

Levels of Serum D-Dimer among Patients with Aortic Intramural Haematoma

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ABSTRACT

Objective: The aim of this study was to evaluate whether there was a difference of serum D-dimer between patients with aortic intramural haematoma and patients with classic acute aortic dissection.

Methods: According to results of computed tomographic angiography, all the patients, who had an established diagnosis of acute aortic syndrome in the past four years in an affiliated hospital, were retrospectively classified into two groups: classic acute aortic dissection (AAD) group and aortic intramural haematoma (AIH) group. The serum D-dimer concentrations at admission and other clinical baseline characteristics between the two groups were compared. Furthermore, the occurrence of the main clinical complications was compared between the two groups. Fifty-one subjects were included. Thirty-eight patients (74.5%) were in the AAD group and thirteen (25.5%) in the AIH group.

Results: D-dimer levels were significantly higher in AAD group (3.50 ± 1.72 mg/mL) than in AIH group (1.54 ± 1.50 mg/mL, $p < 0.05$). All patients with AAD had D-dimer levels above the threshold of 0.50 ng/mL (sensitivity 100%). However, two patients in the AIH group presented with D-dimer levels below the threshold. The sensitivity of the D-dimer test in detecting AIH was 84.6% (11/13). But there was no significant difference in sensitivity between the two groups ($p > 0.05$). The main clinical complication rate was 39.5% (15/38) in the AAD group and 30.8% (4/13) in the AIH group ($p > 0.05$).

Conclusion: D-dimer levels are lower in patients with AIH than those in patients with AAD. Although it shows no difference of sensitivity between AAD and AIH, D-dimer can be negative in AAD patients. Moreover, patients with AIH have a similar clinical evolution during hospitalization compared to patients with AAD.

Keywords: Acute aortic syndrome, D-dimer

Niveles de Dímero-D Plasmático en Pacientes con Hematoma Intramural Aórtico

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RESUMEN

Objetivo: El objetivo de este estudio fue evaluar si existe diferencia de dímero-D plasmático entre pacientes con hematoma intramural aórtico y pacientes con disección aórtica aguda clásica.

Métodos: Según los resultados de la angiografía tomográfica computarizada, todos los pacientes, que tenían un diagnóstico establecido de síndrome aórtico agudo en los últimos cuatro años en un hospital afiliado, fueron clasificados retrospectivamente en dos grupos: Grupo de disección aórtica aguda (DAA) clásica y el hematoma intramural aórtico (HIA). Se compararon las concentraciones séricas del dímero-D a la hora de la admisión y otras características clínicas de base entre los dos grupos. Además, se comparó la aparición de complicaciones clínicas principales entre ambos grupos. Se incluyeron cincuenta y un sujetos. En el grupo DAA había treinta y ocho pacientes (74.5%) y en el grupo HIA había trece (25.5%).

Resultados: El dímero-D fue significativamente mayor en el grupo DAA (3.50 ± 1.72 mg/mL) que en el grupo HIA (1.54 ± 1.50 mg/mL, $p < 0.05$). Todos los pacientes con DAA tenían niveles de dímero-D por encima del umbral de 0.50 ng/mL (100% sensibilidad). Sin embargo, dos pacientes en el grupo HIA presentaron niveles de dímero-D por debajo del umbral. La sensibilidad de la prueba de dímero D en la de-

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tección de HIA fue de 84.6% (11/13). Pero no hubo ninguna diferencia significativa en la sensibilidad entre los dos grupos ($p > 0.05$). La tasa de complicación clínica principal fue 39.5% (15/38) en el grupo DAA y 30.8% (4/13) en el grupo de HIA ($p > 0.05$).

Conclusión: El dímero-D es inferior en los pacientes con HIA, comparado con los pacientes de DAA. Aunque no se muestra ninguna diferencia de sensibilidad entre DAA y HIA, el dímero-D puede ser negativo en los pacientes de DAA. Por otra parte, los pacientes con HIA tienen una evolución clínica similar durante la hospitalización en comparación con los pacientes con DAA.

Palabras claves: Síndrome aórtico agudo, dímero-D

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INTRODUCTION

Both acute intramural haematoma (AIH) and acute aortic dissection (AAD) belong to the acute aortic syndrome (AAS). However, a recent study has revealed that pathogenesis, clinical manifestation, evolution and prognosis of these two diseases can differ from each other dramatically (1).

To improve survival rate and reduce the occurrence of complications, it is extremely important to establish diagnosis at admission and treat the patients appropriately during hospitalization. Therefore, a convenient and quick screening method for either AIH or AAD is valuable in clinical practice. D-dimer, which is a sensitive index for intravascular thrombosis, was firstly used to detect acute pulmonary embolism. With thrombus newly formed in the false lumen, patients with AAD also have significantly elevated levels of D-dimer. Moreover, D-dimer has a high sensitivity but a relatively low specificity in diagnosing AAD (2). However, there is no report so far about the value of D-dimer in diagnosing AIH among an Asian population. Thus, D-dimer levels between patients with AAD and AIH was compared retrospectively to determine whether there is a difference in serum D-dimer between patients with AIH and those with AAD.

SUBJECTS AND METHODS

From April 2004 to May 2009, the diagnosis of either AAD or AIH was confirmed in 51 patients using the standard criteria of computed tomography angiography. Meanwhile, D-dimer concentrations were determined at the patient's presentation to hospital. According to the extent of the enhanced CT signal in the false lumen, patients were divided into AAD group and AIH group, retrospectively. D-dimer levels between the two groups were compared. This study was conducted in accordance with the Declaration of Helsinki. This study was conducted with approval from the Ethics Committee of the Affiliated Hospital of Yangtze University. Written informed consent was obtained from all participants.

The serum D-dimer was performed (Tina-quant assay; Roche Diagnostics; Mannheim, Germany) with the aid of an automated chemical analysis system (model 704; Hitachi, Tokyo, Japan). This test uses a latex-bound monoclonal antibody that is specific to D-dimer. The reaction is followed at an assay temperature of 37 °C via the increase in turbidity at a wavelength ranging from 700 to 950 nm. The result is avail-

able in 15 to 30 minutes. The results were obtained within one hour. Below a cutoff value of 0.5 mg/mL. Major clinical complications were: stroke during hospital, acute renal failure, acute myocardial infarction, acute aortic valve insufficiency and paralysis.

Statistical analysis

Data are presented as percentages and mean \pm SD. Counting data were compared by Chi-squared test. Quantitative data were compared by means of Student's unpaired *t*-test. A value of $p < 0.05$ was considered to be significant.

RESULTS

Baseline characteristics

Clinical characteristics of both groups are shown in Table 1. Only bodyweight showed significant difference between the AIH and AAD groups ($p < 0.05$). There were no significant differences between the two groups in age; gender, occurrence of hypertension, diabetes mellitus, smoking, concomitance of coronary heart disease, stroke and aortic valve disease.

Table 1: Comparison of baseline characteristics between the acute intramural haematoma and acute aortic dissection Group 2

	AAD group (n = 38)	AIH group (n = 13)
Age (y)	53.6 \pm 9.7	58.9 \pm 14.6
Weight(Kg)	82.4 \pm 19.3	70.4 \pm 13.3*
Male (%)	29 (76.3%)	8 (61.5%)
History of hypertension (%)	32 (84.2%)	10 (76.9%)
Smoking history (%)	27 (71.1%)	8 (61.5%)
Diabetes (%)	6 (15.8%)	4 (30.8%)
History of coronary heart disease (%)	8 (21.1%)	5 (38.5%)
History of stroke (%)	2 (5.3%)	1 (7.7%)
Aortic valve disease (%)	1 (2.6%)	0 (0%)
Oral warfarin (%)	0 (%)	1 (7.7%)

*Compared to AAD group, $p < 0.05$

Clinical manifestations

Physical activity was the most common incentive between both AAD group and AIH group. In such clinical presentations as abruptness, severity of pain and localization of pain, no significant differences were found between the two groups ($p > 0.05$). Furthermore, there were no significant differences be-

tween the two groups in hypertension, asymmetry of blood pressure among limbs, abnormal auscultation of aortic valve and shock [$p > 0.05$] (Table 2).

Table 2: Two groups of patients with clinical performance on comparison

	AAD group (n = 38)	AIH group (n = 13)
Symptoms		
Duration (h)	2.7 ± 2.0	3.7 ± 2.8
Onset during activity	34 (89.5%)	9 (69.2%)
Abruptness	32 (84.2%)	8 (61.5%)
Pain severity	32 (84.2%)	10 (76.9%)
Chest pain	15 (39.5%)	7 (53.8%)
Backache	4 (10.5%)	0 (0%)
Stomachache	35 (92.1%)	10 (76.9%)
Signs		
Hypertension	19 (50.0%)	6 (46.2%)
Asymmetry of pressure among limbs	7 (18.4%)	2 (15.3%)
Auscultation abnormalities of aortic valve	4 (10.5%)	1 (7.7%)
Shock	13 (34.2%)	3 (23.1%)

* Compared with AAD group, $p < 0.05$.

D-Dimer level

The D-Dimer concentration of the AAD group and AIH group were 3.50 ± 1.72 mg/mL and 1.54 ± 1.50 mg/mL at admission to hospital, respectively ($p < 0.05$). Taking the > 0.50 mg/mL as a cutoff, the sensitivity of D-Dimer in the AAD group is 100% (38/38). Yet that of the AIH group was 84.6% (11/13).

Classification and treatment

The difference of Stanford classifications between AAD group and AIH group was insignificant ($p > 0.05$). The maximum aortic diameter measured in the computed tomography angiography (CTA) scan of the AAD group was significantly greater than that of the AIH group [$p < 0.05$] (Table 3). Most patients of these two groups underwent conservative therapy because of non-medical reasons and no significant differences were found ($p > 0.05$).

Table 3: Comparison of the Stanford classification, aortic diameter and treatment in the two groups

	AAD group (n = 38)	AIH group (n = 9)
Stanford classification		
A type (%)	25 (65.8%)	6 (46.2%)
B type (%)	13 (34.2%)	7 (53.8%)
Max aortic diameter (mm)	46.0 ± 10.2	42.1 ± 9.0*
Treatments		
Conservative treatment (%)	29 (76.3%)	10 (76.9%)
Stent-graft implantation (%)	5 (13.1%)	2 (15.4%)
Surgical procedures (%)	4 (10.5%)	1 (7.7%)

* Compared to AAD group, $p < 0.05$

Clinical outcome

The incidence rate of clinical complications of the AAD group was 39.5% (15/38) and that of the AIH group was 30.8% [4/13] ($p > 0.05$). Mortality during hospitalization of the AAD group

was 18.4% (7/38) and of the AIH group was 11.1% [1/13] ($p > 0.05$).

DISCUSSION

The patients with acute aortic syndrome usually have acute pain arising from aortic disease, including AAD, AIH, penetrating aortic ulcer and unstable thoracic aortic aneurysms (3). Although AIH has attracted increasing attention recently, its clinical knowledge on it remains limited, especially in terms of a quick diagnostic method (4–6).

The value of D-dimer has been established in the diagnosis of AAD. With a cutoff value of 0.5 mg/mL, the sensibility of D-dimer could reach nearly 100% (7). Other studies proved that the degree of D-dimer elevation and the range of dissection were positively correlated (8, 9). They found that the D-dimer concentrations reflected the anatomical extent of aortic dissection. Furthermore, prior research suggested that the diagnostic significance of D-dimer, in patients with AAD among whom there was no direct blood flow connection between the true lumen and false lumen is relatively limited (10). However, the diagnostic value of D-dimer in patients with AIH has not been fully elucidated.

In this study, with a cutoff value of 0.5 mg/mL, the D-dimer sensitivity in the AIH group showed no significant difference when compared to that in the AAD group. Nevertheless, D-dimer level in patients with AIH is significantly lower than in patients with AAD. The main underlying reasons may be that there is no interlink between the false lumen and true lumen. Thus, D-dimer and other fibrin degradation products have no pathway to get into the blood circulation.

The present study showed that the AIH group accounted for about 20% of all patients with acute aortic syndrome. The proportion is similar to those of former reports (1, 11). From an aetiological aspect, AIH may be associated with the rupture of the nutrient artery of the aortic wall. Acute aortic dissection is related to atherosclerotic plaque rupture that allows high-pressure blood flow to penetrate the intima and get into the medium. The bodyweight of patients in the AAD group was significantly higher than that of the AIH group in our study, but its diagnostic importance and clinical value remains unclear. Prior study has reported that the occurrence of AIH was related to anticoagulation therapy (12). Only one patient of the AIH group in our study had oral warfarin therapy because of chronic atrial fibrillation and recurrent cerebral embolism. The international normalized ratio (INR) was 2.96 when the patient was admitted, which suggested that the anticoagulant therapy might be associated with the occurrence of AIH. Large-scale clinical studies will be needed to clarify the relationship between anticoagulation and AIH.

Patients with AIH and AAD had similar clinical symptoms, of which abrupt severe chest and back-pain was most common. It is remarkable that in both the AAD and AIH group, the onset of pain was associated with the beginning of some physical movements, such as: breath holding, coughing,

changing of posture and trying to have a bowel movement. These differ from the physical exertion triggering angina pectoris, which is usually caused by longer periods of physical exercise and a threshold needs to be reached before the appearance of chest pain. The severity of angina pectoris has the characteristics of crescendo, while the pain of AIH and AAD reaches climax at the moment of onset (13).

The diagnosis of AIH also relies on CT angiography. Without contrast media entering, the intramural haematoma usually showed as thickening of the wall of the aorta. Moreover, AIH has no pseudomembrane and no communication between the true and false lumen. Yet, the most important difference between AIH and AAD is that the false lumen would not be acentrated by contrast medium after intravenous injection of contrast agents (14, 15). Another imaging characteristic of AIH is relatively limited implicated range of aorta. Some research have shown that most of AIH are Stanford B Type. Yet the majority of AAD are Stanford A Type (1). In the present research, 53.8% of AIH patients belonged to Stanford B while only 34.2% of AAD belonged to Stanford B. Furthermore, the maximal aortic diameter of AIH is smaller than that of AAD, which may be associated with the lower pressure in the false lumen.

There has been no guideline for the management of AIH. Some researchers recommended medication therapy, especially for Type B AIH. For Type A AIH with limited range, conservative treatment is also adopted (16). But other experts such as von Kodolitsch considered that emergent surgery was mandatory if the ascending aorta was involved, no matter how large the diameter is and no matter whether there is unstable lesion or not. Type A AIH might compromise both the aortic valve and the coronary artery, therefore, early surgical procedure should be considered (17, 18). In the present study, we found that the main clinical complications and death rates are similar in patients with AAD and AIH, which suggested that even though the AIH haematoma has a self-limited tendency. More attention should be paid to AIH patients, especially among patients with Type A AIH.

There was a report that AIH might derive into AAD. For example, a young woman who suffered from type B AIH turned into Type A AAD after three months of conservative therapy (19). Another patient with Type B AIH receiving medication therapy complained of recurrent chest-pain. The CTA implied that prior haematoma had been absorbed; yet there were another two neo-penetrating ulcers in the aortic wall (20). The mechanism can be that the structure and tenacity of the aortic wall was changed permanently even though the haematoma had been absorbed completely after the AIH, it cannot bear the pressure of the aortic, and then the infiltrating inflammatory cells will further reduce the strength of the aorta wall, eventually leading to lesion progress.

CONCLUSION

In conclusion, we consider that although the plasma D-Dimer concentration of the aortic wall haematoma patients is lower

than the Sandwich separation patients, we find that they are not so different with 0.5 $\mu\text{g/mL}$ for threshold. However, we note that we could misdiagnose because the AIH patients may be in a negative reaction, and what's more, the clinical outcome between the AIH patients is similar to AAD, so we should pay greater attentions to it.

AUTHORS' NOTE

The authors declare no conflict of interest.

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