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**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**

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**Background** Previous reports indicate that D-dimer testing (DT) for acute aortic dissection (AAD) has a sensitivity of 100%, but each study comprised less than 30 patients. The aim of this study was to evaluate the positive rate and factors related to the results of DT for AAD in a larger population.

**Methods and Results** DT (cutoff; upper normal limit) was performed for 113 consecutive AAD patients within 24h of symptom onset. In total, 104 (92%) patients exhibited positive DT. The positive rate of DT showed a low tendency in patients aged less than 70 years and for a time interval from symptom onset to admission within 120 min, and there were significant differences between those with and without a thrombosed false lumen (TFL) (86.4% (n=59) vs 98.1% (n=54), p=0.033), complete TFL (excluding patients with ulcer-like projection (ULP) from those with a TFL) (81.1% (n=37) vs 97.4% (n=76), p=0.005) and length score (1 (n=28); 78.6%, 2 (n=40); 95.0%, 3 (n=45); 97.8%, p=0.005). Multivariate analysis demonstrated age (odds ratio=1.164, p=0.013), complete TFL (0.048, 0.030) and length score (6.271, 0.033) as independent factors.

**Conclusions** Physicians should be aware that younger patients with short dissection length and a TFL without ULP are liable to have false-negative DT results. ([Circ J 2006; 70: 1598-1601])

**Key Words:** Acute aortic dissection; D-dimer; Dissection length; Thrombosed false lumen; Ulcer-like projection

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**A** cute aortic dissection (AAD) results in high mortality and morbidity if it is not recognized and treated promptly. So rapid and accurate diagnosis is essential. Needless to say, advanced image modalities, such as computed tomography (CT), magnetic resonance imaging and transesophageal echocardiography, are intrinsic to the accurate diagnosis and treatment of AAD, but a simple laboratory test that can suggest the presence of AAD would also be useful, particularly in the emergency setting because it could support the use of advanced imaging. Previous reports indicate that D-dimer testing (DT) for AAD has a sensitivity of 100% when the cut off value for D-dimer is set to the upper limit of the normal range, indicating that we could exclude AAD if DT was negative. However, each of those study groups comprised small populations of less than 30 patients.

The aim of this study was to confirm the positive rate of DT for AAD in a larger population in an emergency setting and to verify the factors related to the result of DT. We could review the D-dimer values on admission of a large population of AAD patients because it has been routinely measured from January 2001.

**Methods**

**Study Setting and Patients**

This single-center, retrospective study comprised 113 consecutive patients with AAD who were admitted to the Osaka Mishima Emergency and Critical Care Center within 24h of symptom onset between January 2001 and July 2005. Patients with cardiac arrest on arrival were excluded. The diagnosis of AAD was confirmed by thoracic and abdominal contrast-enhanced CT. Blood samples were taken in the emergency room immediately after admission.

**Study Protocol**

This study was approved by the Human Research Committee at the Osaka Mishima Emergency and Critical Care Center. We reviewed the age, time from the onset of the symptoms to admission (TIME) and serum D-dimer values (latex agglutination, Roche Diagnostic, Tokyo, Japan, normal limit ≤0.4μg/ml). The cut-off value for D-dimer was set to the upper limit of the normal range (ie, 0.4μg/ml) to calculate the positive rate of DT. The positive rate of DT and absolute D-dimer values were compared for each of the
following factors: TIME, age, gender, presence or absence of dissection of the ascending aorta, a thrombosed false lumen (TFL; included all patients with a TFL, regardless of the existence of ulcer-like projection) and complete TFL (excluded patients with ulcer-like projection from those with a TFL), length score (calculated by allocating 1 point for dissection of each portion, including the ascending aorta, descending thoracic aorta and abdominal aorta (full score = 3)), the incidence of shock (defined as a systolic blood pressure <90 mmHg and perspiration or disturbance of consciousness), malperfusion and pericardial effusion (as detected by thoracic and abdominal enhanced CT) and renal dysfunction (defined as serum creatinine level >2.0 mg/dl on admission).

**Statistical Analysis**

For continuous variables, mean ± standard deviation (SD), or median, and the 25% and 75% percentiles values were calculated, and comparison between 2 groups was performed using the Mann-Whitney U-test. The positive rate for each of the above factors was initially analyzed using Fisher's exact test or linear regression test, as appropriate.
Multivariate logistic regression test was subsequently performed as the second step. Correlation between 2 data sets was estimated by Spearman correlation. P-values <0.05 were considered significant. All statistical calculations were performed using a commercially available statistical software package (SPSS II for Windows, Version 11.0, Chicago, IL, USA).

Results

In total, 104 of 113 (92.0%) patients exhibited positive D-dimer test results. The positive rate of DT by 60 min in TIME was relatively low within 120 min (Fig 1) but there was not a significant difference in the D-dimer values between patients with TIME within and those beyond 120 min (mean ± SD 38.1±64.9 (n=50) vs 35.8±81.3 µg/ml (n=63), p=0.400). The positive rate of DT was 100% in patients aged more than 70 years (Fig 2) but there was not a significant difference in the D-dimer values between patients aged less and more than 70 years (39.3±81.7 (n=71) vs 32.5±59.9 µg/ml (n=42), p=0.941). Moreover, statistically significant differences were observed for the D-dimer positive rate between those with and without a TFL and complete TFL, and in length score, but not between males and females, dissection of ascending aorta, shock, malperfusion, pericardial effusion and renal dysfunction (Table 1). Multivariate logistic regression test demonstrated age, complete TFL and length score as independent factors related to positive D-dimer findings (Table 2). Moreover, absolute D-dimer values were also significantly lower in patients with complete TFL than in those without (p=0.001) (Fig 3). There was a significant correlation between length score and absolute D-dimer values (r=0.519, p<0.001) (Fig 4).

Discussion

All of the previous studies concerning DT for AAD have reported that it can achieve a sensitivity of 100%, so to date the only limitation of DT for AAD has been considered its lack of specificity. Even with low specificity, DT has a great advantage if the sensitivity is 100%, because AAD can be excluded by negative D-dimer test results. However, in our study there were 9 AAD patients (8%) with normal D-dimer values, so this is the first report to demonstrate a limitation concerning the sensitivity of DT. Nienaber et al speculated in their response to the letter from Weber et al that AAD patients with intramural hematoma might not exhibit an elevation of the biomarkers for AAD, such as...
smooth muscle myosin heavy chain\(^9\) or soluble elastin fragment;\(^10\) as well as D-dimer, because they are unlikely to leak biomarkers into the blood stream!\(^11\). Although we had already indicated that patients with a TFL exhibited significantly lower D-dimer values than those with a patent false lumen;\(^12\) the present study supports that speculation more strongly because AAD with a TFL without ulcer-like projection (ie, complete TFL in the present study) is more similar to that with intramural hematoma. DT might depend on the presence of a false lumen, in which D-dimers can be formed, that is connected to the circulation. We can also speculate that DT depends on the size of the false lumen to form D-dimer, based on another result that dissection length is an independent factor related to positive DT results for AAD. Thus, AAD patients with a long dissection length can produce D-dimer more abundantly than those with a short dissection length. Therefore, negative DT would be more usual in patients with a short dissection length. It is more difficult to explain the relationship between DT and the last independent factor, age. Some reports have demonstrated the presence of tissue factor in the smooth muscle layer of the aorta, with this factor being abundantly present following progression of atherosclerotic changes.\(^13,14\) Elderly patients have a high incidence of progressive atherosclerotic lesions, which might lead to positive DT results.

It is of importance to consider how DT can be used clinically. If the sensitivity of DT for AAD were 100%, we could use this as the test to exclude AAD, but our current results do not support that. We recommend that DT, which shows high sensitivity, although not 100%, should be used by general physicians rather than cardiologists.

**Study Limitations**

This study was retrospective and evaluated a relatively small number of patients. Particularly, the number of patients with negative DT was very small, so statistical interpretation of our data must be done carefully. The diagnosis of ulcer-like projection on CT was also an important limitation because multislice CT was only used after December 2003 and therefore the detection of ulcer-like projections before this date might not be adequate. Accordingly, we might consider patients with ulcer-like projection as the same as those without it. Moreover, the patients were transferred by ambulance to the institution, rather than as self-referral, which might cause a bias in the data collected.

**Conclusion**

DT for AAD demonstrated high sensitivity but not 100%. Physicians should be aware that younger patients with short dissection length and a thrombosed false lumen without ulcer-like projection are liable to have a false-negative D-dimer test result.

**References**