



86

## Value of D-Dimers in patients with acute aortic dissection

Chuncaai Xue<sup>a,\*</sup>, Yigang Li<sup>b</sup><sup>a</sup>Department of Cardiology, the People's Hospital of Binzhou, Binzhou 256610, China;<sup>b</sup>Department of Cardiology, Xinhua hospital, Shanghai JiaoTong university, Shanghai 200092, China.

Received 6 November 2006

### Abstract

**Objective:** To evaluate the value of D-dimers in patients with acute aortic dissection (AAD). **Methods:** This study consisted of 16 patients with AAD and 27 non-AAD patients. Serum D-dimers were measured by Sta-Liatest D-DI immunoturbidimetric assay. **Results:** D-dimer level was higher ( $P < 0.001$ ) in patients with AAD ( $7.91 \pm 5.52 \mu\text{g/ml}$ ) than that in non-AAD group ( $1.57 \pm 1.24 \mu\text{g/ml}$ ). D-dimer was positive ( $>0.4 \mu\text{g/ml}$ ) in all patients with AAD and in 10 control group patients (37%). Among patients with acute AAD, D-dimers tended to be higher in Stanford A than in Stanford B ( $8.67 \pm 4.31 \mu\text{g/ml}$  vs.  $3.24 \pm 1.27 \mu\text{g/ml}$ ,  $P < 0.01$ ). D-dimer values tended to be higher in more extended disease ( $3.84 \pm 1.65 \mu\text{g/ml}$ ,  $8.57 \pm 3.58 \mu\text{g/ml}$  and  $11.87 \pm 5.69 \mu\text{g/ml}$  in thoracic aorta, thoracic and abdominal aorta, thoracic and abdominal aorta and iliacal arteries, respectively,  $P < 0.05$  for both  $8.57 \pm 3.58$  and  $11.87 \pm 5.69$  vs.  $3.84 \pm 1.65$ ). Including the control group into the analysis, we found a sensitivity of 100%, a negative predictive value of 100%, and a specificity of 66% and a positive predictive value of 64% for D-dimer in diagnosis of AAD in our patients with suspected AAD. **Conclusion:** D-dimer was elevated in patients with AAD. A negative D-dimer test result could be useful in excluding AAD.

**Keywords:** D-dimer; aorta; dissection; coagulation

### INTRODUCTION

Acute aortic dissection (AAD) is a life-threatening disease with a high mortality rate of 1–2% per hour, early after symptom onset.<sup>[1]</sup> In suspected cases, diagnostic speed is of utmost importance. Available noninvasive bedside tests in the emergency department, including physical examination, ECG, chest radiograph, and transthoracic echocardiography can provide important clues to the diagnosis in some patients, but they usually are not sufficient to rule out the disease. More accurate tests are semi-invasive (e.g., transesophageal echocardiography) or time-consuming and not available at bedside (e.g., CT scanning, MRI, and angiography). Until now, blood testing has played only a minor role in diagnosing acute aortic dissection. In this study, we evaluated the value of D-dimers in patients with AAD.

### MATERIALS AND METHODS

#### Patients

Between March 2002 and April 2006, we recruited 43 consecutive chest pain patients in whom AAD was suspected or not ruled out. These patients were admitted to our emergency department or CCU within 48 h from onset of symptoms.

Diagnosis of AAD was confirmed using the recommended criteria by imaging technique (TEE, CT, and MRI)<sup>[2]</sup>. The patients were divided into an AAD group (n=16) and non-AAD group (n=27) served as control group. The final diagnosis in non-AAD patients was non-ST-elevation myocardial infarction in 8 cases (30%), ST-elevation myocardial infarction in 6 cases (22%), pericarditis in 4 (15%), esophageal/gastric disease in 4 (15%), pulmonary embolism (PE) in 2 (7%), neuroradicular pain in 2 (7%), and musculoskeletal pain in 1 (4%).

#### D-Dimer Test

\*Corresponding author.

E-mail address: [xuehc@yahoo.com.cn](mailto:xuehc@yahoo.com.cn).

D-Dimer level was measured in all patients and control group using quantitative Sta-Liatest D-DI immunoturbidimetric assay (Diagnostica Stago, France) that measured the changes in absorbance at 540 nm of a microlatex suspension coated covalently with two complementary monoclonal antibodies, specific for fibrin degradation products. The range of detection of the assay was 0.22-20  $\mu\text{g/ml}$ . The cutoff value was 0.4 $\mu\text{g/ml}$  with results above this threshold reported as positive.

### Statistical analysis

Data was expressed as numbers, percentages, mean  $\pm$ SD. Differences between-groups were analyzed by *t* test.

## RESULTS

Sixteen patients (9 man and 7 woman) were diagnosed as AAD using standard criteria<sup>[2]</sup>, with a mean age of  $58 \pm 17$  years (ranged from 35-78 years). Comorbid conditions for 16 AAD patients were as follows: hypertension, 13(81%) patients; coronary heart disease, 4(25%) patients; smoking, 5(31%) patients; diabetes mellitus, 2(12.5%) patients. Dissection types, management and clinical outcomes were shown in *Tab 1*.

**Tab 1 Dissection type, management and in-Hospital outcome**

	Type	Number. (%)
Stanford classification	Type A	7(44)
	Type B	9(56)
Extent of dissection	Thoracic aorta	5(31)
	Thoracic and abdominal aorta	4(25)
	Thoracic and abdominal aorta and iliacal arteries	7(44)
Therapy	Stents	3(19)
	Operations	2(13)
	Conservative	11(69)
In-Hospital Outcome	Discharged	9(56)
	Died	7(44)

D-dimer level was higher ( $P < 0.001$ ) in patients with AAD ( $7.91 \pm 5.52 \mu\text{g/ml}$ ) than that in non-AAD group ( $1.57 \pm 1.24 \mu\text{g/ml}$ ). D-dimer was positive ( $> 0.4 \mu\text{g/ml}$ ) in all patients with AAD and in 10 control group patients (37%). Among patients with AAD, D-dimers tended to be higher in Stanford A than in Stanford B ( $8.67 \pm 4.31 \mu\text{g/ml}$  vs.  $3.24 \pm 1.27 \mu\text{g/ml}$ ,  $P < 0.01$ ). D-dimer values tended to be higher in more extended diseases ( $3.84 \pm 1.65 \mu\text{g/ml}$ ,  $8.57 \pm 3.58 \mu\text{g/ml}$  and  $11.87 \pm 5.69 \mu\text{g/ml}$  in thoracic aorta, thoracic and abdominal aorta, thoracic and abdominal aorta and iliacal arteries, re-

spectively,  $P < 0.05$  for both  $8.57 \pm 3.58$  and  $11.87 \pm 5.69$  vs.  $3.84 \pm 1.65$ ). The mean value of D-dimer in different groups was shown in *Tab 2*.

**Tab 2 The mean values of D-dimer in different groups**

different groups	mean value of D-dimer ( $\mu\text{g/ml}$ )
AAD	$7.91 \pm 5.52$
Stanford A	$8.67 \pm 4.31$
Stanford B	$3.24 \pm 1.27$
Different extended AAD	
thoracic aorta	$3.84 \pm 1.65$
thoracic and abdominal aorta	$8.57 \pm 3.58$
thoracic, abdominal aorta and iliacal arteries	$11.87 \pm 5.69$
non-AAD	$1.57 \pm 1.24$

Including control group, we found a sensitivity of 100%, a negative predictive value of 100%, a specificity of 66% and a positive predictive value of 64% for D-dimer in diagnosis of AAD in our patients with suspected AAD.

## DISCUSSION

Acute aortic dissection (AAD) is a life-threatening illness and should be diagnosed as soon as possible. Evaluation of AAD is based on clinical presentation but mainly relies on imaging techniques. So far, there is no laboratory test as opposed to acute coronary syndrome to aid the diagnosis. Determination of smooth muscle myosin heavy chains or soluble elastin fragments has been shown to detect AAD with high sensitivity and specificity<sup>[3, 4]</sup>, but these tests are not widely used today.

Recently, elevations of circulating D-dimers have been reported in patients with aortic dissection, suggesting that D-dimer may be a biomarker of this disease<sup>[5-8]</sup>. Weber *et al*<sup>[5]</sup> reported on 24 patients with AAD in whom D-dimer was tested as a part of initial diagnostic strategy. They found that all patients with AAD had elevated levels of D-dimer. In contrast, only 31% of control group patients who had chest pain of other origin had increased D-dimer concentrations. They concluded that D-dimer test was a useful tool in the diagnostic strategy of suspected acute aortic dissection. Ohlmann *et al*<sup>[8]</sup> studied 94 consecutive patients with confirmed AAD and 94 controls presenting with clinical suspicion of dissection, they found that D-Dimers were elevated in patients with AAD and provided valuable diagnostic and prognostic information. D-Dimer might be a useful complementary tool to the current diagnostic work-up of patients with suspected AAD.

Our data showed that D-dimer measurement had a

high sensitivity and a low specificity in diagnosing AAD. D-dimer was influenced by the anatomical extension and by the type of the dissection. In our study, D-dimer values tended to be higher in more extended diseases and were higher in Stanford A than in Stanford B. In patients with chest pain and elevated D-dimer, AAD should be taken into account.

D-dimer is a typical degradation product of crosslinked fibrin. Elevation of D-dimer is due to activation of the extrinsic pathway of the coagulation cascade at the site of vessel (aortic) wall injury by tissue factor [5]. Elevated D-dimer values reflect a profound fibrinolytic activity. The role of D-dimer in patients with suspected DDA is similar to its role in pulmonary embolism and deep vein thrombosis. It shows very high sensitivity and low specificity for deep vein thrombosis and/or pulmonary embolism [9]. D-dimer also has been used in other clinical conditions with ongoing fibrinolysis such as acute coronary syndrome [10,11], malignancy [12], burn [13], liver cirrhosis [14] and aortic aneurysm [15]. Our data showed that D-dimer was elevated in patients with AAD and a negative D-dimer test result could be useful in excluding AAD. Larger, prospective multicenter studies are needed to elucidate the value of D-dimers in the screening of patients with chest pain and suspected AAD.

## References

- [1] Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, Evangelista A, Fattori R, Suzuki T, Oh JK, Moore AG, Malouf JF, Pape LA, Gaca C, Sechtem U, Lenferink S, Deutsch HJ, Diedrichs H, Marcos y Robles J, Llovet A, Gilon D, Das SK, Armstrong WF, Deeb GM, Eagle KA. The International Registry of Acute Aortic Dissection (IRAD): New insights into an old disease. *JAMA* 2000; 283: 897-903
- [2] Erbel R, Alfonso F, Boileau C, Dirsch O, Eber B, Haverich A, Rakowski H, Struyven J, Radegran K, Sechtem U, Taylor J, Zollikofer C, Klein WW, Mulder B, Providencia LA. Diagnosis and management of aortic dissection. *Eur Heart J* 2001; 22:1642-81
- [3] Suzuki T, Katoh H, Tsuchio Y, Hasegawa A, Kurabayashi M, Ohira A, Hiramori K, Sakomura Y, Kasanuki H, Hori S, Aikawa N, Abe S, Tei C, Nakagawa Y, Nobuyoshi M, Misu K, Sumiyoshi T, Nagai R. Diagnostic implications of elevated levels of smooth-muscle myosin heavy-chain protein in acute aortic dissection: the smooth muscle myosin heavy chain study. *Ann Intern Med* 2000;133:537-41.
- [4] Shinohara T, Suzuki K, Okada M, Shiigai, M. Shimizu, T. Maehara, and F. Ohsuz.. Soluble elastin fragments in serum are elevated in acute aortic dissection. *Arterioscler Thromb Vasc Biol* 2003;23:1839-44.
- [5] Weber T, Hogler S, Auer J, Berent, R., Lassnig, E., Kvas, E., Eber, B. D-dimer in acute aortic dissection. *Chest* 2003; 123:1375-78
- [6] Perez A, Abbet P, Drescher MJ. D-dimers in the emergency department evaluation of aortic dissection. *Acad Emerg Med* 2004; 11:397-400
- [7] Eggebrecht H, Naber CK, Bruch C, Kroger K, von Birgelen C, Schmermund A, Wichert M, Bartel T, Mann K, Erbel R. Value of plasma fibrin D-dimers for detection Acad Emerg Med of acute aortic dissection. *J Am Coll Cardiol* 2004; 44:804-9
- [8] Ohlmann P, Faure A, Morel O, Petit H, Kabbaj H, Meyer N, Cheneau E, Jesel. Diagnostic and Prognostic Value of Circulating D-Dimers in Patients With Acute Aortic Dissection. *Crit Care Med* 2006;34:1358-64.
- [9] Brown MD, Rowe BH, Reeves MJ, Bermingham JM, Goldhaber SZ. The accuracy of the enzyme-linked immunosorbent assay D-dimer test in the diagnosis of pulmonary embolism: A meta-analysis. *Ann Emerg Med* 2002; 40:133-144
- [10] Ridker PM, Hennekens CH, Cerskus A, Stampfer MJ. Plasma concentration of cross-linked fibrin degeneration product (D-dimer) and the risk of future myocardial infarction among apparently healthy men. *Circulation* 1994; 90: 2236-40.
- [11] Bayes-Genis A, Mateo J, Santalo M, Oliver A, Guindo J, Badimon L, Martinez-Rubio A, Fontcuberta J, Schwartz RS, De Luna AB. D-dimer is an early diagnostic marker of coronary ischemia in patients with chest pain. *Am Heart J* 2000; 140: 379-384.
- [12] Beer JH, Haeberli A, Vogt A, Woodtli K, Henkel E, Furrer Th, Fey MF. Coagulation markers predict survival in cancer patients. *Thromb Haemost* 2002; 88: 745-749.
- [13] Garcia-Avello A, Lorente JA, Cesar-Perez J, Garcia-Frade LJ, Alvarado R, Arevalo JM, Navarro JL, Esteban A. Degree of hypercoagulability and hyperfibrinolysis is related to organ failure and prognosis after burn trauma. *Thromb Res* 1998; 89: 59-64.
- [14] Violi F, Ferro D, Basili S, Quintarelli C, Musca, A Cordova C, Balsano F. Hyperfibrinolysis resulting from clotting activation in patients with different degree of cirrhosis. *Hepatology* 1993; 17: 78-83.
- [15] Yamazumi K, Ojio M, Okumura H, Aikou T. An activated state of blood coagulation and fibrinolysis in patients with abdominal aortic aneurysm. *Am J Surg* 1998; 175: 297-301.