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ORIGINAL ARTICLE

Predictive Value of Serum D-Dimer and Prothrombin Time for Adverse Events in Patients with Acute Myocardial Infarction

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SUMMARY

Background: **This study aimed to investigate the predictive value of D-dimer (D-D) and prothrombin time for severity and adverse cardiovascular events in patients with acute myocardial infarction (AMI).**
Methods: **A total of 314 patients who were diagnosed with AMI and underwent percutaneous coronary intervention (PCI) in the Department of Cardiology, Linquan People's Hospital, from January 2020 to December 2023 were selected. According to Killip classification, patients were divided into severe and non-severe AMI groups. Within 2 hours after admission, 3 mL of cubital venous blood were drawn for blood biochemical and coagulation tests. According to the patient's electrocardiogram, coronary angiography, and other tests, the diagnosis of acute myocardial infarction was confirmed.**
Results: **D-D and prothrombin time (PT) in the severe group were significantly higher than those in the non-severe group, and the difference was statistically significant ($p < 0.05$). The number of patients with PCI of left circumflex artery, right coronary artery stent implantation, single and double stent implantation in the severe group was higher than that in the non-severe group, and the results were statistically significant ($p < 0.05$). The results of ROC curve showed that the area under the curve, sensitivity, and specificity of D-D and PT were significantly better than those of cardiac troponin T(cTnT) and N-terminal pro-brain natriuretic peptide (NT-proBNP) in patients with severe myocardial infarction ($p < 0.05$). In addition, the results of bivariate regression analysis showed that D-D and PT were significantly correlated with Killip classification ($p < 0.05$). Multivariate logistic regression analysis showed that previous history of heart failure, left ventricular ejection fraction, PT, and D-D were independent risk factors for adverse cardiovascular events in patients with AMI ($p < 0.05$).**
Conclusions: **Serum D-D and PT have important predictive value for adverse cardiovascular events in patients with AMI.**
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KEYWORDS

acute myocardial infarction, D-dimer, prothrombin time, PCI

INTRODUCTION

AMI, characterized by thrombosis caused by the rupture of atherosclerotic plaques, is a critical condition with high mortality. AMI is an important cause of death in patients with coronary heart disease [1-3]. According to statistics, the mortality rate of AMI in the United States is as high as 71% in men and 22% in women. Approxi-

mately 1.5 million people suffer an acute myocardial infarction each year [4-6]. The main clinical manifestation of patients with acute myocardial infarction is chest pain, and it is necessary to use electrocardiogram combined with progressive elevation of serum troponin for diagnosis and differential diagnosis. However, the elevation of troponin level in the early stage of myocardial infarction is not obvious, so it is easy to be misdiagnosed and for treatment to be delayed, which eventually leads to the aggravation of the patient's condition and poor prognosis.

As a simple, effective, and low-cost inflammatory predictor, neutrophil-to-lymphocyte ratio (NLR) and high-sensitivity C-reactive protein (hs-CRP) have been shown to be risk signals for in-hospital death in patients with acute myocardial infarction, with high predictive value [7-10]. Further studies suggested that the risk of recurrent coronary events in patients with acute myocardial infarction was increased by 45% - 55% when the D-D level was greater than 273 μg/L [11]. Patients with AMI after PCI have significant abnormalities in thrombosis- and inflammation-related indicators, and it is not clear whether these abnormal indicators have certain predictive value for the severity of AMI.

The purpose of this study was to explore the indicators with predictive value for the severity of AMI through the retrospective analysis of blood biochemical and coagulation indicators in patients with AMI, so as to achieve the purpose of using simple and low-cost indicators to accurately judge the prognosis of AMI, which is conducive to clinicians' early intervention.

MATERIALS AND METHODS

General information

The medical records of 314 patients who were diagnosed with AMI and underwent PCI in the Department of Cardiology, Linquan County People's Hospital, from January 2020 to December 2023 were retrospectively collected. Inclusion criteria: 1) age ≥ 18 years and complete medical records; 2) AMI according to the cri-teria of 2013 American College of Cardiology Guide-lines for the Treatment of ST-segment Elevation Myo-cardial Infarction and 2014 American Heart Association Guidelines for the Treatment of Patients with Non-ST-segment Elevation Acute Coronary Syndromes; and 3) patients who underwent PCI. Exclusion criteria: 1) patients with congenital heart disease, malignant arrhythmia, acute cerebrovascular disease, or tumor; 2) patients with infectious diseases, liver and kidney dysfunction; 3) patients with hematological diseases and psychiatric diseases; and 4) incomplete medical records. There were 163 male and 64 female patients with mild acute myocardial infarction. The mean age was (61.08 ± 11.482) years (range: 34 - 85 years). There were 66 males and 18 females in the severe acute myocardial infarction group, aged 31 to 89 years, with an average age of (65.82 ± 12.477) years. Patients with myocardial infarction in the severe group were older than those in the non-severe group, and the difference was statistically significant, but there was no significant difference in gender between the two groups.

Medical record information

A. The basic data of the patients included age, gender, and blood pressure.
B. Past medical history: history of smoking, alcohol consumption, hypertension, diabetes, hyperlipidemia, arrhythmia, and adverse cardiovascular events.
C. Medication history: aspirin, clopidogrel, β-blockers, ACEI, statins, and nitrates.

Blood biochemical and hematological indexes were detected

All patients were tested for coagulation indicators within 2 hours after admission, and blood biochemical indicators were tested after 12 hours of fasting to exclude the influence of diet on the test results. hs-CRP was detected by Sysmex XN-3700 automatic blood routine analyzer. The Hitachi 760-020 automatic biochemical analyzer was used to detect the levels of cTnT, NT-pro-BNP, creatine kinase (CK), creatine kinase isoenzyme (CK-MB), lactate dehydrogenase (LDH), albumin, globulin, total cholesterol (TC), low-density lipoprotein (LDL), and high-density lipoprotein (HDL). The levels of prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), fibrinogen, and D-D were measured by Stago Evelution coagulator. The level of left ventricular ejection fraction (LVEF) was measured by electrocardiogram.

Angiographic analysis

Patients with chest pain lasting 30 minutes were all treated with PCI within 12 hours. If chest pain persisted beyond the therapeutic window, PCI was also performed. All patients were treated with clopidogrel (75 mg orally, once a day for 12 months) and aspirin (100 mg continuously) after PCI, and were given anti-platelet aggregation, anticoagulation, lipid-lowering, and other treatments. The results of coronary angiography were collected: 1) coronary artery stenosis diameter > 50% was defined as diseased vessel; 2) diseased vessels (anterior descending artery, left lateral branch, right coronary artery, left coronary artery); 3) the number of stents implanted; and 4) stent implantation vessels.

Indicators of observation

Adverse cardiovascular events including death, malignant arrhythmia, heart failure, and cardiogenic shock were recorded.

Group

Each patient was divided into two groups according to Killip classification: Killip classification ≤ 2 was defined as the non-severe group, and Killip classification > 2 was defined as the severe group.

Table 1. Basic characteristics of patients with acute myocardial infarction.

	All patients n = 314	Non-severe group n = 227	Severe group n = 87	p-value
Age (years)	62.39 ± 11.936	61.08 ± 11.482	65.82 ± 12.477	0.002
Male gender	229 (72.9%)	163 (71.8%)	66 (75.9%)	0.718
Smoking history	117 (37.3%)	90 (39.6%)	27 (31.0%)	0.374
Drinking history	52 (16.6%)	38 (16.7%)	14 (16.1%)	0.890
Hypertension history	149 (47.5%)	102 (44.9%)	47 (54.0%)	0.370
Diabetes history	33 (10.5%)	26 (11.5%)	7 (8%)	0.781
Hyperlipidemia history	6 (1.9%)	4 (1.8%)	2 (2.3%)	0.959
Myocardial infarction history	2 (0.6%)	1 (0.4%)	1 (1.1%)	0.106

Table 2. Comparison of serological and coagulation indexes in patients with acute myocardial infarction.

	All patients n = 314	Non-severe group n = 227	Severe group n = 87	p-value
hs-CRP, mg/L	13.00 ± 24.120	13.86 ± 27.029	10.77 ± 13.804	0.311
cTnT, ng/mL	20.80 ± 18.62	20.39 ± 17.84	31.876 ± 20.58	0.027
NT-proBNP, ng/mL	3,341.64 ± 4,742.89	2,880.65 ± 3,652.04	4,547.73 ± 6,697.65	0.005
CK, IU/L	4,450.91 ± 196.44	4,446.67 ± 231.04	4,462.00 ± 0.00	0.537
CK-MB, U/L	160.03 ± 122.06	158.95 ± 120.65	162.85 ± 126.35	0.800
LDH, U/L	636.07 ± 344.17	626.89 ± 311.51	660.01 ± 418.68	0.446
Albumin, g/L	38.24 ± 3.13	38.29 ± 2.90	38.12 ± 3.68	0.677
Globulin, g/L	24.05 ± 3.97	24.08 ± 3.80	23.97 ± 4.41	0.828
TC, mmol/L	4.76 ± 1.00	4.79 ± 1.06	4.69 ± 0.85	0.434
LDL, mmol/L	2.98 ± 0.84	2.98 ± 0.89	2.95 ± 0.72	0.680
HDL, mmol/L	1.26 ± 0.30	1.25 ± 0.29	1.28 ± 0.32	0.428
LVEF, %	57.24 ± 7.59	57.15 ± 6.96	57.49 ± 9.06	0.716
PT, sec	13.53 ± 1.35	13.18 ± 0.80	14.45 ± 1.93	< 0.001
APTT, sec	35.289 ± 12.64	34.71 ± 9.68	36.793 ± 18.20	0.192
TT, sec	23.041 ± 24.02	21.949 ± 20.87	25.890 ± 30.72	0.194
Fibrinogen, g/L	3.41 ± 1.08	3.40 ± 1.08	3.43 ± 1.09	0.863
D-D, μg/mL	0.61 ± 0.89	0.45 ± 0.49	1.03 ± 1.40	< 0.001

hs-CRP - hypersensitive C-reactive protein, cTnT - cardiac troponin T, NT-proBNP - N-terminal pro-brain natriuretic peptide, CK - creatine kinase, CK-MB - creatine kinase isoenzymes, LDH - lactate dehydrogenase, TC - total cholesterol, LDL - low-density lipoprotein, HDL - high-density lipoprotein, LVEF - left ventricular ejection fraction, PT - prothrombin time, APTT - activated partial prothrombin time, TT - thrombin time, D-D - D-dimer.

Stastistic

All statistical data were analyzed by SPSS 25.0 software. The measurement data in accordance with normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$). One-way analysis of variance was used for comparison between groups. χ^2 test was used for comparison of count data between groups. The sensitivity and specificity of D-D, PT, TT, and NT-proBNP were analyzed by ROC curve. Bivariate regression analysis was used to evaluate the correlation between D-D, PT, TT, NT-proBNP, and Killip grade and cardiovascular adverse events. Multivariate logistic regression analysis was used to evaluate the potential predictors of acute myocardial infarction. $p < 0.05$ was considered statistically significant.

Table 3. Comparison of history of stent implantation in patients with acute myocardial infarction undergoing PCI.

	All patients n = 314	Non-severe group n = 227	Severe group n = 87	p-value
Anterior descending branch	145 (46.2%)	104 (45.8%)	41 (47.1%)	0.469
Left circumflex branch	58 (18.5%)	44 (19.4%)	14 (16.1%)	0.001
Right coronary artery	122 (38.9%)	88 (38.8%)	34 (39.1%)	0.031
Left coronary artery	4 (1.3%)	3 (1.3%)	1 (1.1%)	0.903
Single branch	163 (51.9%)	115 (50.7%)	48 (55.2%)	< 0.001
Double branch	124 (39.5%)	89 (39.2%)	35 (40.2%)	< 0.001
Heart failure	53 (16.9%)	35 (15.4%)	18 (20.7%)	< 0.001
Cardiogenic shock	2 (0.6%)	0 (0%)	2 (2.3%)	0.106
Adverse cardiovascular events	55 (17.5%)	38 (16.7%)	17 (19.5%)	< 0.001

Table 4. Bivariate regression analysis was used to analyze the correlation between serological and coagulation indexes.

	D-D	PT	cTn-T	NT-proBNP	Killip
D-D	-	R = 0.3110 p < 0.001	R = 0.265 p < 0.001	R = 0.103 p = 0.070	R = 0.388 p < 0.001
PT	R = 0.311 p < 0.001	-	R = 0.079 p = 0.163	R = 0.136 p = 0.016	R = 0.319 p < 0.001
cTn-T	R = 0.265 p < 0.001	R = 0.079 p = 0.163	-	R = 0.11 p = 0.53	R = 0.027 p = 0.637
NT-proBNP	R = 0.103 p = 0.070	R = 0.136 p = 0.016	R = 0.11 p = 0.53	-	R = 0.103 p = 0.069

cTnT - cardiac troponin, NT-proBNP - N-terminal pro-brain natriuretic peptide, PT - prothrombin time, D-D - D-dimer.

RESULTS

Basic characteristics of patients with acute myocardial infarction

There were 66 males and 25 females in the severe myocardial infarction group, aged 40 to 85 years, with an average age of (65.82 ± 12.477) years. There were 163 males and 60 females in the non-severe group, aged 34 - 84 years, with an average age of (61.08 ± 11.482) years. There was a significant difference in age between the two groups ($p = 0.002$), but no significant difference in gender, smoking history, drinking history, hypertension history, diabetes history, hyperlipidemia history, and arrhythmia history between the two groups ($p > 0.05$) (Table 1).

Comparison of serological and coagulation indexes in patients with AMI

The results showed that the levels of troponin and brain natriuretic peptide, prothrombin time, and D-dimer in the severe group were significantly higher than those in the non-severe group, and the difference was statistically significant ($p < 0.05$) (Table 2).

Comparison of stent implantation during PCI in patients with AMI

The results of Table 3 show that the patients with AMI in the severe group had a history of stent implantation in the left circumflex artery and the right coronary artery, a history of single or double stent implantation, and a history of heart failure and adverse cardiovascular events, which were significantly higher than those in the non-severe group, with statistically significant differences ($p < 0.05$).

The sensitivity and specificity of cardiac function indexes and coagulation indexes were compared

ROC curve results showed that the cutoff value of D-D was 0.475 (area under the curve (AUC) 0.74, sensitivity 66.3%, specificity 78.2%, $p < 0.001$). The cutoff value of prothrombin time was 14.45 (AUC 0.692, sensitivity 37.2%, specificity 95.1%, $p < 0.001$). The cutoff value of troponin T was 4.745 (AUC 0.501, sensitivity 87.2%, specificity 16%, $p = 0.985$), and the cutoff value of brain natriuretic peptide was 5,319 (AUC 0.554, sensitivity 26.7%, specificity 87.6%, $p = 0.140$). See Figure 1A - B.

Table 5. Multivariate logistic regression was used to analyze the independent risk factors of acute myocardial infarction.

	B	OR	95% CI - upper	95% CI - lower	p-value
Age	**-0.025**	**0.975**	**1.019**	**0.933**	**0.265**
Smoking history	**-0.326**	**0.721**	**1.961**	**0.265**	**0.522**
Drinking history	**0.822**	**2.275**	**7.708**	**0.672**	**1.87**
Hyperlipidemia history	**0.737**	**2.089**	**25.446**	**0.172**	**0.563**
Hypertension history	**-0.897**	**0.408**	**0.984**	**0.169**	**0.046**
Diabetes history	**-0.778**	**0.459**	**2.234**	**0.094**	**0.335**
Heart failure history	**8.750**	**6,311.432**	**162,300.120**	**245.435**	**< 0.001**
hs-CRP	**0.037**	**1.038**	**1.087**	**0.991**	**0.117**
cTnT	**0.003**	**1.003**	**0.897**	**1.053**	**0.956**
NT-proBNP	**0.000**	**1.000**	**1.000**	**1.000**	**0.076**
CK	**-0.004**	**0.996**	**0.996**	**0.996**	**0.378**
CK-MB	**0.00**	**1.000**	**1.007**	**0.994**	**0.921**
LDH	**0.00**	**1.000**	**1.003**	**0.998**	**0.724**
Albumin	**-0.056**	**0.945**	**1.083**	**0.825**	**0.416**
Globulin	**0.035**	**1.036**	**1.164**	**0.922**	**0.551**
TC	**0.663**	**1.941**	**6.635**	**0.568**	**0.291**
LDL	**-0.727**	**0.483**	**1.778**	**0.131**	**0.274**
HDL	**-0.324**	**0.723**	**5.686**	**0.092**	**0.758**
LVEF	**-0.208**	**0.812**	**0.886**	**0.744**	**< 0.001**
PT	**0.747**	**2.474**	**0.744**	**0.302**	**0.001**
APTT	**0.036**	**1.036**	**1.102**	**0.974**	**0.258**
TT	**-0.009**	**0.991**	**1.016**	**0.966**	**0.49**
Fibrinogen	**-0.262**	**0.77**	**1.254**	**0.473**	**0.293**
D-D	**0.758**	**2.469**	**0.984**	**0.223**	**0.045**

hs-CRP - hypersensitive C-reactive protein, cTnT - cardiac troponin T, NT-proBNP - N-terminal pro-brain natriuretic peptid, CK - creatine kinase, CK-MB - creatine kinase isoenzymes, LDH - lactate dehydrogenase, TC - total cholesterol, LDL - low-density lipoprotein, HDL - high-density lipoprotein, LVEF - left ventricular ejection fraction, PT - prothrombin time, APTT - activated partial prothrombin time, TT - thrombin time, D-D - D-dimer.

The correlation between D-D, PT, cTnT, NT-proBNP, Killip grade, and adverse cardiovascular events was evaluated

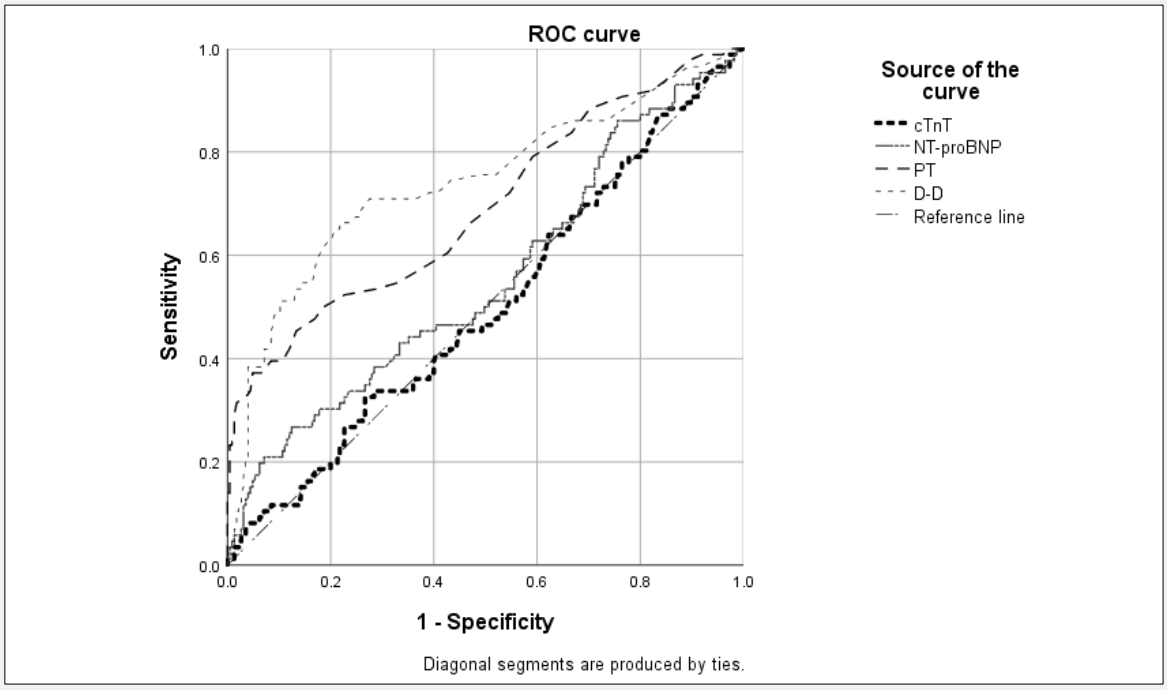
Bivariate regression analysis showed that D-D was significantly correlated with prothrombin time ($R = 0.311$, $p < 0.001$), troponin T ($R = 0.265$, $p < 0.001$), and Killip ($R = 0.388$, $p < 0.001$) grades. Similarly, PT was also significantly correlated with NT-proBNP ($R = 0.136$, $p = 0.016$) and Killip grade ($R = 0.319$, $p < 0.001$). There was no significant correlation between cTnT ($R = 0.027$, $p = 0.637$) and brain natriuretic peptide ($R = 0.103$, $p = 0.069$) and Killip classification (Table 4).

Multivariate logistic regression was used to analyze the independent risk factors of AMI

Multivariate logistic regression analysis showed that previous history of heart failure, LVEF, PT, and D-D were independent risk factors for AMI ($p < 0.05$) (Table 5).

DISCUSSION

AMI is a common cardiovascular disease that can lead to death in patients, and most patients have a poor prognosis. Therefore, it is particularly important to find new economic and accurate predictors. Previous studies have shown that D-D has important diagnostic value for patients with chest pain in the emergency department [12, 13]. The results of our study also demonstrated that D-D was more sensitive and specific than cTnT and NT-proBNP in the diagnosis of AMI and had an important correlation with Killip classification. Multivariate logistic regression analysis showed that D-D could be used as an independent risk factor for AMI.



	D-D	PT	cTnT	NT-proBNP
Cutoff value	**0.475**	**14.45**	**4.745**	**5,319**
AUCs	**0.74**	**0.692**	**0.501**	**0.554**
Sensitivity (%)	**66.3%**	**37.2%**	**87.2%**	**26.7%**
Specificity (%)	**78.2%**	**95.1%**	**16%**	**87.6%**
p-value	**< 0.001**	**< 0.001**	**0.985**	**0.140**

Figure 1. The ROC curve analysis of cTnT, NT-proBNP, PT, and D-D.

(A) The ROC curve analysis of cTnT, NT-proBNP, PT, and D-D. (B) Statistical data obtained from the ROC curves of cTnT, NT-proBNP, PT, and D-D.
AUCs - areas under the curve, cTnT - cardiac troponin T, NT-proBNP - N-terminal pro-brain natriuretic peptide, PT - prothrombin time, D-D - D-dimer.

The PT mainly reflects the function of the exogenous coagulation pathway, and a longer PT indicates inadequate coagulation, thereby increasing the risk of bleeding [14]. Patients with coronary heart disease often have abnormal blood coagulation function [15]. Natural PT is not a direct indicator for the diagnosis of coronary heart disease, but it is related to the state of blood coagulation, and abnormal blood coagulation may affect the progression and treatment of coronary heart disease. Our results suggest that PT has important predictive value for the diagnosis and prognosis of AMI, and it has high sensitivity and specificity. It can also play a role as an independent risk factor for AMI. Previous studies have suggested that active and effective anti-thrombotic and anti-infective interventions can effectively improve the prognosis of AMI patients with high levels of D-D and hs-CRP after PCI, which supports our study conclusion [16].

However, our study has certain limitations. First of all, our study is a retrospective analysis, which may lead to some errors due to the inevitable subjectivity of data collection. Although we demonstrated that both D-D and PT can be used as independent predictors of adverse cardiovascular events in patients with AMI, further studies with a larger sample size and prospective studies are needed to minimize the existence of such errors.

The results of our study provide an economic, simple,

and accurate predictor for the diagnosis of AMI, which can help clinicians to determine the risk of complications after PCI in time and take effective intervention measures as soon as possible, which has important value.

Declaration of Interest:

No potential conflicts of interest regarding the research, authorship, or publication of this article were disclosed.

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