: 1.047, 95% CI: 1.003-1.092), diabetes mellitus (OR: 5.896, 95% CI: 2.496-13.927), anemia (OR: 3.488, 95% CI: 1.308-9.306), and total bilirubin (OR: 0.946, 95% CI: 0.904-0.992) were independent predictors of CI-AKI. The incidence of major adverse cardiovascular and cerebral events and all-cause mortality within 30 days, 6 months, and 1 year after PCI in the highest quartile of the D-dimer groups were higher than those in the other 3 groups. In conclusion, increasing D-dimer levels were independently associated with the incidence of CI-AKI and adverse outcomes in patients with STEMI after PCI.

Keywords

D-dimer, acute myocardial infarction, percutaneous coronary intervention, contrast-induced acute kidney injury, major adverse cardiovascular and cerebral events.

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Introduction

Acute ST-segment elevation myocardial infarction (STEMI) is one of the leading causes of death globally. Early restoration of coronary antegrade flow by percutaneous coronary intervention (PCI) plays a critical role in improving the prognosis of patients with STEMI. Contrast-induced acute kidney injury (CI-AKI) is defined as acute renal damage that develops secondary to contrast media exposure and is the third leading cause of in-hospital acute kidney injury.[1] Contrast-induced acute kidney injury occurs frequently in patients with STEMI undergoing PCI due to hemodynamic instability and inadequate prophylaxis[2,3] and is related to long-term morbidity and mortality.[4-6] Vascular endothelial dysfunction, vasoconstriction, inflammation, free radical damage, tubular cell toxicity, reactive oxygen species, and oxidative stress have been proposed as pathophysiological mechanisms of CI-AKI.[7] At

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present, there are no operative prophylactic–therapeutic measures for CI-AKI.[8] Therefore, early identification of high-risk groups and active intervention are essential to prevent CI-AKI. D-dimer is a product of the degradation of cross-linked fibrin, an indicator of ongoing fibrinolysis and the severity of a hypercoagulable state. Previous studies have shown that when vascular endothelial cells are damaged, tissue factors are released to activate the coagulation fibrinolysis system, resulting in hypercoagulation and hyperfibrinolysis of the blood.[9] Wakabayashi and Masuda[10] showed that a hypercoagulable state of blood in patients with diabetes mellitus severely affected glomerular filtration function. In addition, Simes et al demonstrated that D-dimer was correlated with the level of high-sensitivity C-reactive protein, and high D-dimer levels reflected an inflammatory state.[11] However, few studies have explored the correlation between D-dimer, a marker of thrombosis and hypercoagulable state, and CI-AKI. Furthermore, D-dimer testing might be useful in the diagnosis and prognosis of patients with acute coronary syndromes (ACSs).[12,13] However, the prognostic value of D-dimer in patients with ACS has long been controversial. Some previous studies revealed that D-dimer levels were not predictive of cardiovascular events.[14,15] In contrast, Fiotti et al found that D-dimer levels on admission were associated with worse in-hospital prognosis in patients with unstable angina pectoris.[16] Thus, the purpose of this study was to investigate whether D-dimer levels on admission predict CI-AKI after PCI, as well as to evaluate the prognostic value of D-dimer levels in patients with STEMI and to provide ideas for improving STEMI and CI-AKI risk stratification.

Methods

Study Population

This is a retrospective observational cohort study. From December 2013 to January 2017, consecutive patients with STEMI admitted to Zhongda Hospital and treated with PCI were enrolled. The inclusion criteria were as follows: (1) age between 18 and 80 years old and (2) patients with STEMI who were diagnosed based on the Guidelines for the Diagnosis and Treatment of Acute ST-segment Elevation Myocardial Infarction in 2015[17] and underwent PCI. The exclusion criteria were as follows: (1) allergy to iodine or iodine contrast medium, (2) end-stage renal failure requiring peritoneal dialysis, hemodialysis, and kidney transplantation, (3) severe cardiac insufficiency and valvular heart disease with unstable hemodynamics, (4) definite bacterial and fungal infections, acute and chronic inflammatory diseases, autoimmune diseases, or tumors, (5) antibiotics use before admission, (6) contrast medium administration within 2 weeks before admission, and (7) nephrotoxic drug application during hospitalization. The study was approved by the medical ethics committee of Zhongda Hospital, and all methods were performed in accordance with the relevant guidelines and regulations. All patients included volunteered to participate in this clinical study and signed an informed consent form.

Grouping

The patients were divided into 4 groups according to D-dimer by using the 4-quantile method: group 1 ($n = 100$, D-dimer ≤ 109 μg/L), group 2 ($n = 100$, $110 \leq$ D-dimer ≤ 195 μg/L), group 3 ($n = 100$, $196 \leq$ D-dimer ≤ 377 μg/L), and group 4 ($n = 100$, D-dimer ≥ 378 μg/L).

Laboratory Investigations

Serum creatinine (SCr) concentration was measured before and 2 to 3 days after contrast media exposure. Renal function was measured using the estimated glomerular filtration rate (eGFR) with the modified MDRD formula ($eGFR = 175 \times \text{creatinine}^{-1.234} \times \text{age}^{-0.179} \times [0.79\ (\text{female})]$) according to data from Chinese patients with CKD. Plasma D-dimer was tested via an enzyme immunoassay using INNOVANCE D-dimer (SIEMENS), and the D-dimer level was reported in fibrinogen equivalent units. Total bilirubin, alanine aminotransferase, aspartate aminotransferase, blood glucose, total cholesterol, triglycerides (TGs), high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, albumin, and other biochemical indicators were measured after an overnight fast $\geq$12 hours.

Coronary Angiography

All patients were given aspirin (300 mg), ticagrelor (180 mg), or clopidogrel (300 mg) before the operation. Selective coronary arteriography was performed by cardiologists specializing in interventional treatments. The corresponding diseased vessels were treated according to the specific results of the coronary angiography. Nonionic and low-osmotic contrast agents (Iopromide injection, Bayer Vital GmbH) were used during the operation, and the amounts were recorded.

Percutaneous Coronary Intervention

Percutaneous coronary intervention included balloon dilation and/or stent implantation for infarct-related vessels and was performed by experienced operators according to standard techniques. Hydration therapy was given to patients with an eGFR <60 mL/min/1.73 m^2 and consisted of intravenous administration of isotonic saline (1.0-1.5 mL/kg/h) at 3 to 12 hours before the operation and 6 to 24 hours after the operation. Isotonic saline solution was intravenously given at 0.5 mL/kg/h if left ventricular ejection fraction (LVEF) <35% or NYHA >2. Aspirin (100 mg, one daily), ticagrelor (90 mg, twice daily), or clopidogrel (75 mg, once daily) were administered after surgery. Statins, β-blockers, nitrates, and angiotensin-converting enzyme inhibitors were commonly used in all patients without contraindications.

Study Protocol: End Points and Follow-Up

The primary end point was CI-AKI. Contrast-induced acute kidney injury was defined as a rise in SCr of 44.2 μmol/L or

Table 1. Baseline Clinical Data and Therapy at Admission of the 4 Groups.a

Variable	Group 1 (n = 100)	Group 2 (n = 100)	Group 3 (n = 100)	Group 4 (n = 100)	*P* value
Age, years	55.2 ± 11.0	59.2 ± 11.6	65.1 ± 11.8	70.5 ± 9.5	<.001
Male	90 (90.0)	83 (83.0)	75 (75.0)	68 (68.0)	.001
SBP (mm Hg)	129.8 ± 19.4	128.3 ± 21.3	128.3 ± 21.9	127.8 ± 23.8	.924
Smoker	62 (62.0)	51 (51.0)	42 (42.0)	35 (35.0)	.001
Hypertension	55 (55.0)	59 (59.0)	63 (63.0)	71 (71.0)	.111
Diabetes mellitus	23 (23.0)	20 (20.0)	25 (25.0)	33 (33.0)	.178
Anemia	4 (4.0)	8 (8.0)	13 (13.0)	26 (26.0)	<.001
Previous AMI	1 (1.0)	1 (1.0)	2 (2.0)	4 (4.0)	.382
Atrial fibrillation	1 (1.0)	2 (2.0)	4 (4.0)	12 (12.0)	.001
CI-AKI	11 (11.0)	14 (14.0)	12 (12.0)	29 (29.0)	.001
Therapy at admission					
Aspirin	98 (98.0)	96 (96.0)	99 (99.0)	91 (91.0)	.028
β-blockers	81 (81.0)	72 (72.0)	80 (80.0)	68 (68.0)	.325
Statins	94 (94.0)	98 (98.0)	97 (97.0)	97 (97.0)	.681
ACEI/ARB	74 (74.0)	61 (61.0)	60 (60.0)	59 (59.0)	.051

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; CI-AKI, contrast induced acute kidney injury; SBP, systolic blood pressure.
[a]Data are presented as the mean ± SD or n (%).

a 25% increase from the baseline value within 2 to 3 days after contrast media exposure.[18] The secondary end points were the main adverse cardiovascular and cerebrovascular events (MACCEs) and hospitalization for kidney failure during the follow-up period (30 days, 6 months, 1 year after PCI). The MACCEs included all-cause death, target vessel revascularization, myocardial infarction during follow-up, unstable angina pectoris requiring hospitalization, heart failure, stroke, or transient cerebral ischemia. Each patient's baseline clinical data (including demographic data, previous medical history, and vital signs on admission), biochemical and angiographic variables, and echocardiography results were recorded. The patients made a follow-up visit 30 days, 6 months, and 1 year after the operation. Follow-up data were obtained from hospital records or via interviews (in person or by telephone) with patients and their families conducted by at least 2 cardiologists.

Statistical Analysis

Analyses were performed using SPSS software, version 16.0 (SPSS, Inc). Continuous variables are expressed as the means ± SDs or medians (interquartile ranges). Categorical variables are expressed as frequencies with percentages. Univariable and multivariable logistic regression analyses were used to determine CI-AKI predictors. Variables with univariable *P* values <.10 were selected for multivariable analysis and expressed as odds ratios (ORs) with 95% CIs. Survival was graphically represented using Kaplan-Meier curves. Differences in survival rates were compared using the log-rank test. The area under the receiver operating characteristic (ROC) curves (AUCs) were used to indicate the predictive value of D-dimer level on CI-AKI. All tests were 2 tailed, and statistical significance was defined as $P < .05$.

Results

Patient Characteristics

This study included 400 patients with STEMI who underwent PCI, and CI-AKI occurred in 66 (16.5%) patients. All patients were subdivided into 4 groups according to D-dimer level. Baseline clinical data and therapy at admission for the 4 groups are shown in Table 1. The biochemical and angiographic variables and echocardiography results of the 4 groups are shown in Table 2. There were statistically significant differences among the 4 groups in terms of the incidence of CI-AKI ($P = .001$), age ($P < .001$), proportion of female patients ($P = .001$), smoking history ($P = .001$), anemia ($P < .001$), atrial fibrillation (AF; $P = .001$), hemoglobin ($P < .001$), albumin ($P < .001$), glucose ($P = .034$), TGs ($P = .004$), SCr ($P < .001$), eGFR ($P < .001$), and LVEF ($P < .001$), and there were no statistically significant differences in the other indicators. The incidence of CI-AKI after PCI was higher among patients with STEMI, with D-dimer levels in the highest quartile (group 4). Patients in the high dimer group were older, had higher glucose and creatinine levels, and had lower hemoglobin, albumin, eGFR, and LVEF. D-dimer levels were higher in anemic and AF patients.

Risk Factors for CI-AKI

Baseline clinical data and therapy at admission of the CI-AKI and non-CI-AKI groups are given in Table 3. The biochemical and angiographic variables and echocardiography results of the CI-AKI and non-CI-AKI groups are shown in Table 4. The proportions of females (31.8% vs 18.9%, *P*, .018), diabetes mellitus (47.0% vs 21.0%, $P < .001$), and anemia (31.8% vs 9.0%, $P < .001$) in the CI-AKI group were higher than those in the non-CI-AKI group. There were statistically significant differences ($P < .05$) between the CI-AKI and non-CI-AKI groups

Table 2. Biochemical and Angiographic Variables of the 4 Groups.a

Variable	Group 1 (n = 100)	Group 2 (n = 100)	Group 3 (n = 100)	Group 4 (n = 100)	*P* value
Biochemical indicators					
D-dimer, μg/L (IQR)	74.0 (58.0-89.5)	146.0 (128.0-162.5)	256.5 (215.0-320.5)	576.0 (458.5-762.5)	<.001
NT-proBNP, pg/mL (IQR)	504.5 (102.1-2725.3)	636.3 (82.9-3102.5)	562.5 (182.7-2325.9)	693.0 (137.2-3503.2)	.205
Hemoglobin, g/L	142.3 ± 15.7	142.1 ± 19.9	136.8 ± 18.3	129.6 ± 20.9	<.001
White blood cells, 10^9/L	10.3 ± 3.3	10.5 ± 4.0	10.1 ± 3.4	10.2 ± 4.1	.902
Neutrophil ratio	75.6 ± 12.2	75.9 ± 13.3	75.2 ± 12.0	75.8 ± 12.4	.981
Platelet, 10^9/L	219.7 ± 54.3	215.5 ± 64.3	209.7 ± 60.8	204.0 ± 72.3	.325
Albumin, g/L	38.5 ± 4.1	38.1 ± 4.9	36.7 ± 4.9	34.5 ± 5.3	<.001
Total bilirubin, μmol/L	13.9 ± 7.7	13.3 ± 7.0	14.1 ± 6.7	13.8 ± 7.9	.891
Glucose, mmol/L	8.1 ± 3.5	8.2 ± 3.4	8.6 ± 4.0	9.7 ± 5.3	.034
TC, mmol/L	4.7 ± 1.3	4.6 ± 1.3	4.7 ± 1.0	4.3 ± 1.2	.059
Triglycerides, mmol/L	2.1 ± 1.8	2.0 ± 1.7	1.7 ± 1.1	1.4 ± 0.9	.004
HDL-C, mmol/L	1.1 ± 0.2	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	.609
LDL-C, mmol/L	2.9 ± 0.9	2.9 ± 0.9	2.9 ± 0.8	2.7 ± 0.8	.274
Uric acid, μmol/L	325.0 ± 92.8	333.8 ± 99.0	312.4 ± 110.6	340.2 ± 113.6	.263
SCr, μmol/L	77.3 ± 19.1	85.7 ± 27.0	90.6 ± 31.6	112.5 ± 85.3	<.001
eGFR, mL/min	101.5 ± 39.6	87.7 ± 35.5	76.3 ± 26.2	66.2 ± 34.1	<.001
Coronary angiography					
Contrast agent, mL	112.3 ± 26.5	111.0 ± 21.5	110.4 ± 22.6	108.4 ± 19.7	.676
Lesion vessels	3.0 ± 1.6	3.1 ± 1.4	3.0 ± 1.5	3.2 ± 1.6	.599
Three-vessel disease	51 (51.0)	52 (52.0)	41 (41.0)	55 (55.0)	.550
LVEF	0.58 ± 0.10	0.54 ± 0.11	0.51 ± 0.11	0.52 ± 0.14	<.001

Abbreviations: eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; NT-proBNP, NT-proB-type natriuretic peptide; SCr, serum creatinine concentration; TC, total cholesterol.
[a]Data are presented as the IQR, mean ± SD, or n (%).

Table 3. Baseline Clinical Data and Therapy at Admission of the CI-AKI and Non-CI-AKI Groups.[a]

Variable	CI-AKI (n = 66)	Non-CI-AKI (n = 334)	*P* value
Male	45 (68.2)	271 (81.1)	.018
Smoker	28 (42.4)	162 (48.5)	.366
Hypertension	42 (63.6)	206 (61.9)	.786
Diabetes mellitus	31 (47.0)	70 (21.0)	<.001
Anemia	21 (31.8)	30 (9.0)	<.001
Previous AMI	3 (4.5)	5 (1.5)	.106
Atrial fibrillation	4 (6.1)	15 (4.5)	.584
Three-vessel disease	39 (59.1)	164 (49.1)	.138
Therapy at admission			
Aspirin	63 (95.5)	321 (96.1)	.805
β-blockers	53 (80.3)	264 (79.0)	.817
Statins	65 (98.5)	321 (96.1)	.337
ACEI/ARB	43 (65.2)	211 (63.2)	.760

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; CI-AKI, contrast-induced acute kidney injury.
[a]Data are presented as n (%).

in terms of D-dimer, age, hemoglobin, neutrophil ratio, albumin, total bilirubin, glucose, SCr, and eGFR.

Univariable and multivariable analyses and predictors for CI-AKI are presented in Table 5. Univariable logistic regression showed that D-dimer, age, sex, diabetes mellitus, anemia, neutrophil ratio, albumin, blood glucose, total bilirubin, and eGFR were risk factors for CI-AKI in patients with STEMI after PCI. Multivariable logistic regression showed that a low D-dimer level was significantly associated with a decreased risk of CI-AKI in patients with STEMI after PCI independent of confounding factors, with an OR of 0.487 (95% CI: 0.178-0.931, $P = .041$) for those in the first quartile compared with those in the highest quartile. In addition, multivariable logistic regression also showed that age (OR: 1.047, 95% CI: 1.003-1.092), diabetes mellitus (OR: 5.896, 95% CI: 2.496-13.927), anemia (OR: 3.488, 95% CI: 1.308-9.306), and total bilirubin (OR: 0.946, 95% CI: 0.904-0.992) were independent predictors of CI-AKI in patients with STEMI after PCI (all $P < .05$). Multivariable logistic regression models were created which included D-dimer, age, sex, diabetes mellitus, anemia, neutrophil ratio, albumin, blood glucose, total bilirubin, and eGFR ($P < .10$).

The ROC curves for D-dimer as a marker to differentiate CI-AKI in patients with STEMI after PCI are illustrated in Figure 1. The AUC of D-dimer for predicting the occurrence of CI-AKI in patients with STEMI after PCI was 0.702 (95% CI: 0.627-0.778; $P = .039$). The Youden index was used to find the best cutoff in the ROC curve. The cutoff of normality used by the specific laboratory was 437 μg/L. When the detection cutoff point of D-dimer was >437 μg/L for the diagnosis of CI-AKI, the sensitivity and specificity of D-dimer in predicting CI-AKI were 59.6% and 83.5%, respectively.

The occurrence of MACCE in each D-dimer group is shown in Table 6. The Kaplan-Meier survival curves that depict follow-up without an MACCE (MACCE-free) for the CI-AKI group and non-CI-AKI group are illustrated in Figure 2.

Table 4. Biochemical and Angiographic Variables of the CI-AKI and Non-CI-AKI Groups.[a]

Variable	Overall (N = 400)	CI-AKI (n = 66)	Non-CI-AKI (n = 334)	*P* value
Biochemical indicators				
D-dimer, μg/L(IQR)	194.5 (108.5-377.5)	273.0 (130.0-611.8)	184.5 (104.0-335.0)	.011
Age, years	62.5 ± 12.4	67.1 ± 10.4	61.6 ± 12.6	.001
SBP (mm Hg)	128.5 ± 21.6	127.6 ± 21.8	128.7 ± 21.6	.687
NT-proBNP, pg/mL (IQR)	586.5 (88.5-2985.7)	637.4 (92.5-2795.4)	549.6 (98.9-2602.3)	.145
Hemoglobin, g/L	137.7 ± 19.4	127.5 ± 23.8	139.8 ± 17.8	<.001
White blood cells, 10^9/L	10.3 ± 3.7	10.1 ± 3.5	10.3 ± 3.7	.638
Neutrophil ratio	75.6 ± 12.4	79.1 ± 10.4	74.9 ± 12.7	.012
Platelet, 10^9/L	212.2 ± 63.2	215.9 ± 74.1	211.5 ± 60.9	.607
Albumin, g/L	37.0 ± 5.0	35.8 ± 5.8	37.2 ± 4.8	.040
Total bilirubin, μmol/L	13.8 ± 7.3	11.6 ± 5.7	14.2 ± 7.5	.008
Glucose, mmol/L	8.6 ± 4.1	9.8 ± 5.5	8.4 ± 3.8	.014
TC, mmol/L	4.6 ± 1.2	4.5 ± 1.2	4.6 ± 1.2	.474
Triglycerides, mmol/L	1.8 ± 1.5	1.6 ± 0.9	1.9 ± 1.6	.213
HDL-C, mmol/L	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.2	.773
LDL-C, mmol/L	2.8 ± 0.9	2.8 ± 0.9	2.8 ± 0.8	.813
Uric acid, μmol/L	327.9 ± 104.5	343.9 ± 110.3	324.7 ± 103.2	.172
SCr, μmol/L	91.5 ± 50.0	117.0 ± 101.0	86.5 ± 30.0	<.001
eGFR, mL/min	83.6 ± 36.8	69.7 ± 53.1	86.1 ± 32.4	.004
Coronary angiography				
Contrast agent, mL	110.5 ± 22.7	109.2 ± 21.4	110.8 ± 23.0	.616
Lesion vessels	3.0 ± 1.5	3.3 ± 1.5	3.0 ± 1.5	.187
LVEF	0.54 ± 0.12	0.52 ± 0.12	0.54 ± 0.12	.328

Abbreviations: CI-AKI, contrast-induced acute kidney injury; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; NT-proBNP, NT-proB-type natriuretic peptide; SBP, systolic blood pressure; SCr, serum creatinine concentration; TC, total cholesterol.
[a]Data are presented as the IQR or mean ± SD.

Table 5. Univariable and Multivariable Analysis and Predictors for CI-AKI.

	Univariate analysis			Multivariate analysis		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
D-dimer grouping						
Group 4	1			1		
Group 1	0.334	0.159-0.701	.004[a]	0.487	0.178-0.931	.041[b]
Group 2	0.399	0.196-0.812	.011[a]	0.585	0.258-1.131	.157
Group 3	0.303	0.141-0.648	.002[a]	0.354	0.213-1.097	.078
Age	1.039	1.015-1.064	.001[a]	1.047	1.003-1.092	.036[b]
Male	0.498	0.277-0.895	.020[a]	0.737	0.306-1.777	.497
Smoker	0.782	0.459-1.333	.367			
Hypertension	1.079	0.624-1.866	.786			
Diabetes mellitus	3.340	1.926-5.793	<.001[a]	5.896	2.496-13.927	<.001[b]
Anemia	4.729	2.495-8.964	<.001[a]	3.488	1.308-9.306	.013[b]
Previous AMI	3.133	0.730-13.445	.124			
Atrial fibrillation	1.372	0.441-4.273	.585			
NT-proBNP, pg/mL	1.027	0.298-3.016	.383			
White blood cells, 10^9/L	0.982	0.913-1.057	.637			
Neutrophil ratio	1.031	1.006-1.056	.013[a]	1.031	0.998-1.066	.070
Platelet, 10^9/L	1.001	0.997-1.005	.606			
Albumin, g/L	0.947	0.898-0.998	.041[a]	1.002	0.923-1.087	.965
Glucose, mmol/L	1.069	1.012-1.130	.018[a]	0.979	0.895-1.072	.647
Total bilirubin, μmol/L	0.938	0.894-0.984	.009[a]	0.946	0.904-0.992	.040[b]
TC, mmol/L	0.919	0.730-1.157	.473			
Triglycerides, mmol/L	0.854	0.664-1.098	.217			
HDL-C, mmol/L	0.853	0.289-2.515	.773			
LDL-C, mmol/L	0.962	0.697-1.328	.812			
Uric acid, umol/L	1.003	0.998-1.005	.173			
eGFR, mL/min	0.985	0.975-0.995	.004[a]	0.994	0.979-1.021	.277
Contrast agent, mL	0.997	0.985-1.009	.615			
Lesion vessels	1.121	0.946-1.329	.188			
Three-vessel disease	1.497	0.876-2.558	.140			
LVEF	0.310	0.030-3.236	.328			

Abbreviations: AMI, acute myocardial infarction; CI-AKI, contrast-induced acute kidney injury; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; NT-proBNP, NT-proB-type natriuretic peptide; SBP, systolic blood pressure; TC, total cholesterol.
[a]Univariate logistic regression showed that D-dimer, age, sex, diabetes mellitus, anemia, neutrophil ratio, albumin, blood glucose, total bilirubin, and eGFR were risk factors for CI-AKI in patients with ST-segment elevation myocardial infarction (STEMI) after percutaneous coronary intervention (PCI).
[b]Multivariate logistic regression showed that D-dimer, age, diabetes mellitus, anemia, and total bilirubin were independent predictors of CI-AKI in patients with STEMI after PCI.

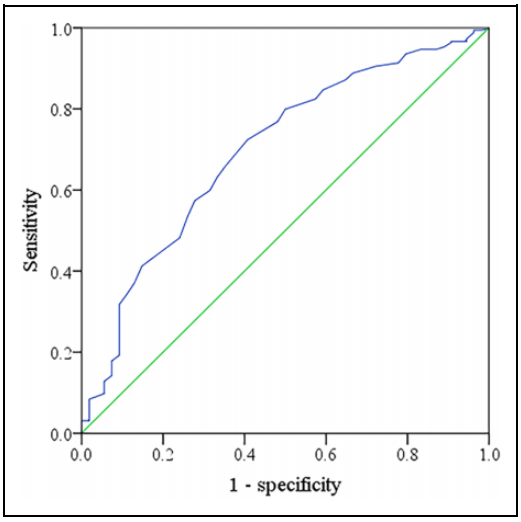

Figure 1. Receiver operating characteristic (ROC) curves for D-dimer as a marker to differentiate contrast-induced acute kidney injury (CI-AKI) in patients with ST-segment elevation myocardial infarction (STEMI) after percutaneous coronary intervention (PCI). The area under the ROC curves (AUCs) of D-dimer predicting the occurrence of CI-AKI in patients with STEMI after PCI was 0.702 (95% CI: 0.627-0.778; $P = .039$).

The incidence of MACCEs within 30 days (21%), 6 months (32%), and 1 year (47%) after PCI were higher among patients with STEMI, with D-dimer levels in the highest quartile (group 4). The cumulative probability of the overall survival of the 4 groups at the 1-year follow-up is illustrated in Figure 3. The incidence of all-cause mortality within 30 days (7%), 6 months (9%), and 1 year (10%) after PCI were higher among patients with STEMI, with D-dimer levels in the highest quartile (group 4). As shown in Table 7, the incidence of hospitalization for kidney failure within 6 months and 1 year after PCI in group 4 were higher than that in the other 3 groups.

Discussion

Contrast-induced acute kidney injury is characterized by acute impairment of renal function following exposure to contrast agents,[19] is an independent predictor of worse outcomes, and is significantly associated with long-term mortality.[20] Previous studies have shown that congestive heart failure, chronic renal insufficiency, diabetes mellitus, intravascular volume depletion, and the use of a large amount of contrast agent were considered important predisposing factors.[21] The diagnosis of CI-AKI has traditionally relied on SCr, which is a delayed indicator of CI-AKI.[22] Early identification of high-risk groups and active intervention are indispensable to prevent CI-AKI.

Several risk scores and risk factors have been established for the prediction of CI-AKI, but none is recommended for use in daily practice due to a lack of sufficient verification in the literature.[7,23] Advances in biomarkers for predicting CI-AKI have been made recently. Neutrophil gelatinase-associated lipocalin has been strongly correlated with SCr levels and have been considered in the diagnosis of CI-AKI.[24] Cystatin C levels have been shown to be a more accurate early marker of GFR reduction and were less influenced by nonrenal variables than SCr levels.[25,26] Procalcitonin, a novel marker of systemic inflammatory conditions, has been recently demonstrated to predict CI-AKI in patients with ACS.[27] Unfortunately, although such biomarkers are promising, no standard cutoffs for the diagnosis of CI-AKI have been established, and existing data on clinical outcomes are inadequate.

D-dimer is the ultimate product of fibrin degradation by plasmin, the plasma concentrations of which are increased during ongoing or recent thrombosis. The measurement of D-dimer is routinely used in combination with clinical parameters in the initial assessment of suspected venous thromboembolism.[28] Furthermore, there is an increasing trend toward using D-dimer to exclude aortic dissection.[29]

This study showed that D-dimer, a marker of thrombosis and hypercoagulable state, was negatively correlated with eGFR and that D-dimer levels were higher in anemic and AF patients. In addition, patients with higher D-dimer levels were significantly older and more frequently female. The incidence of CI-AKI after PCI was higher among patients with STEMI, with D-dimer levels in the highest quartile. Multivariable logistic regression showed that D-dimer was an independent predictor of CI-AKI in patients with STEMI after PCI ($P < .05$). The AUC of D-dimer for predicting the occurrence of CI-AKI in patients with STEMI after PCI was 0.702. When the detection cutoff point of D-dimer for the diagnosis of CI-AKI was >437 μg/L, the sensitivity and specificity of D-dimer in predicting CI-AKI were 59.6% and 83.5%, respectively. Moreover, multivariable logistic regression also showed that age (OR: 1.047, 95% CI: 1.003-1.092), diabetes mellitus (OR: 5.896, 95% CI: 2.496-13.927), anemia (OR: 3.488, 95% CI: 1.308-9.306), and total bilirubin (OR: 0.946, 95% CI: 0.904-0.992) were independent predictors of CI-AKI in patients with STEMI after PCI.

Table 6. MACCE Occurrence in Each D-dimer Group.[a]

Variable	Group 1 (n = 100)	Group 2 (n = 100)	Group 3 (n = 100)	Group 4 (n = 100)	*P* value
MACCE occurrence (30 days after PCI)	4 (4.0%)	4 (4.0%)	12 (12.0%)	21 (21.0%)	<.001[b]
MACCE occurrence (6 months after PCI)	12 (12.0%)	14 (14.0%)	22 (22.0%)	32 (32.0%)	.001[b]
MACCE occurrence (1 year after PCI)	26 (26.0%)	33 (33.0%)	36 (36.0%)	47 (47.0%)	.001[b]

Abbreviations: MACCEs, main adverse cardiac and cerebrovascular events; PCI, percutaneous coronary intervention.
[a]Data are presented as n (%).
[b]The incidence of MACCE within 30 days, 6 months, and 1 year after PCI in group 4 were higher than that in the other 3 groups.

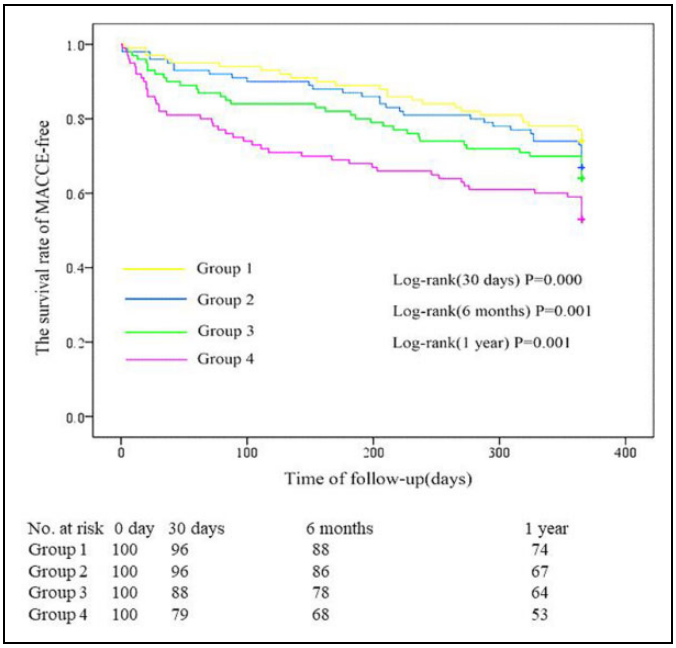

Figure 2. Survival curves for follow-up without an main adverse cardiovascular and cerebrovascular event (MACCE-free) for the 4 groups. The incidence of MACCEs within 30 days, 6 months, and 1 year after percutaneous coronary intervention (PCI) in group 4 were higher than that in the other 3 groups ($P < .01$).

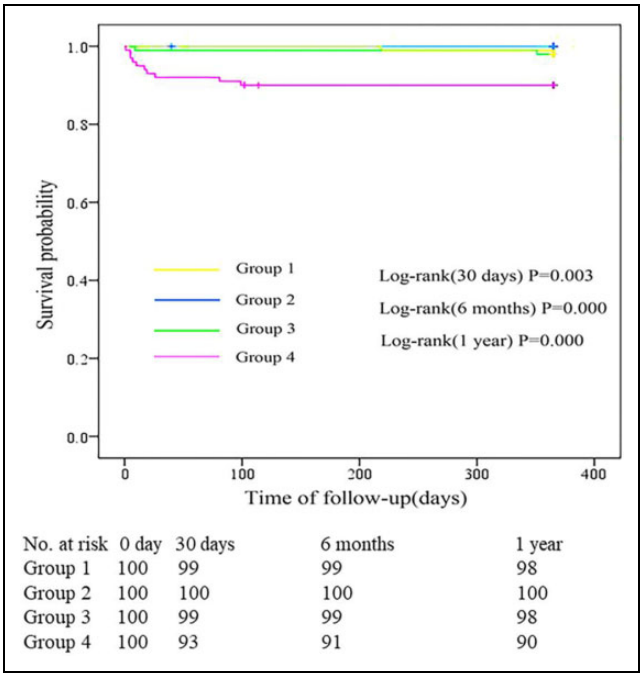

Figure 3. Cumulative probability of the overall survival for the 4 groups at the 1-year follow-up. The incidence of all-cause mortality within 30 days, 6 months, and 1 year after percutaneous coronary intervention (PCI) in group 4 were higher than that in the other 3 groups ($P < 0.01$).

The prognostic value of D-dimer in patients with ACSs has long been debated. In our study, Kaplan-Meier analysis showed a significantly increased cumulative risk of MACCEs within 30 days, 6 months, and 1 year after PCI for patients with D-dimer levels in the fourth quartile (Figure 2). Likewise, Kaplan-Meier survival analysis revealed significantly lower survival rates within 30 days, 6 months, and 1 year after PCI for patients with D-dimer levels in the fourth quartile (Figure 3). Overall, this study indicated that the incidence of MACCEs and all-cause mortality within 30 days, 6 months, and 1 year after PCI were higher among patients with STEMI, with D-dimer levels in the highest quartile.

Study Limitations

The following limitations of the present study should be addressed. First, this study was not a standard randomized controlled trial. There was a selection bias, and whether these defects will affect the results also requires a prospective study with larger samples. Second, it was more reasonable to measure D-dimer several times during hospitalization. In addition, the changes in D-dimer during the follow-up period were not measured or analyzed. Third, the role of potential preventive strategies for CI-AKI, such as hydration and drug therapy, was not assessed. Although we adjusted for several known confounding variables in the multiple logistic regression model, other unknown factors might have played roles in CI-AKI. A greater sample size, more D-dimer subgroups, more thrombosis parameters, a longer follow-up time, and multicenter trials are necessary to further determine the cutoff point of D-dimer and other thrombosis parameters for patients to provide ideas for improving STEMI and CI-AKI risk stratification.

Conclusion

In conclusion, the current study demonstrated that higher D-dimer levels represent a strong independent indicator of

Table 7. Hospitalization for Kidney Failure in Each D-Dimer Group.[a]

Variable	Group 1 (n = 100)	Group 2 (n = 100)	Group 3 (n = 100)	Group 4 (n = 100)	*P* value
Hospitalization for kidney failure (30 days after PCI)	0 (0.0%)	1 (1.0%)	1 (1.0%)	3 (3.0%)	.278
Hospitalization for kidney failure (6 months after PCI)	1 (1.0%)	1 (1.0%)	2 (2.0%)	8 (8.0%)	.009[b]
Hospitalization for kidney failure (1 year after PCI)	3 (3.0%)	4 (4.0%)	6 (6.0%)	12 (12.0%)	.040[b]

Abbreviation: PCI, percutaneous coronary intervention.
[a]Data are presented as n (%).
[b]The incidence of hospitalization for kidney failure within 6 months and 1 year after PCI in group 4 were higher than that in the other 3 groups ($P < .05$).

increased risk of CI-AKI in patients with STEMI after PCI. Age, diabetes mellitus, anemia, and total bilirubin were independent predictors of CIN in patients with STEMI after PCI. In addition, increasing D-dimer levels were associated with the incidence of MACCE and all-cause mortality within 30 days, 6 months, and 1 year in patients with STEMI after PCI. Based on these solid results, D-dimer levels may help to screen patients with STEMI with a relatively high risk of CI-AKI and MACCEs on admission and help physicians select the best treatment options.

Authors' Note

Erfei Luo and Dong Wang contributed equally to this work and should be considered co-first authors.

Declaration of Conflicting Interests

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