Can D-dimer testing help emergency department physicians to detect acute aortic dissections?

D-dimer testi akut aort disseksiyonlarını belirlemede acil servis hekimlerine yardımcı olabilir mi?

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ABSTRACT

Objective: To determine the diagnostic accuracy of D-dimer testing for detection of acute aortic dissection.
Methods: This study is a retrospective chart review of patients who had been evaluated with suspicion of acute aortic dissection. All patients' D-dimer levels were determined prior to their further work up in the emergency department. The study was conducted in a tertiary care center between February 2006-August 2008. The D-dimer assay used was the immunoturbidimetric assay, with a normal range up to 0.246 µg/ml. Statistical analysis was accomplished using Chi-square test, Student's t-test and a receiver-operating characteristics (ROC) curve analysis.
Results: Ninety-nine patients were included in the study, 30 patients were diagnosed as having acute aortic dissection and 69 patients were evaluated in non-acute aortic dissection group. In comparison of the two groups, positive D-dimer results were found to be significantly higher in acute aortic dissection group than in non-acute aortic dissection group ($p<0.001$). Sensitivity of the D-dimer test in detection of acute aortic dissection was found as 96.6% and the negative predictive value of the test was 97.3%. Specificity and positive predictive value of the D-dimer test were 52.2% and 46.8%, respectively. The area under the ROC curve yielded an acceptable certainty for excluding acute aortic dissection on base of negative results (AUC: 0.764; CI 95%: 0.674-0.855; $p<0.001$).
Conclusion: D-dimer testing is helpful for emergency physicians in detection of patients with suspected acute aortic dissection in the emergency department. *(Anadolu Kardiyol Derg 2010; 10: 434-9)*
Key words: Acute aortic dissection, D-dimer, fibrin degradation products, emergency department, diagnostic value of tests

ÖZET

Amaç: D-dimer testinin akut aort disseksiyonunu belirlemede tanısal değerini saptamak.
Yöntemler: Bu çalışma retrospektif bir çalışmadır. Acil serviste akut aort disseksiyonu şüphesi mevcut olan ve ileri tetkik öncesi D-dimer testi istenen hastalar çalışmaya dâhil edilmiştir. 3. basamak bir sağlık kuruluşunda gerçekleştirilen çalışmada, Şubat 2006-Ağustos 2008 tarihleri arasındaki kayıtlar incelenmiştir. Kullanılan D-dimer ölçüm yöntemi immunoturbidimetrik yöntemdir ve 0.246 µg/ml'ye kadar olan sonuçlar normal olarak kabul edilmiştir. İstatistiksel analizde Ki-kare testi, Student's t-testi kullanılmış, ayrıca ROC eğrisi analizi yapılmıştır.
Bulgular: Çalışmaya 30 akut aort disseksiyonu mevcut, 69 akut aort disseksiyonu mevcut olmayan kontrol grubu olmak üzere 99 hasta dâhil edilmiştir. Bu iki gruba ait D-dimer ölçümlerinin karşılaştırılmasında akut aort disseksiyonu olan hastaların olmayanlara göre istatistiksel anlamlı olarak daha fazla pozitif sonucunun olduğu görülmüştür ($p<0.001$). Akut aort disseksiyonunu saptamada D-dimer testinin duyarlılığı %96.6 özgünlüğü %52.2 negatif prediktif değeri %97.3 pozitif prediktif değeri ise %46.8 olarak bulunmuştur. ROC analizi sonucunda eğri altında kalan (AUC) değeri 0.764 (CI %95: 0.674-0.855) ve $p<0.001$) olarak saptanmıştır.
Sonuç: D-dimer testinin acil serviste akut aort disseksiyonu şüphesi olan hastalarda akut disseksiyonun saptanması için kullanımı faydalıdır. *(Anadolu Kardiyol Derg 2010; 10: 434-9)*
Anahtar kelimeler: Akut aort disseksiyonu, D-dimer, fibrin yıkım ürünleri, acil servis, testlerin tanısal değeri

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This work was presented at the 5th Mediterranean Emergency Medicine Congress, 14-17 September, 2009, Valencia, Spain
Accepted/Kabul Tarihi: 05.05.2010

doi:10.5152/akd.2010.142

Introduction

Acute aortic dissection (AAD) is a relatively uncommon but severe disease with a high mortality rate increasing gradually hour by hour after onset of the symptoms (1, 2).

It is a challenge for the emergency physicians (EP) to diagnose AAD because of overwhelming and occult symptoms of the disease. The clinical criteria for the diagnosis of AAD is not clearly defined, this further leads to complication of the diagnosis. Because AAD is a highly lethal disorder, diagnostic testing should be performed in any patient for whom AAD is suspected, even when the probability is believed to be low (3). Contrast enhanced computed tomography (CT) is the current choice of diagnostic test for AAD, however it is costly and may result in contrast material related problems in some patients.

There is no gold standard simple laboratory test method to exclude or diagnose aortic catastrophes identified in clinical practice. Therefore EP's need a screening test to identify patients with suspected AAD, before considering to perform advanced imaging studies.

D-dimer is a typical degradation product of cross-linked fibrin, which is considered as the best available laboratory marker of coagulation activation, and levels have been found to correlate with the extent of thrombosis (4-6).

In the last years, many trials showing that D-dimer testing can be used to exclude aortic dissection safely were reported (6-19). In numerous studies, in which different techniques and cut-off levels have been used, the sensitivity of D-dimer test in diagnosis of aortic dissection were found between 88-100% (6-19). In some studies the sensitivity of D-dimer test reached up to 100% (6-8, 10, 17). However, the role of D-dimer test for diagnosis of AAD has not been incorporated into formal guidelines and clinical practice yet. Today, the appropriate laboratory technique of choice and the threshold value for D-dimer testing is a current topic of discussion.

We aimed to determine the diagnostic accuracy of D-dimer measurements in the diagnostic evaluation of patients with suspected AAD.

Methods

Study design: This study is a retrospective chart review of patients who had been evaluated for suspected AAD in the emergency department (ED). Because it was a retrospective study, neither informed consent nor Ethics committee approval for the study was required under the Turkish law.

Study setting and population: The study was carried out in a tertiary care centers Department of Emergency Medicine with 70000/year adult patient attendances. Patient records, who were evaluated for AAD at our institution, were investigated retrospectively between February 2006 and August 2008 January.

Study protocol: Emergency department records were queried for International Classification of Diseases (ICD-10) code I 71.0 corresponding to dissection of aorta and R 07 corresponding to chest pain. Patients who had a D-dimer determination in the ED as a part of their work up were included to the study. D-dimer testing have been routinely ordered for patients with suspicion of AAD in last years in our ED. Patients diagnosed as acute aortic rupture, patients who re-attended during the study period and patients who had missing data on their charts were excluded from the study.

Charts were reviewed for patient demographics, medical history, signs and symptoms on presentation, type of dissection, management, and outcome. Patients were divided in two groups as patients who had a AAD and as those who did not. Two groups were compared for demographic characteristics, major complaints on the attendance, comorbid conditions, vital signs, physical findings, mediastinal enlargement on the chest X-ray and D-dimer test results.

Acute aortic dissection was diagnosed on basis of CT findings of an intimal flap. Aortic dissection was considered to be chronic, at least 14 days after onset of aortic dissection (AD) defined by the initial episode of intense pain (20). Dissections were classified on the basis of false lumen propagation to the ascending aorta (DeBakey 1, 2, and 3) (21).

Contrast enhanced thorax CT angiogram results were evaluated by a blinded radiologist and the diagnosis report of this radiologist was the gold standard for identifying AAD. Additionally, operation records were obtained from our cardiovascular surgery department if the patient had undergone surgery in our institution.

We identified consecutive 113 cases in which a D-dimer test had been performed prior to CTA scan. However, 14 patients were excluded from the study. Two patients were excluded because of re-attendances in the study period, and 6 patients were excluded because of missing data on the charts and 6 patients were diagnosed as acute aortic rupture and excluded from the study too. Of the 113 patients, 99 were enrolled into the study.

A control group was selected from patients and named as non-AAD group, in whom AAD had been ruled out and in whom D-dimer test had been performed. The D-dimer assay used by the institution during the study was a quantitative immunoturbidimetric assay (Dade Behring, Germany,). Normal levels for D-dimer were accepted between 0.064-0.246 µg/ml. The cut-off value was 0.246 µg/ml, with results above this threshold reported as positive. A limitation was the upper limit of the test, which was 0.771 µg/ml.

Statistical analysis

Statistical analysis was performed, owing to a commercially available statistical package (SPSS for Windows, Version 11.0, SPSS, Chicago, Illinois, USA). Data are expressed as numbers, percentages, mean±SD. The differences between two groups with the diagnostic and demographic parameters were analyzed using Fisher exact tests and Pearson Chi-square tests for categorical variables, and comparison of continuous variables between two groups were performed using a Student's t-test.

Sensitivity, specificity, positive (PPV) and negative predictive (NPV) values, and likelihood ratios (LR) were calculated with 95% confidence interval in relation to the final diagnosis, that is, having confirmed AAD. A receiver-operating characteristics (ROC) curve analysis was done for estimation of the certainty for excluding AAD on base of negative D-dimer results. The area under the curve (AUC) was also calculated and shown with 95% confidence interval (CI). A value $p<0.05$ was considered to be significant.

Results

The baseline characteristics of the study patients are given in Table 1. The two groups were similar in the ratio of gender and mean age. No statistically significant differences in patients clinical presentation, past medical history and physical findings were found between AAD and non-AAD groups (p>0.05 for all). However, patients in non-AAD group were more likely to be diabetic (p=0.006), and AAD group patients are more likely to have chest pain (p=0.027), back pain (p=0.019) and pulse deficit (p=0.021).

When comparing D-dimer results, there were statistically significant difference between the AAD and the non-AAD groups: positive D-dimer results (cut-off value: 0.246 µg/ml) were found to be 96.6% and 47.8% in AAD and non-AAD groups respectively, (p<0.001).

Sensitivity of the D-dimer test in detection of AAD was found to be 96.6% and NPV of the test was 97.3%. Specificity of the D-dimer test was 52.2% and PPV was calculated as 46.8%. Positive LR and negative LR were found to be 2.02 and 0.06, respectively. The only patient who had a negative D-dimer result with an AAD was at the limit of chronic aortic dissection, she attended to the ED nearly two weeks after the onset of her symptoms.

The ROC curve analysis AUC value yielded an acceptable certainty for excluding acute aortic dissection on base of negative results (AUC: 0.764; CI 95%: 0.674-0.855; p< 0.001) (Fig. 1).

In 30 patients AAD was identified after thoracoabdominal CT imaging. Final diagnosis of the patients are given in Table 2. Cardiovascular surgeons planned emergent surgery for 24 patients and medical treatment for 6 patients. Two of those emergent surgery planned patients died before operation, 2 patients did not give informed consent for operation, and 3 of them referred to another institution because of unavailability of operation rooms, therefore 17 of the patients were operated finally.

In the non-AAD group, 19 patients had an aortic aneurysm (AA) and one of them was operated previously. Eight patients had chronic aortic dissection. Three of them had previously known chronic dissections, four of them were operated previously, and one of them identified in the ED and operated electively later. Patients with AA were mostly evaluated with CT, because of the mediastinal enlargement on chest X-ray in ED and diagnosed non-specific chest and abdominal pain eventually. CT reports of all those non-AAD patients were evaluated again with cardiovascular surgeons and no emergent operation due to presenting symptoms was considered.

Table 1. Clinical characteristics of patients with and without AAD

Variables	AAD Group (n=30)	Non-AAD Group (n=69)	p*
Patient's demographics			
• Age, years	62.8 ±13.4	67.8 ±11.8	0.064
• Male gender, n (%)	19 (63.3)	44 (63.8)	1.000
• Hypertension, n (%)	22 (73.3)	46 (66.7)	0.639
• Coronary artery disease, n (%)	5 (16.7)	16 (23.2)	0.596
• Diabetes mellitus, n (%)	1 (3.3)	19 (27.5)	0.006
Symptoms and physical examination findings of study patients			
• Chest pain, n (%)	22 (73.3)	33 (47.8)	0.027
• Back pain, n (%)	9 (30.0)	7 (10.1)	0.019
• Abdominal pain, n (%)	2 (6.7)	11 (15.9)	0.333
• Syncope, n (%)	1 (3.3)	3 (4.5)	1.000
• Pulse deficit, n (%)	6 (20.0)	3 (4.3)	0.021
• Focal neurological deficit, n (%)	1 (3.3)	2 (2.9)	1.000
• Blood pressure asymmetry, n (%)	6 (20.0)	5 (7.2)	0.084
• Pulsatile mass, n (%)	2 (6.7)	1 (1.4)	0.217
• Trill, n (%)	4 (11.1)	2 (2.9)	0.067
• Hypertensive (SBP≥150 mmHg), n (%)	11 (36.7)	16 (23.2)	0.220
• Hypotensive (SBP<100 mmHg), n (%)	4 (13.3)	12 (17.4)	0.770
• Enlarged mediastinum, n (%)	18 (81.8)†	44 (72.1)‡	0.568
D-dimer results			
• Negative D-dimer results, n (%)	1 (3.3)	36 (52.2)	<0.001

Data are presented as mean±SD (range) and proportions (percentages).
*Student's t-test, Chi square test , † - n=22 ; ‡- n=61
AAD - acute aortic dissection, SBP - systolic blood pressure

Discussion

We found the sensitivity of the D-dimer test detecting AAD to be 96.6% and NPV 97.3%. Our results are parallel to the recent

Table 2. Final diagnosis of the patients

AAD group (n=30)	n (%)
DeBakey 1, n (%)	13 (43.4)
DeBakey 2, n (%)	5 (16.6)
DeBakey 3, n (%)	12 (40.0)
Non-AAD group (n= 69)	
Aortic aneurysm and chronic dissection subgroup (n= 27)*	
Thoracic aortic aneurysm, n (%)	10 (14.5)
Abdominal aortic aneurysm, n (%)	9 (13.0)
Chronic dissection, n (%)	8 (11.6)
Other subgroups (n=42)	
Acute coronary syndrome (UAP/NSTEMI/STEMI)†, n (%)	11 (15.9)
Nonspecific chest pain, n (%)	13 (18.9)
Pulmonary etiology (embolism, cancer, pneumonia), n (%)	4 (5.8)
Acute arterial occlusion, n (%)	2 (2.9)
Others, n (%)	12 (17.4)

* Included operated dissections and aneurysms
AAD - acute aortic dissection, †NSTEMI - Non-ST elevated myocardial infarction, STEMI - ST elevated myocardial infarction, UAP - unstable angina

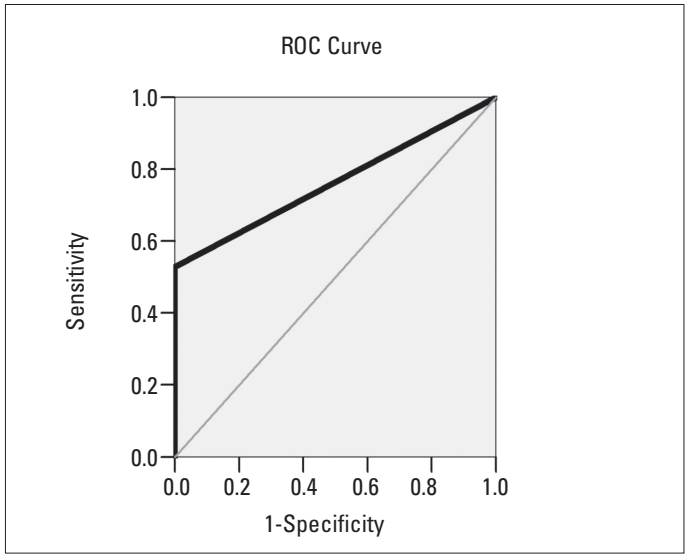

Figure 1. Receiver-operating characteristics (ROC) curves for excluding AAD on base of negative D-dimer testing

AUC - 0.764; 95% CI - (0.674-0.855); p<0.001
AAD - acute aortic dissection

studies. However, the upper limit of D-dimer values were set as 0.771 µg/ml at our institution, therefore in our study to compare D-dimer levels according to time of onset of the symptoms or outcome was not possible. Also ROC curve analysis yielded a good certainty for excluding AAD on base of negative results. Whereas, the only patient with false negative D-dimer test result in this study, had an onset of symptoms 2 weeks ago and that period of time is circa at the limit of chronic dissection. The reason of this decreased D-dimer value may be the endothelialization of the patent false lumen of the dissection.

AAD is a serious catastrophic disease of the emergency medicines daily practice. The presentation of thoracic aortic dissection is highly variable, and the diagnosis can not be ruled out based on medical history, examination, or plain radiography findings (22). Absence of chest radiograph abnormalities, sudden-onset pain, and a history of hypertension all decrease the likelihood of the diagnosis. However, advanced imaging studies such as CT, magnetic resonance imaging (MRI), digital subtraction angiography (DSA), and echocardiography will still be required to confirm to rule out the diagnosis (20, 23, 24). At this point D-dimer will help physicians as a sensitive test for AAD diagnosis, and potentially a useful test for patients who present with a low likelihood of this disease (absence of tearing or ripping aortic pain, mediastinal widening, pulse and blood pressure differentials) (25, 26).

Other markers such as smooth muscle myosin heavy chain (SMMHC) and soluble elastin have been proposed as specific markers of AAD too, but rapid measurement systems of those markers are not clinically available (27). Also, SMMHC's high sensitivity (90%) for detection of AAD decreases rapidly with time, and soluble elastin has a 0% sensitivity in patients with a thrombosed false lumen (27, 28). Therefore D-dimer has an advantage over SMMHC and soluble elastin in differentiating AAD. The Task Force of European Society of Cardiology recommends measuring D-dimer values in the initial management of patients with suspected AAD (21).

D-dimer is a typical degradation product of cross-linked fibrin. The hypothesized mechanism in elevation of D- dimer levels in AAD is the activation of the extrinsic pathway of the coagulation cascade by tissue factor, that is largely exposed at the site of the injured aortic wall (6). The difference in D-dimer levels between acute and chronic dissections may be explained by the fact that the patent false lumen becomes endothelialized during the chronic course of aortic dissection; as a consequence, the coagulation cascade and fibrinolytic status is no longer activated (7). However, another pathway for elevation of D-dimer levels had been previously described. A tissue factor, which is located in the smooth muscle layer of the aorta, would pour into the bloodstream after dissection and activate the coagulation cascade, stimulating fibrinolytic activity and the formation of D-dimer (29).

It has been shown that D-dimer has a very high sensitivity (up to 100%) to exclude AAD(6-8, 10, 17), however the specificity of the test is reported to be low as 34-80 %. The results of studies investigating the role of D-dimer levels in diagnosis of AAD are given in Table 3.

Akutsu K. et al. (10) found 100% sensitivity for rapid bedside D-dimer testing and D-dimer levels were elevated only one hour after onset of symptoms in all patients regardless the type of AAD (type A or B, patent or thrombosed). However, in some trials sensitivity of D-dimer for detecting AAD found to be lower than in other studies (93-82%) (9, 13, 14, 16, 18). Wiegand et al. (16) reported sensitivity of D-dimer testing as 88%. He pointed out that until the results of large studies including consecutive series of patients with suspicion of AAD and a rationale for an optimal cut-off value become available, D-dimer tests are not safe enough to rule out AAD. However, Wiegand et al. (16) reported no association between the level of the D-dimer reading and time of the symptom onset. Time of the symptom onset of all the three false negative cases was lower or equal than one hour. As Hazui et al. (13) reported previously, D-dimer levels in AAD patients were relatively lower in the first two hours after symptoms onset. Young patients and patients who have thrombosed false lumen (TFL) without ulcer like projections are liable to have false-negative D-dimer results, and there was a significant correlation between length of dissection and absolute D-dimer values too (13).

Sodeck et al. (17) found D-dimer's sensitivity for AAD as 100% at cut-off level 0.1 µg/ml and 98% at 0.5 µg/ml, and 86% at 0.9 µg/ml. Therefore, authors were criticized for choosing a very low D-dimer cut-off value to reach high sensitivity, but poor specificity (30). Sensitivities of D-dimer testing for detection of AAD vary between 82-100 % (6-18). The major reason of those different sensitivities found in previous trials, may be the different measurement techniques and cut-off levels which are chosen for D-dimer assay.

One of the latest studies (18) evaluating D-dimer's sensitivity for detection of AAD found the lowest sensitivity ever founded in the literature as 82%. Authors pronounced also a word of caution regarding the NPV of D-dimer test in the diagnosis of aortic

Table 3. A review of current studies on the subject

Author/Date	Study Design	D-dimer assay	Cut-off, value µg/ml	Number of patients AAD / Control	Sensitivity, %	Specificity, %
Weber T. et al. 2003[6]	Pro-and retrospective	Turbidimetric	0.5	24 / 35	100	68
Eggebrecht H. et al. 2004[7]	Pro-and retrospective	Turbidimetric	0.62	16 / 80	100	73
Perez A. et al. 2004[8]	Retrospective	LA†	0.5	7 / -	100	-
Hazui H. et al. 2005[9]	Pro-and retrospective	LA†	0.9	29 / 49	93	80
Akutsu K. et al. 2005[10]	Prospective	ELISA	0.5	30 / 48	100	54
Ohlmann P. et al. 2006[11]	Retrospective	Turbidimetric	0.4	94 / 94	99	34
Weber T.et al. 2006[12]	Pro-and retrospective	Turbidimetric	0.5	27 / -	-	-
Hazui H. et al. 2006[13]	Retrospective	LA†	0.4	113 / -	92	-
Spinner T. et al. 2006[14]	Prospective	LA†	0.3	26 / 24	92	-
Sbarouni E. et al. 2007[15]	Prospective	ELISA	0.7	18 / 29	94	59
Wiegand J. et al. 2007[16]	Retrospective	ELISA	0.5	25 / -	88	-
Sodeck G. et al. 2007[17]	Prospective	LA†	0.1	65 / -	100	-
Paprella D. et al. 2009[18]	Prospective	Turbidimetric	0.4	61 / -	82	-
Suzuki T. et al. 2009[19]	Prospective	ELISA	0.5	87 / 133	96	46
Current study	Retrospective	Turbidimetric	0.246	30 / 69	96	52

AAD - acute aortic dissection, ELISA - enzyme-linked immunosorbent assay, †LA - latex agglutination

dissection, and they recommend to search for a novel specific biomarker for diagnosis od AAD (18).

On the other hand, in a recent meta-analysis, the pooled sensitivity of D-dimer testing remains at 94%, which is extracted from eleven original article and a total of 349 acute aortic dissection patients (25). The authors of this meta-analysis concluded that serum D-dimer is sensitive for diagnosis of AAD and potentially represents a useful test for patients who present with a low likelihood of this disease.

A very recent study (19) supports findings of the previous and our study. In that prospective multicenter study, 220 patients with initial suspicion of having AAD were enrolled, of whom 87 were diagnosed with AAD and 133 with other final diagnoses. Sensitivity and NPV of the test were found to be 96% and 97% respectively. According to the results of the study, D-dimer test can reliably rule out aortic dissections, even at the widely used cut-off level of 500 ng/mL used for ruling out pulmonary embolism, within the first 24 hours after symptom onset. Authors pointed out that D-dimer levels may be useful in risk stratifying patients with suspected aortic dissection to rule out aortic dissection (19).

Some authors recommend that D-dimer tests should be a part of the current initial diagnostic work-up of patients with chest pain and suspected AAD and D-dimer levels may represent a complementary tool for the diagnostic and prognostic evaluation of AAD (7, 13, 31). In a recent review (31) according to a proposed algorithm for acute chest pain, the author pointed out that, patients with low clinical suspicion of aortic dissection, and with normal D-dimer test results, may be discharged safely from the ED. Hazui et al. (9) used D-dimer test to differentiate AAD from acute coronary syndromes. D-dimer may play a role for decision making to give patients thrombolytic agents in acute myocardial infarction with ST segment elevation. Unfortunately, the database of this study was not large enough to reliably investigate this relationship statistically.

D-dimer levels were also found to be correlated with anatomic extension and with the type of the disease (6, 11). In a large series with 94 patients, a sensitivity of 99% observed (11). Only one patient with a localized intramural hematoma had a normal D-dimer value (<0.400 µg/ml). In the same trial, D-dimer levels in De Bakey I type dissections were found to be higher than type II and III. According to this, D-dimer increases proportionally to the surface of contact between the bloodstream and the thrombogenic components of the false lumen, and D-dimer levels are significantly lower in patients with intramural hematoma than in patients with patent false lumen (11). Additionally, D-dimer concentrations on admission may provide independent prognostic information about patients with acute aortic type A dissection (12). Eggebrecht et al . (7) and Ohlmann et al. (11) found that D-dimer levels tended to be higher in patients who died during the in-hospital period. However, Weber et al. (6) and Sbarouni et al. (15) did not observe a difference on D-dimer levels between patients' outcome (mortality) and type of aortic dissection.

According to our and the recent literature results, D-dimer test has a high sensitivity for detection of AAD. Clinical suspicion and chest radiography findings are the only tools, but they are not sensitive and specific in determination of patients who require further imaging. Therefore D-dimer measurement will help physicians to risk stratify patients and decide to perform further analysis in patients with suspected AAD (17, 19). Using D-dimer test in low probability patients as an additional risk stratifying tool in exclusion of AAD would result in increased diagnostic efficiency and cost savings. It will also spare the patients from unnecessary radiation and contrast material load when the great majority of negative imaging studies performed is considered.

Study limitations

The retrospective nature of the study is a methodological limitation because the evaluation and management were not standardized. Our study analyzed D-dimer results in retrospectively created patient groups, and we cannot completely rule out that selection bias may have influenced the results of this study. In our study exact D-dimer levels over 0.771 µg/ml were not assessed. Because of, 18 patients in AAD and 6 patients in non-AAD groups had a D-dimer value over 0.771 µg/ml, a reliable statistical analysis was not possible. However, this limitation would not affect our primary goal to show D-dimers sensitivity and NPV is enough valuable high for detecting AAD.

Conclusion

Findings of our study have shown that negative D-dimer test has a high sensitivity and NPV for detecting AAD in the emergency department patients, however D-dimer test is not sensitive enough to rule out AAD. Nevertheless, it seems to be a useful diagnostic tool in assessing for AAD and may aid the clinician in low probability patients where diagnostic uncertainty remains. We believe that, further, well-organized large scale prospective trials should be designed specifically to investigate the reasons of the false negative results.

Conflict of interest: None declared.

References

1. Mehta RH, Suzuki T, Hagan PG, Bossone E, Gilon D, Llovet A, et al. Predicting death in patients with acute type a aortic dissection. Circulation 2002; 105: 200-6.
2. Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, et al. The International Registry of Acute Aortic Dissection (IRAD): New insights into an old disease. JAMA 2000; 283: 897-903.
3. Sarasin FP, Louis-Simonet M, Gaspoz JM, Junod AF. Detecting acute thoracic aortic dissection in the emergency department: time constraints and choice of the optimal diagnostic test. Ann Emerg Med 1996; 28: 278-88.
4. Sie P. The value of laboratory tests in the diagnosis of venous thromboembolism. Haematologica 1995; 80: 57-60.
5. The DVTENOX Study Group. Markers of haemostatic system activation in acute deep venous thrombosis evolution during the Şrst days of heparin treatment. Thromb Haemost 1993; 70: 909-14.
6. Weber T, Högler S, Auer J, Berent R, Lassnig E, Kvas E, et al. D-dimer in acute aortic dissection. Chest 2003; 123: 1375-8.
7. Eggebrecht H, Naber CK, Bruch C, Kröger K, Von Birgelen C, Schmermund A, et al. Value of plasma fibrin D-dimers for detection of acute aortic dissection. J Am Coll Cardiol 2004; 44: 804-9.
8. Perez A, Abbet P, Drescher MJ. D-dimers in the emergency department evaluation of aortic dissection. Acad Emerg Med 2004; 11: 397-400.
9. Hazui H, Fukumoto H, Negoro N, Hoshiga M, Muraoka H, Nishimoto M, 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.
10. Akutsu K, Sato N, Yamamoto T, Morita N, Takagi H, Fujita N, 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.
11. Ohlmann P, Faure A, Morel O, Petit H, Kabbaj H, Meyer N, et al. Diagnostic and prognostic value of circulating D-Dimers in patients with acute aortic dissection. Crit Care Med 2006; 34: 1358-64.
12. Weber T, Rammer M, Auer J, Maurer E, Aspoeck G, Eber B. Plasma concentrations of D-dimer predict mortality in acute type A aortic dissection. Heart 2006; 92: 836-7.
13. Hazui H, Nishimoto M, Hoshiga M, Negoro N, Muraoka H, Murai 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.
14. Spinner T, Spes C, Mudra H. Elevated D-dimer at acute chest pain: Pulmonary embolism or aortic dissection? Intensivmedizin und Notfallmedizin 2006; 43: 570-4.
15. Sbarouni E, Georgiadou P, Marathias A, Geroulanos S, Kremastinos DT. D-dimer and BNP levels in acute aortic dissection. Int J Cardiol 2007; 122: 170-2.
16. Wiegand J, Koller M, Bingisser R. Does a negative D-dimer test rule out aortic dissection? Swiss Med Wkly 2007; 137: 462.
17. Sodeck G, Domanovits H, Schillinger M, Ehrlich MP, Endler G, Herkner H, et al. D-dimer in ruling out acute aortic dissection: a systematic review and prospective cohort study. Eur Heart J 2007; 28: 3067-75.
18. Paparella D, Malvindi PG, Scrascia G, De Ceglia D, Rotunno C, Tunzi F, et al. D-dimers are not always elevated in patients with acute aortic dissection. J Cardiovasc Med (Hagerstown) 2009; 10: 212-4.
19. Suzuki T, Distante A, Zizza A, Trimarchi S, Villani M, Salerno Uriarte JA, 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.
20. Knaut AL, Cleveland JC Jr. Aortic emergencies. Emerg Med Clin North Am 2003; 21: 817-45.
21. Erbel R, Alfonso F, Boileau C, Dirsch O, Eber B, Haverich A, et al. Task Force on Aortic Dissection, European Society of Cardiology. Diagnosis and management of aortic dissection. Eur Heart J 2001; 22: 1642-81.
22. Suzuki T, Katoh H, Watanabe M, Kurabayashi M, Hiramori K, Hori S, et al. Novel biochemical diagnostic method for aortic dissection. Results of a prospective study using an immunoassay of smooth muscle myosin heavy chain. Circulation 1996; 93: 1244-9.
23. Khan IA, Nair CK. Clinical, diagnostic, and management perspectives of aortic dissection. Chest 2002; 122: 311-28.
24. Woo Y, Bavaria J, Mohler M. Clinical features and diagnosis of thoracic aortic aneurysm. [CDROM] In: Rose BD, ed. UpToDate. Wellesley, MA: UpToDate; 2004. 2 CDROMs.
25. 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.
26. Von Kodolitsch Y, Schwartz AG, Nienaber CA. Clinical prediction of acute aortic dissection. Arch Intern Med 2000; 160: 2977-82.
27. Shinohara T, Suzuki K, Okada M, Shiigai M, Shimizu M, Maehara T, et al. Soluble elastin fragments in serum are elevated in acute aortic dissection. Arterioscler Thromb Vasc Biol 2003; 23: 1839-44.
28. Suzuki T, Katoh H, Tsuchio Y, Hasegawa A, Kurabayashi M, Ohira A, et al. Diagnostic implications of elevated levels of smooth-muscle myosin heavy-chain protein in acute aortic dissection. Ann Intern Med 2000; 133: 537-41.
29. Rapaport SI, Rao LV. The tissue factor pathway: How it has become a "prima ballerina". Thromb Haemost 1995; 74: 7-17.
30. Salvagno GL, Targher G, Franchini M, Lippi G. Plasma D-dimer in the diagnosis of acute aortic dissection. Eur Heart J 2008; 29: 1207.
31. Mir MA. Aortic dissection in pursuit of a serum marker. Am J Emerg Med 2008; 26: 942-5.