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ORIGINAL ARTICLE

Value of D-dimer and C reactive protein in predicting inhospital death in acute aortic dissection

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ABSTRACT

Objective To evaluate the role of D-dimer and C reactive protein (CRP) in predicting inhospital death in acute aortic dissection (AD).

Design A single-centre prospective study.

Setting University hospital in China.

Patients 114 patients with acute AD.

Intervention Admission D-dimer and CRP concentrations were assayed.

Main outcome measures To observe the association of D-dimer and CRP with inhospital death.

Results Increased levels of plasma D-dimer (9.84±3.53 vs 4.28±1.99, $P < 0.001$), CRP (14.08±2.81 vs 11.18 ±1.85, $P < 0.001$) and aortic diameter (45.2±9.5 vs 40.3±6.0, $p = 0.007$) were found in dead patients compared with those survived. Moreover, plasma D-dimer concentrations in type A were higher than that in type B (6.51±4.11 vs 4.87±2.29, $p = 0.013$). Plasma D-dimer concentrations had positive correlations with CRP levels ($r=0.527$, $P < 0.001$) and aortic diameter ($r=0.227$, $p = 0.015$), and had negative correlations with the type of AD ($r=-0.232$, $p = 0.013$) and the time from onset ($r=-0.264$, $p = 0.005$). D-dimer and CRP levels and the type of AD were strongly associated with inhospital mortality. The OR and 95% CI were 3.272, 1.638 to 6.535; 2.322, 1.134 to 4.757; and 0.126, 0.019 to 0.853, respectively. Furthermore, the sensitivity and specificity of D-dimer ≥5.67 μg/mL in predicting inhospital death in acute AD were 90.3% and 75.9% (95% CI 0.85 to 0.96), respectively. Moreover, the sensitivity and specificity of CRP levels ≥11.21 mg/L were 100% and 54.2%, respectively (95% CI 0.74 to 0.89).

Conclusions D-dimer ≥5.67 μg/mL, CRP ≥11.21 mg/L and type A acute AD were important risk factors and independently associated with acute AD inhospital death.

INTRODUCTION

Acute aortic dissection (AD) is a severe cardiovascular disease demonstrating the characteristics of acute onset, rapid development, and high morbidity and mortality. Data showed that the mortality of AD per hour early after the onset of symptoms was about 1%–2%.[1 2] Although electrocardiography, chest radiography, CT, nuclear MRI, and transthoracic or transesophageal echocardiography are commonly used modalities in diagnosing AD, they are either unavailable at bedside or time-consuming. Many patients with AD die before diagnosis. The misdiagnosis rate could up to approximately 38% in the initial assessment of AD.[3]

Activated coagulation and fibrinolytic systems are found in the pathogenesis of AD. The release of tissue factor and false lumen thrombosis lead to the activation of extrinsic and intrinsic pathways of the coagulation cascade reaction. Subsequently, fibrinolytic systems are also activated, and cross-linked fibrin is degraded. D-dimer, a kind of degradation product of cross-linked fibrin, indicating fibrinolytic activities in AD, could be detected in peripheral blood within 10 min. Various studies have confirmed the value of D-dimer in early diagnosis, differential diagnosis and predicting prognosis with its potential sensitivity and specificity.[4–13]

However, whether D-dimer could provide valuable clinical prediction information for inhospital death in acute AD is still lacking systematic investigations. This present study is undertaken therefore to assess the plasma levels of D-dimer in acute AD and indicate its value in predicting inhospital risk of death.

MATERIALS AND METHODS

Study population

We consecutively enrolled 114 patients with acute AD between January 2007 and October 2011. Among these 114 patients, 83 patients survived and 31 died during hospitalisation. Thus, the study subjects comprised two groups: survival and death. All the subjects enrolled in this study had normal hepatic and renal function. The study subjects with coronary heart disease, heart failure and Marfan syndrome were excluded. And those who recently had a surgery or infectious diseases were also excluded. All the included patients were informed and consented with regard to their participation in this study.

Definitions

The diagnosis of AD was confirmed in all patients by history, chest radiography, transthoracic or transesophageal echocardiography, and contrast-enhanced CT. We classified AD according to Stanford classification.[1] AD is characterised by acute and chronic phases. The dissection is considered as acute AD if the time from the onset of the symptoms to admission is within 14 days, while chronic AD is that over 14 days.[2]

Hypertension was established by a clinic record of systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, or the use of antihypertensive agents. Diabetes mellitus was defined as treatment with oral hypoglycaemic agents or insulin, fasting glucose level ≥126 mg/dL, or a glycosylated haemoglobin A1c≥6.5%.

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Smoking status was defined when the subjects were current smokers according to self-report. Marfan syndrome was diagnosed by the Ghent criteria.[14] Glomerular filtration rate ≤60 mL/min was defined as impaired renal function.

Serum measurements

Venous blood was drawn from all patients in a fasting state after admission (within 48 h after onset without premedications) before surgery. Plasma were obtained after rapidly centrifugation and were immediately stored at −20°C for further analysis. Plasma D-dimer was assayed by immunoturbidimetric method (Diagnostica Stago, France, normal limit ≤0.5 μg/mL). C reactive protein (CRP) was determined by a high-sensitivity assay using a BN II nephelometer (Dade Behring, Marburg, Germany). The detection of value was as low as 0.17 mg/L. Total cholesterol, triglyceride, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol were determined by standard quantitative assay techniques in the hospital Clinical Laboratory Center according to the manufacturers' instructions. All assays were run in duplicate.

Statistical analysis

Continuous variables were compared by means of t test and analysis of variance for normally distributed data, and nonparametric Mann–Whitney U test for abnormally distributed data. Categorical variables were compared by χ^2 test or Fisher's exact test. Correlations were assessed using Spearman's rank correlation. Univariate analysis and multiple logistic regression analysis were used to simultaneously analyse the influence of multiple factors on a variable. Receiver operating characteristic analysis was performed to determine the cut-off value for D-dimer and CRP in predicting inhospital mortality with high sensitivity and specificity. p Value<0.05 was considered statistically significant. Data analysis was performed using a commercially available statistical software package (SPSS II for windows, V.18.0, Chicago, Illinois, USA).

RESULTS

Plasma levels of biomarkers

Among the 114 patients with acute AD, 83 patients survived and 31 died during hospitalisation. Therefore, the study subjects comprised survived and dead groups. In our findings, the percentage of type A AD (83.9% vs 45.8%, p<0.001), plasma D-dimer (9.84±3.53 vs 4.28±1.99 μg/mL, p<0.001), CRP (14.08±2.81 vs 11.18±1.85 mg/L, p<0.001) concentrations and aortic diameter (45.2±9.5 vs 40.3±6.0 mm, p=0.007) were significantly higher in death than in survival group (table 1 and figures 1 and 2).

Correlation analysis

Our findings showed that D-dimer levels had positive correlations with CRP levels (r=0.527, p<0.001) and aortic diameter (r=0.227, p=0.015), and had negative correlations with the type of AD (r=−0.232, p=0.013) and the time from onset of symptoms to hospital admission (r=−0.264, p=0.005) (figure 3). Moreover, increased D-dimer levels were observed in type A AD compared with type B AD (6.51±4.11 vs 4.87±2.29 μg/mL, p=0.013).

Univariate analysis and multiple logistic regression analysis for inhospital mortality

The data indicated that there were eight variables associated with hospital short-term mortality including the type of AD, history of smoking, admission systolic blood pressure, admission diastolic blood pressure, aortic diameter, onset of symptoms to hospital admission, D-dimer and CRP with a p value about 0.1 in univariate analysis (table 2). And then, we put these eight variables into multiple logistic regression analysis and found that D-dimer (OR, 3.272; 95% CI 1.638 to 6.535; p=0.001), CRP (OR, 2.322; 95% CI 1.134 to 4.757; p=0.021) and the type of AD (OR, 0.126; 95% CI 0.019 to 0.853; p=0.034) were significantly associated with hospital short-term mortality (table 3). In addition, hospital short-term mortality in type A AD (39%) was higher than that in type B AD (12%).

In addition, we also performed univariate and multiple logistic regression analyses stratified by the type of AD. However, in either type A or type B AD, we observed no statistically

Table 1 Baseline clinical characteristics of patients with acute aortic dissection (AD)

Clinical variables	Survival	Death	p Value
Number	83	31	—
Type A AD, n (%)	38 (45.8)	26 (83.9)	<0.001
Age (year)	48.9±7.6	48.6±7.6	0.934
Males, n (%)	69 (83.1)	27 (87.1)	0.422
History of smoking, n (%)	54 (65.1)	15 (48.4)	0.081
History of hypertension, n (%)	65 (78.3)	27 (87.1)	0.218
History of DM, n (%)	26 (31.3)	6 (19.4)	0.151
Admission SBP (mm Hg)	164±26	174±38	0.327
Admission DBP (mm Hg)	101±16	107±20	0.136
Aortic diameter (mm)	40.3±6.0	45.2±9.5	0.007
Medications before admission, n (%)			
Aspirin	36 (43.4)	14 (45.2)	0.515
Nitroglycerin	44 (53.0)	13 (41.9)	0.200
Serum measurements			
D-dimer (μg/mL)	4.28±1.99	9.84±3.53	<0.001
CRP (mg/L)	11.18±1.85	14.08±2.81	<0.001
TC (mmol/L)	4.82±0.79	4.86±0.97	0.926
TG (mmol/L)	1.18±0.64	1.22±0.58	0.954
HDL-C (mmol/L)	1.13±0.43	1.09±0.33	0.526
LDL-C (mmol/L)	2.29±1.30	2.36±0.72	0.189
Time from admission to death (day)	–	4.3±2.7	–

CRP, C reactive protein; DBP, diastolic blood pressure; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

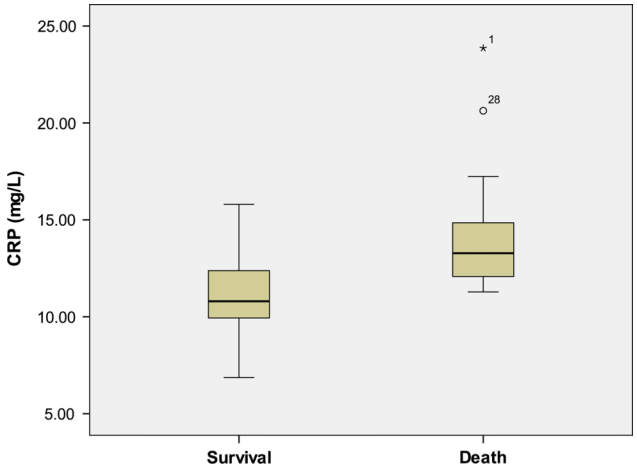

Figure 1 Comparison of D-dimer values between survival and death groups.

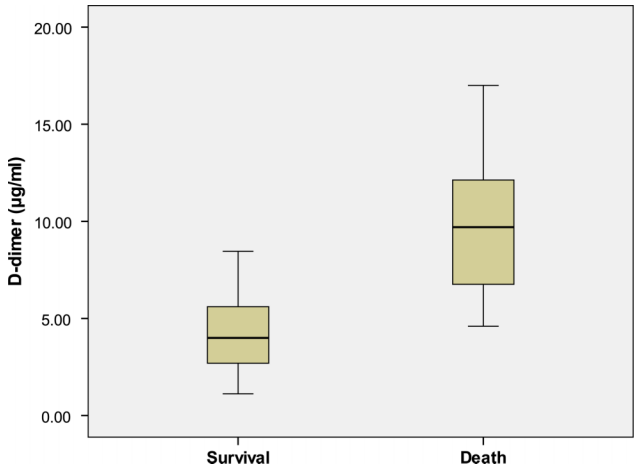

Figure 2 Comparison of C reactive protein values between survival and death groups.

significant correlations between any of variables included in this study and inhospital death.

Sensitivity and specificity of D-dimer and CRP in predicting inhospital mortality

We performed receiver operating characteristic analysis to determine the cut-off value of D-dimer and CRP in evaluating inhospital mortality. The cut-off values were 5.67 μg/mL for D-dimer, and 11.21 mg/L for CRP with their higher sensitivity and specificity, respectively. The area under the curve was 0.917 and 0.822 for D-dimer and CRP, respectively. When D-dimer was ≥5.67 μg/mL, the sensitivity and specificity in predicting inhospital death were 90.3% and 75.9% (95% CI 0.85 to 0.96; p<0.001), respectively. When CRP was ≥11.21 mg/L, the sensitivity and specificity were 100% and 54.2% (95% CI 0.74 to 0.89; p<0.001), respectively (table 4 and figure 4). D-dimer ≥5.67 μg/mL and CRP ≥11.21 mg/L were important risk factors for hospital short-term mortality in acute AD.

When D-dimer was ≥4.43 μg/mL, its sensitivity in predicting inhospital death was up to 100%; while when D-dimer was ≥8.37 μg/mL, the specificity could reach 100%. In addition, when CRP was ≥15.12 mg/L, the specificity could reach 100% but with lower sensitivity (table 5). Furthermore, better predicting inhospital death performance was shown when combining use of both D-dimer and CRP assays with a sensitivity of 81.9% and a specificity of 96.8% (table 4 and figure 4).

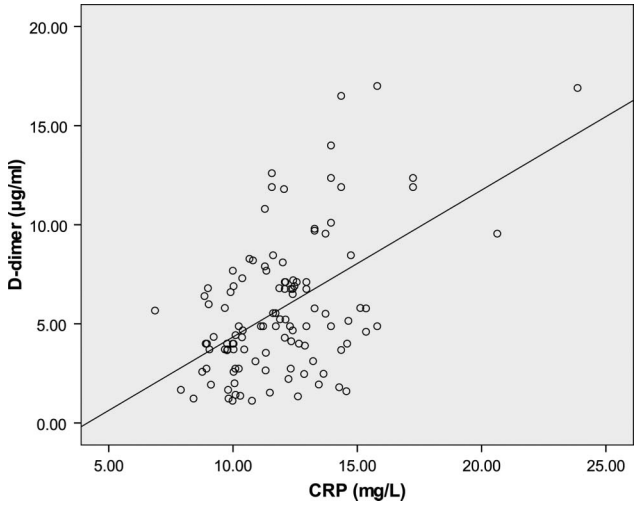

Figure 3 Correlations between plasma D-dimer and C reactive protein levels.

Table 2 Univariate analysis for hospital short-term mortality

Clinical variables	95% CI	p Value
Age	0.943 to 1.052	0.883
Type of AD	0.057 to 0.464	0.001
Male	0.221 to 2.417	0.607
History of smoking	0.218 to 1.162	0.108
History of hypertension	0.579 to 6.039	0.296
History of DM	0.193 to 1.437	0.210
Admission SBP (mm Hg)	0.998 to 1.025	0.102
Admission DBP (mm Hg)	0.997 to 1.045	0.085
Aortic diameter (mm)	1.033 to 1.166	0.003
Aspirin	0.469 to 2.466	0.866
Nitroglycerin	0.278 to 1.473	0.297
Onset of symptoms to hospital admission (h)	0.642 to 1.059	0.127
Time of surgery (h)	0.968 to 1.013	0.399
Surgical treatment	0.721 to 3.967	0.227
D-dimer (μg/mL)	1.644 to 3.247	<0.001
CRP (mg/L)	1.449 to 2.566	<0.001
TC (mmol/L)	0.650 to 1.739	0.810
TG (mmol/L)	0.562 to 2.135	0.791
HDL-C (mmol/L)	0.273 to 2.181	0.629
LDL-C (mmol/L)	0.742 to 1.491	0.778

AD, aortic dissection; CRP, C reactive protein; DBP, diastolic blood pressure; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

DISCUSSION

Numerous studies have demonstrated the value of D-dimer in early diagnosis of acute AD.[4 5 7 9 15] However, the role of D-dimer in predicting inhospital death in acute AD still lacks systemic investigations. This study assessed the plasma D-dimer levels and indicated the clinical value of D-dimer in predicting hospital short-term death in acute AD. The data showed that D-dimer levels had significant positive correlation with CRP levels. When D-dimer was ≥5.67 μg/mL, the sensitivity and specificity in predicting hospital short-term mortality were 90.3% and 75.9%, respectively. When CRP was ≥11.21 mg/L, the

Table 3 Multiple logistic regression for hospital short-term mortality

Clinical variables	OR	95% CI	p Value
D-dimer (μg/mL)	3.272	1.638 to 6.535	0.001
CRP (mg/L)	2.322	1.134 to 4.757	0.021
Type of AD	0.126	0.019 to 0.853	0.034
History of smoking	0.485	0.082 to 2.886	0.427
Admission SBP (mm Hg)	1.013	0.987 to 1.039	0.332
Admission DBP (mm Hg)	0.994	0.941 to 1.049	0.817
Aortic diameter (mm)	1.109	0.964 to 1.274	0.147
Onset of symptoms to hospital admission (h)	1.154	0.629 to 2.119	0.643

AD, aortic dissection; CRP, C reactive protein; DBP, diastolic blood pressure; SBP, systolic blood pressure

Table 4 Diagnostic value of D-dimer and C reactive protein (CRP) for hospital short-term mortality

	AUC	Cut-off value	Sensitivity (%)	Specificity (%)	95% CI	p Value
D-dimer (μg/mL)	0.917	5.67	90.3	75.9	0.85 to 0.96	<0.001
CRP (mg/L)	0.822	11.21	100	54.2	0.74 to 0.89	<0.001
D-dimer+CRP	0.948	–	81.9	96.8	0.89 to 0.98	<0.001

AUC: area under the curve.

sensitivity and specificity were 100% and 54.2%, respectively. D-dimer ≥5.67 μg/mL, CRP ≥11.21 mg/L and type A acute AD were important risk factors and independently associated with acute AD hospital short-term death.

D-dimer, a kind of cross-linked fibrin polymer, has become a major screening indicator in suspected pulmonary embolism, deep vein thrombosis, disseminated intravascular coagulation, and so on with its high sensitivity and low specificity. Plasma D-dimer concentrations are associated with the area and volume of blood clots. Moreover, increased D-dimer levels could also be observed in the elderly, infection, tissue necrosis, surgery, trauma, acute coronary syndrome, pregnancy, cancer and so on.[15–18] Arterial media smooth muscle ischaemia, degeneration, necrosis and elastic fibre rupture, fibrosis and intimal rupture, and thus the formation of intramural haematoma, and ultimately the formation of true and false lumens are considered to have contributed to the pathogenesis of AD.[1 19] During these processes, the ingredients of the aorta are injured resulting in the release of tissue factor into blood flow, which leads to the activation of extrinsic pathway of the coagulation cascade reaction. In addition, false lumen thrombosis activates the intrinsic pathway of the coagulation cascade reaction. Subsequently, fibrinolytic system is also activated, cross-linked fibrin is degraded and then D-dimer is formed.[4 5 7 20] D-dimer levels may increase as early as 1 h after the onset of acute AD, and the rapid D-dimer assay could be completed within 10 min. At the same time, D-dimer has a longer half-life and high sensitivity.[7] Therefore, it is a meaningful biomarker in acute AD.

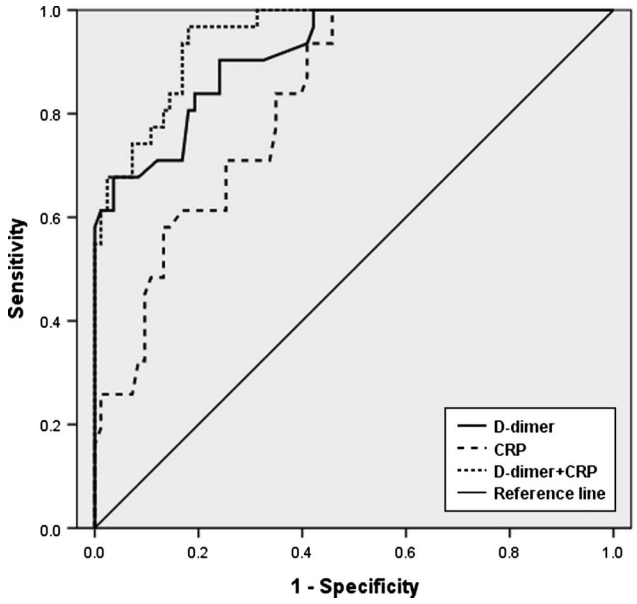

Figure 4 Diagnostic value of D-dimer and C reactive protein for inhospital death.

Various studies have reported the clinical value of D-dimer in early diagnosis, differential diagnosis and predicting prognosis with its potential sensitivity and specificity in acute AD.[4 5 7 9] Within the first 24 h after onset, when the cut-off value was at 0.5 μg/mL, the sensitivity and negative predictive values could almost reach 100%, and the specificity was about 54%–68.6%.[5 7] The specificity increased to 73% when the cut-off value was 0.626 μg/mL.[4] These demonstrate great diagnostic performance within the first 24 h of the onset of symptoms. Negative D-dimer test could be almost rule out acute AD because of its high negative predictive value. Many studies have recognised it as a rule-out tool for acute AD. Acute AD would be excluded when D-dimer levels were below 0.1 μg/mL with a sensitivity of 100%.[9]

Furthermore, significantly elevated plasma D-dimer levels were observed in acute AD with high sensitivity.[4 5 7 11 12] D-dimer values were associated with the type of AD and clinical events and prognosis. Elevated D-dimer levels were reported in patients with type A acute AD, those with severe complications or those who died during hospitalisation.[2 4 6 8 21] D-dimer >5200 ng/mL was considered as an independent predictor of inhospital mortality.[21] Moreover, D-dimer values had some relationships with the length, size and the features of lesion in the dissected aorta.[5 21 22] In addition, the correlation between D-dimer levels and the time after onset of symptoms in acute AD is controversial.[2 23 24]

Our findings also indicated that significantly increased levels of plasma D-dimer concentrations were investigated in patients died, and in type A patients with acute AD compared with those who survived and type B AD, respectively. When D-dimer was ≥5.67 μg/mL, the sensitivity and specificity in predicting inhospital death were 90.3% and 75.9%, respectively. D-dimer ≥5.67 μg/mL was an important risk factor for inhospital death in acute AD. When D-dimer was ≥4.43 μg/mL, its sensitivity in predicting inhospital death was up to 100%; while when D-dimer was ≥8.37 μg/mL, the specificity could reach 100%. In addition, D-dimer levels had positive correlations with CRP levels and aortic diameter, while they had negative correlations with the time after onset of symptoms to hospital admission. All these data further elucidate that D-dimer may be used in typing and predicting poor prognosis in acute AD.

Table 5 The sensitivity and specificity in predicting hospital mortality with different D-dimer and C reactive protein (CRP) concentrations

	Concentrations	Sensitivity (%)	Specificity (%)
D-dimer (μg/mL)	4.43	100	57.8
	8.37	61.3	100
CRP (mg/L)	11.21	100	54.2
	15.12	25.8	100

Recent research suggested that the sensitivity of D-dimer for AD decreases when patients presented with intramural haematoma or a thrombosed false lumen. D-dimer assay may show negative in patients with intramural haematoma.[19 25 26] Negative results of D-dimer test may be shown in young patients with short dissection length and a thrombosed false lumen without ulcer-like projection. D-dimer assay was prone to be positive in elderly patients because many older people have atherosclerosis which makes more D-dimers to be released into blood.[24 27] In our study, at the cut-off value of 5.67 μg/mL, D-dimer presented higher specificity but lower sensitivity, which may be caused by the formation of intramural haematoma, thrombosed false lumen or relatively younger age. As far as the older subjects in this study were concerned, elevated D-dimer levels were not simply due to AD, which could induce false-positive.

CRP, a sensitive and non-specific inflammatory biomarker, is mainly produced in the liver by the stimulation of various cytokines. Its plasma levels vary with inflammatory stages and are time-dependent. CRP has been recognised to be closely related to the occurrence and development of AD. CRP values were significantly higher in patients with complications of acute AD such as impaired oxygenation, pleural effusion, as well as in patients who died during hospitalisation.[4 23 28–31] CRP levels above 15 mg/L was an important indicator of impaired oxygenation and poor prognosis.[28] Schillinger *et al*[29] demonstrated the prognostic value of CRP as an independent predictor of poor prognosis in patients with acute AD. Higher CRP levels indicated higher mortality in AD. When the value of CRP was over 6.3 mg/L, short-term risk of death was significantly high.

This present study further confirmed the CRP value in predicting poor prognosis in acute AD, which is partly consistent with our previous study.[32] When CRP was ≥11.21 mg/L, the sensitivity in predicting inhospital death could reach 100%. CRP≥11.21 mg/L was an important risk factor for inhospital death in acute AD. When CRP was ≥15.12 mg/L, the specificity could reach 100% but with lower sensitivity. Furthermore, CRP levels had significant positive correlations with D-dimer levels. Therefore, increased CRP values in dead patients were also observed compared with those who survived. Moreover, combining use of both D-dimer and CRP assays could increase the specificity in assessing inhospital death up to 96.8%.

Therefore, as far as the prognostic value of D-dimer and CRP was concerned, we thought that D-dimer and CRP should be evaluated immediately after admission because of the high sensitivity demonstrated. When the plasma concentrations of either D-dimer or CRP were above the cut-offs which we have provided above, there would be a high risk of inhospital death. In the meanwhile, when both D-dimer and CRP were all above the cut-off levels, the risk of death was significantly increased and death may occur. These findings may guide clinicians implement appropriate treatment strategies in emergent setting for acute AD.

In addition, a relatively high mortality rate was reported to be associated with acute AD, and acute type A AD is a surgical emergency with a potentially higher mortality rate than type B AD.[1] Our data also indicated elevated mortality rate in type A compared with type B AD. Moreover, type A AD was an important risk factor for inhospital death in acute AD. However, we did not find a significant association of emergent surgical treatment and inhospital survival. This may be due to the fact that some patients have demonstrated severe complications before surgery and the relatively small sample size.

CONCLUSIONS

D-dimer ≥5.67 μg/mL, CRP ≥11.21 mg/L and type A acute AD were important risk factors and independently associated with acute AD inhospital death. These findings still need larger sample and prospective clinical studies to be further verified in order to contribute to prognostic assessment in acute AD.

Contributors DW contributed the concept, design, data analysis and writing. XD, J-ZD, X-LZ and C-SM reviewed this manuscript and approved the final version to be published.

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Competing interests None.

Patient consent Obtained.

Ethics approval This study was in agreement with the guidelines of the Ethics Committee of the hospital.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management: part I: from etiology to diagnostic strategies. *Circulation* 2003;108:628–35.
2 Hagan PG, Nienaber CA, Isselbacher EM, *et al*. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. *JAMA* 2000;283:897–903.
3 Spittell PC, Spittell JA Jr, Joyce JW, *et al*. Clinical features and differential diagnosis of aortic dissection: experience with 236 cases (1980 through 1990). *Mayo Clin Proc* 1993;68:642–51.
4 Eggebrecht H, Naber CK, Bruch C, *et al*. Value of plasma fibrin D-dimers for detection of acute aortic dissection. *J Am Coll Cardiol* 2004;44:804–9.
5 Weber T, Hogler S, Auer J, *et al*. D-dimer in acute aortic dissection. *Chest* 2003;123:1375–8.
6 Sbarouni E, Georgiadou P, Marathias A, *et al*. D-dimer and BNP levels in acute aortic dissection. *Int J Cardiol* 2007;122:170–2.
7 Akutsu K, Sato N, Yamamoto T, *et al*. A rapid bedside D-dimer assay (cardiac D-dimer) for screening of clinically suspected acute aortic dissection. *Circ J* 2005;69:397–403.
8 Weber T, Rammer M, Auer J, *et al*. Plasma concentrations of D-dimer predict mortality in acute type A AD. *Heart* 2006;92:836–7.
9 Sodeck G, Domanovits H, Schillinger M, *et al*. D-dimer in ruling out acute aortic dissection: a systematic review and prospective cohort study. *Eur Heart J* 2007;28:3067–75.
10 Sutherland A, Escano J, Coon TP. D-dimer as the sole screening test for acute aortic dissection: a review of the literature. *Ann Emerg Med* 2008;52:339–43.
11 Marill KA. Serum D-dimer is a sensitive test for the detection of acute aortic dissection: a pooled meta-analysis. *J Emerg Med* 2008;34:367–76.
12 Suzuki T, Distante A, Zizza A, *et al*. Diagnosis of acute aortic dissection by D-dimer: the International Registry of Acute Aortic Dissection Substudy on Biomarkers (IRAD-Bio) experience. *Circulation* 2009;119:2702–7.
13 Hazui H, Fukumoto H, Negoro N, *et al*. Simple and useful tests for discriminating between acute aortic dissection of the ascending aorta and acute myocardial infarction in the emergency setting. *Circ J* 2005;69:677–82.
14 De Paepe A, Devereux RB, Dietz HC, *et al*. Revised diagnostic criteria for the Marfan syndrome. *Am J Med Genet* 1996;62:417–26.
15 Shimony A, Filion KB, Mottillo S, *et al*. Meta-analysis of usefulness of d-dimer to diagnose acute aortic dissection. *Am J Cardiol* 2011;107:1227–34.
16 Correia LC, Noya-Rabelo M. The D-dimer approach for troponin in the diagnosis of myocardial infarction: is it really useful? *J Am Coll Cardiol* 2012;59:1570–1.
17 Goldhaber SZ, Bounameaux H. Pulmonary embolism and deep vein thrombosis. *Lancet* 2012;379:1835–46.
18 Tripodi A. D-dimer testing in laboratory practice. *Clin Chem* 2011;57:1256–62.
19 Tran TP, Khoynezhad A. Current management of type B aortic dissection. *Vasc Health Risk Manag* 2009;5:53–63.
20 Hatakeyama K, Asada Y, Marutsuka K, *et al*. Localization and activity of tissue factor in human aortic atherosclerotic lesions. *Atherosclerosis* 1997;133:213–19.
21 Ohlmann P, Faure A, Morel O, *et al*. Diagnostic and prognostic value of circulating D-Dimers in patients with acute aortic dissection. *Crit Care Med* 2006;34:1358–64.
22 Iyano K, Kawada T, Aiba M, *et al*. Correlation of hemostatic molecular markers and morphology of the residual false lumen in chronic aortic dissection. *Ann Thorac Cardiovasc Surg* 2004;10:106–12.
23 Sugano Y, Anzai T, Yoshikawa T, *et al*. Serum C-reactive protein elevation predicts poor clinical outcome in patients with distal type acute aortic disection: association with the occurrence of oxygenation impairment. *Int J Cardiol* 2005;102:39–45.

24 Paparella D, Malvindi PG, Scrascia G, *et al*. D-dimers are not always elevated in patients with acute aortic dissection. *J Cardiovasc Med (Hagerstown)* 2009;10:212–14.
25 Evangelista A, Mukherjee D, Mehta RH, *et al*. Acute intramural hematoma of the aorta: a mystery in evolution. *Circulation* 2005;111:1063–70.
26 Ohlmann P, Faure A, Morel O, *et al*. Lower circulating Sta-Liatest D-Di levels in patients with aortic intramural hematoma compared with classical aortic dissection. *Crit Care Med* 2009;37:899–901.
27 Hazui H, Nishimoto M, Hoshiga M, *et al*. Young adult patients with short dissection length and thrombosed false lumen without ulcer-like projections are liable to have false-negative results of D-dimer testing for acute aortic dissection based on a study of 113 cases. *Circ J* 2006;70:1598–601.
28 Sakakura K, Kubo N, Ako J, *et al*. Peak C-reactive protein level predicts long-term outcomes in type B acute aortic dissection. *Hypertension* 2010;55:422–9.
29 Schillinger M, Domanovits H, Bayegan K, *et al*. C-reactive protein and mortality in patients with acute aortic disease. *Intensive Care Med* 2002;28:740–5.
30 Komukai K, Shibata T, Mochizuki S. C-reactive protein is related to impaired oxygenation in patients with acute aortic dissection. *Int Heart J* 2005;46:795–9.
31 Kin H, Kawazoe K, Nakajima T, *et al*. Perioperative serum procalcitonin concentrations in patients with acute aortic dissection. *Eur Surg Res* 2003;35:451–4.
32 Wen D, Wu HY, Jiang XJ, *et al*. Role of plasma C-reactive protein and white blood cell count in predicting in-hospital clinical events of acute type A aortic dissection. *Chin Med J (Engl)* 2011;124:2678–82.

Value of D-dimer and C reactive protein in predicting inhospital death in acute aortic dissection

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