The Value of D-dimer in the Prognosis and Clinical Classification of Acute Aortic Dissection

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Abstract: Objective: To investigate the prognostic and clinical classification value of D-dimer in acute aortic dissection (AAD), thereby providing a foundation for early clinical attention and proactive intervention. Methods: The clinical data of 74 patients with acute aortic dissection were retrospectively analyzed. Based on the prognosis, they were categorized into two groups: death group and survival group. Univariate and multivariate logistic regression analyses were employed to investigate the risk factors associated with in-hospital mortality in patients with acute aortic dissection (AAD). Similarly, regression analysis was conducted to identify the risk factors for Stanford A acute aortic dissection according to the Stanford classification criteria. Additionally, the prognostic value of D-dimer for both AAD and Stanford A dissection was evaluated using ROC curve analysis. Results: Significant differences were observed in Stanford type A, creatinine, D-dimer, and N-terminal pro-brain natriuretic peptide (NT proBNP) levels between the death group and survival group ($P < 0.05$). Multivariate regression analysis revealed that D-Dimer (odds ratio [OR] = 1.26, 95% confidence interval [CI]: 1.09-1.46, $P = 0.002$) and creatinine (OR = 1.02, 95% CI: 1.00-1.03, $P = 0.022$) independently contributed to the risk of mortality in patients with acute aortic dissection (AAD). The area under the curve (AUC) for D-dimer in predicting in-hospital death was found to be 0.77 with an optimal cut-off point of 6.5 mg/l; yielding a sensitivity of 86% and specificity of 62%. Significant differences were also observed between Stanford A and Stanford B classifications among female patients regarding clinical classification as well as D-Dimer levels ($P <0.05$). Multivariate analysis demonstrated that D-Dimer (OR=1.18,95 % CI : 1.05-1.32, P=0.005) and female gender (OR=4. 07, 95% CI: 1.24-13.29, P=0.02) were associated with increased risk of Stanford A dissection.The AUC for D-dimer was calculated as 0.69 with a critical point at 10.73mg/L,sensitivity ranged from 55%,and specificity reached 81%. Conclusion: The elevated levels of D-dimer not only serve as a prognostic indicator for mortality in acute aortic dissection but also act as a predisposing factor for Stanford A dissection.

Keywords: D-Dimer; Acute Aortic Dissection; Prognosis; Clinical Classification

Introduction

Acute Aortic Dissection (AAD) typically exhibits a rapid onset and can directly result in sudden death. Relevant studies have demonstrated that the average incidence of this disease is 3 to 6 cases per 100,000 individuals, with higher rates observed among the elderly at up to 15 cases per 100,000 individuals. Furthermore, there has been a consistent year-on-year increase in its incidence [1-2]. The direct out-of-hospital mortality rate for AAD exceeds 20%, while even with timely treatment, in-hospital mortality can reach as high as 30%. Following diagnosis, the risk of death for AAD patients escalates by approximately 1%-2% per hour [3]. In recent years, an increasing number of laboratory indicators have been employed for prognostic evaluation of in-hospital outcomes related to AAD. D-dimer serves as a routine admission test indicator and is commonly utilized for diagnosing various diseases; it also holds certain diagnostic value for AAD patients. Several studies have indicated that elevated D-dimer levels are associated with poor prognosis among AAD patients [4]. Routine laboratory

tests are extensively used in clinical practice due to their intuitive data presentation and prompt results acquisition. Establishing correlations between laboratory findings and prognosis/classification plays a pivotal role in early warning systems, timely attention allocation, and proactive intervention during clinical practice. This study aims to analyze in-hospital data from AAD patients to identify risk factors linked to in-hospital mortality and susceptibility factors specific to Stanford type A dissection. Additionally, we aim to further elucidate the impact of D-dimer on the prognosis of AAD along with any disparities across clinical classifications.

1. Data and Methods

1.1 Study Population

A total of 74 patients diagnosed with acute aortic dissection were enrolled from December 2019 to December 2020 at the Emergency Department of the Second Hospital of Hebei Medical University. The cohort consisted of 53 males and 21 females, with a mean age at onset of (50.93±10.68) years. Among them, there were 21 cases in the deceased group and 53 cases in the survival group, including 38 cases classified as Stanford A type and 36 cases classified as Stanford B type.

1.2 Inclusion and exclusion criteria

Inclusion criteria: patients with acute aortic dissection were diagnosed by aortic CT angiography (CTA); All patients were acute onset, the onset time was less than 14 days. All of them had no previous history of AAD and were the first onset of AAD.

Exclusion criteria: acute cerebral infarction, pulmonary embolism, chronic obstructive pulmonary disease, deep venous thrombosis of lower extremities, pregnancy, infection, tumor, autoimmune system disease, basic liver and kidney insufficiency, coagulation dysfunction.

1.3 Methods

The age, gender, chest pain, onset time, past medical history, personal history, laboratory routine test indicators, clinical classification and prognosis in hospital were collected. D-dimer, N-terminal pro-brain natriuretic peptide (NT-proBNP) and high-sensitivity troponin I (hs-cTnI) were detected by Raylaike Bioscience TZ301 detector, and the detection principle was immunofluorescence method. Other laboratory indicators were uniformly detected by the laboratory department of our hospital.

1.4 Statistical analysis

Using SPSS21.0 statistical software, t test and non-parametric test were used to analyze the difference of measurement data between groups, and X^2 test and Fisher's exact probability test were used to analyze the difference of count data. logistic regression analysis was used to explore the relationship between D-dimer and the prognosis and clinical classification of acute aortic dissection. The receiver operating characteristic curve (ROC) was drawn and the area under the curve was calculated. $P<0.05$ was considered statistically significant.

2. Results

2.1 Regression analysis according to prognostic outcome

Univariate analysis of patients with acute aortic dissection between the death group and the survival group, the proportion of Stanford type A, creatinine, D-dimer and N-terminal pro-brain natriuretic peptide (NT-proBNP) in the death group were significantly higher than those in the survival group, with statistical differences. See Tables 1 and 2 for details.

Table 1 Univariate analysis of the death and survival groups of acute aortic dissection

General information	Total (n=74)	Death group (n=21)	Survival group (n=53)	t/X^2	*P*
Age y(M±SD)	50.93 + / - 10.68	50.29 + / - 12.44	51.19 + / - 10.01	0.33	0.75
Time of onset h[M	10.50 (5.00,	8.00 (3.50, 24.00)	24.00 (5.00,24.00)	1.09	0.27

(P25-P75)]	24.00))				
Chest pain n(%)	49 (66.2)	16 (76.2)	33 (62.3)	1.30	0.25
Hypertension n(%)	53 (71.6)	13 (61.9)	40 (75.5)	1.36	0.24
Smoking n(%)	27 (36.5)	6 (28.6)	21 (39.6)	0.79	0.37
Drinking n(%)	31 (41.9)	9 (42.9)	22 (41.5)	0.01	0.92
Stanford type A n(%)	38 (51.4)	16 (76.2)	22 (41.5)		
Stanford B type n(%)	36 (48.6)	5 (23.8)	31 (58.5)	7.24	0.007
Male n(%)	53(71.6)	17(81)	36(67.9)		
Female n(%)	21 (28.4)	4 (19)	17 (32.1)	1.26	0.26

Table 2 Comparison of laboratory indexes between the death group and the survival group of acute aortic dissection M (P25, P75)

Laboratory indexes	Death group (n=21)	Survival group (n=53)	Z	*P*
WBC(*10^9/L)	10.70 (8.10, 13.75)	11.40 (9.10, 13.30)	0.42	0.68
Hs-CRP(mg/L)	4.60 (1.45, 31.45)	7.90 (2.00, 20.27)	0.72	0.47
MYO(ng/mL)	81.00 (44.50, 350.50)	58.00 (38.00, 120.50)	1.31	0.19
CK(U/L)	100.00 (71.00, 246.50)	113.00 (68.50, 204.00)	1.00	0.92
CK-MB(U/L)	28.00 (18.50, 39.00)	25.00 (20.00, 33.50)	0.28	0.78
LDH(U/L)	268.00 (227.50, 346.00)	258.00 (206.00, 325.00)	0.88	0.38
HBDH(U/L)	198.00 (164.50, 246.50)	181.00 (152.00, 242.00)	1.37	0.17
ALT(U/L)	18.70 (13.60, 27.40)	18.10 (11.65, 32.75)	0.02	0.99
AST(U/L)	20.70 (15.45, 31.65)	20.10 (16.70, 29.25)	0.07	0.95
Creatinine (μmol/L)	102.00 (74.00, 165.50)	78.00 (66.00, 97.00)	2.29	0.02
TG(mmol/L)	1.51(0.88, 1.56)	1.51(1.09, 1.56)	0.97	0.33
D-dimer (mg/L)	12.00(6.89, 12.00)	3.30 (1.66, 11.65)	3.71	< 0.001
NT-proBNP(pg/mL)	524.3(250.9,910.3)	224.60(76.25,438.60)	2.60	0.009
Hs-cTnI(ng/ml)	0.05 (0.03, 0.05)	0.03 (0.03, 0.05)	1.41	0.16

Multivariate logistic regression analysis of in-hospital death outcome of acute aortic dissection showed that Stanford type A, D-dimer, creatinine and NT-proBNP were the risk factors for AAD death, which were included as independent variables, and the prognosis of death was used as the dependent variable for binary logistic regression. Binary logistic regression analysis showed that elevated D-dimer and creatinine were independent risk factors for in-hospital death in patients with AAD. The specific assignment is shown in Table 3.

Table 3 Risk factors for prognosis of AAD death in multivariate analysis

Indicators	OR value	95%CI	*P* value
Creatinine	1.02	1.00, 1.03	0.022
D-dimer	1.26	1.09, 1.46	0.002

ROC curve of D-dimer for predicting in-hospital death risk of acute aortic dissection and the best cut-off value The area under the curve of D-dimer for predicting AAD was 77%, the best cut-off value was 6.5, the sensitivity was 86%, and the specificity was 62%. The ROC curve is shown in Figure 1 for details, and the cut-off values are shown in Table 4.

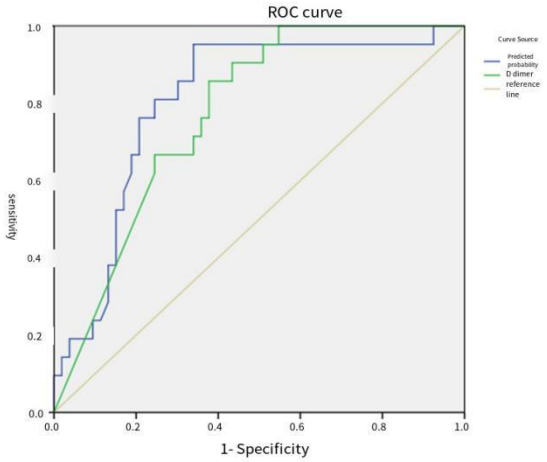

Figure 1 ROC curve of D-dimer for predicting in-hospital mortality risk of acute aortic dissection

Table 4 cut-off values of D-dimer for predicting in-hospital mortality risk in AAD

Indicators	AUC	95%CI	*P*	The Cut-off value	Sensitivity	Specificity
Prediction probability	0.81	0.70-0.91	< 0.01	0.22	0.95	0.66
D-dimer	0.77	0.67-0.88	< 0.01	6.5	0.86	0.62

2.2 Risk factors analysis of Stanford type A dissection

Comparison of clinical data between Stanford type A and Stanford type B acute aortic dissection, there were statistical differences in gender and D-dimer between the two groups. The proportion of female patients in Stanford type A was higher than that in Stanford type B. The value of D-dimer in Stanford A type was significantly higher than that in Stanford B type. See Table 5.

Table 5 Comparison of data between the Stanford type A group and the Stanford type B group of acute aortic dissection

Indicators	Stanford Type A	Stanford Type B	$t/X^2/Z$	*P*
Sex ratio (male/female)	23:15	5:1	4.73	0.03
Age (y)	50.47 + / - 10.67	51.42 + / - 10.82	0.38	0.71
Time of onset (h)	10.00 (4.75,24.00)	24.00 (5.25, 60.00)	1.14	0.26
Chest pain n(%)	26 (68.4)	23 (63.9)	0.17	0.68
Hypertension n (%)	27 (71.1%).	26 (72.2%).	0.01	0.91
Smoking n(%)	12 (31.6%).	15 (41.7%).	0.81	0.37
Drinking n(%)	14 (36.8%).	17 (47.2%).	0.82	0.37
White blood cells (*109/L)	11.50 (9.18, 14.00)	10.65 (7.78, 13.28)	1.44	0.15
Hs-CRP(mg/L)	5.50 (1.40, 19.66)	11.75 (2.13, 22.05)	1.44	0.15
MYO(ng/mL)	68.50 (35.75, 146.25)	56.50 (43.25, 111.75)	0.60	0.55
CK(U/L)	110.50 (73.75, 203.50)	109.50 (64.00, 247.75)	0.49	0.63
CK-MB(U/L)	27.50 (19.75, 40.50)	25.00 (19.25, 32.75)	0.73	0.47
LDH(U/L)	270.50 (226.25, 325.00)	247.50 (201.25, 321.75)	1.44	0.15
HBDH(U/L)	188.00 (159.75, 244.75)	180.00 (145.50, 254.44)	0.94	0.35
ALT(U/L)	17.60 (12.08, 32.13)	21.05 (12.38, 31.25)	0.42	0.68

AST(U/L)	20.60 (17.08, 31.53)	19.30 (16.18, 29.93)	0.83	0.41
Creatinine (μmol/L)	90.96 (69.00, 128.50)	78.50 (68.00, 96.25)	1.03	0.30
TG(mmol/L)	1.54(1.13, 1.56)	1.30 (0.93, 1.56)	0.76	0.45
D-dimer (mg/L)	11.76 (3.33, 12.00)	2.83 (1.60, 9.60)	2.92	0.004
NT-proBNP(pg/mL)	329.60(182.75, 784.18)	220.75 (58.93,648.90)	1.76	0.08
Hs-cTnI(ng/ml)	0.04 (0.03, 0.06)	0.03 (0.03, 0.05)	1.11	0.27

Logistic regression analysis of Stanford type A dissection included gender and D-dimer with significant differences in clinical classification into multivariate regression analysis, and the results showed that female and high D-dimer were risk factors for Stanford type A dissection. See Table 6.

Table 6 logistic regression analysis of Stanford type A acute aortic dissection

Indicators	OR value	95%CI	*P* value
D-dimer	1.18	1.05-1.32	0.005
Women	4.07	1.24-13.29	0.02

ROC curve and optimal cut-off value of D-dimer in predicting Stanford type A acute aortic dissection, the area under the curve of D-dimer in predicting Stanford type A acute aortic dissection was 69%, the optimal cut-off value was 10.73, the sensitivity was 55%, and the specificity was 81%. For details, please refer to Figure 2 and Table 7.

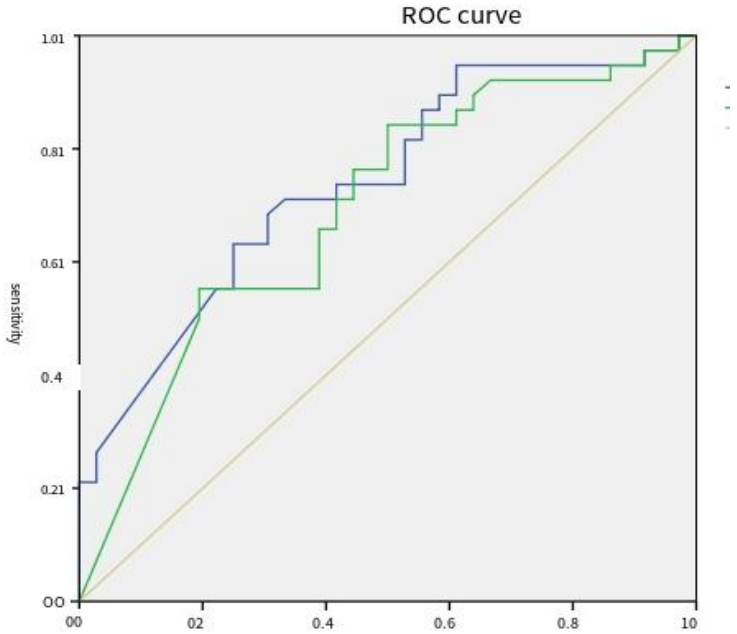

Figure 2 ROC curve of D-dimer for predicting Stanford type A acute aortic dissection

Table 7 Cut-off values of D-dimer for predicting Stanford type A AAD

Indicators	AUC	95%CI	*P*	The Cut-off value	Sensitivity	Specificity
Prediction probability	0.74	0.63-0.85	< 0.001	0.60	0.63	0.75
D-dimer	0.69	0.57-0.81	0.004	10.73	0.55	0.81

3. Discussion

Bedside D-dimer detection is short, fast and convenient, and has a high value in the diagnosis of a variety of clinical

diseases, especially in the emergency department. D-dimer is a product of fibrin degradation, which can be used to diagnose venous thromboembolism and other thrombotic diseases[5,6]. At the same time, in patients with acute cerebral infarction, D-dimer is directly[7] proportional to the severity of infarction. A number of previous studies have shown that D-dimer has the value of differential diagnosis of ADD, and a large number of literature in recent years has also summarized its value[8] in predicting the prognosis of patients with acute aortic dissection. This study found that D-dimer in the death group of AAD was significantly higher than that in the survival group, which is consistent[9,10] with previous results in this direction. We conclude that a D-dimer level of 6.5μg·ml^{-1} has a sensitivity of 86% for prognostic outcomes. Li Dandan et al. found that when the optimal critical point was 4.85 μg·mL^{-1}, the sensitivity could reach 85.7%[11]. The cut-off value of D-dimer for predicting in-hospital death of acute aortic dissection was different from each experiment. It was considered to be related to the extent of aortic tear and the state of false lumen formed with the progress of the disease after aortic tear, and D-dimer increased with the increase[12,13] of tear length. However, in the clinical treatment process, there are some acute aortic dissection with negative D-dimer, which should be paid special attention[13,14] to.

The value of D-dimer in Stanford A type was significantly higher than that in Stanford B type. The results of this study showed that D-dimer could be used as an independent factor to predict Stanford type A dissection. When the cut-off value was 10.73, the specificity was 81%, but the sensitivity was low. The D-dimer level of Debakey type II dissection is lower than that of Debakey type I dissection. Although both type I and type II dissection are Stanford type A, the false lumen formed by Debakey type I tear is longer[15]. It can be seen that the difference in classification is significantly related to the range of vessels involved, which is also consistent with the effect of the degree of tear on D-dimer. Stanford type A dissection involves a wider range of vessels than Stanford type B dissection, which leads to the formation[16,17] of D-dimer. In addition, the dynamic monitoring of D-dimer level is especially necessary for the diagnosed Stanford type B dissection. When the value is abnormally higher than before, it should be alert to the expansion of the dissection area or the occurrence[18] of complications such as pulmonary embolism and lower extremity venous thrombosis.

In conclusion, D-dimer level is an independent factor affecting the prognosis of patients with AAD, and has a certain predictive value for the prognosis and classification of AAD patients. The D-dimer level should be dynamically monitored in emergency clinical work. When it is abnormally high, CTA examination should be performed as soon as possible to further confirm the diagnosis, and active intervention should be taken to improve the survival rate of patients.

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