# Does a negative D-dimer test rule out aortic dissection?

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# **Background**

Early and accurate diagnosis is crucial for the management of patients with acute aortic dissection (AD). Recent studies [1-6] claimed that the D-dimer test may be a valuable addition to the diagnostic work-up in patients with suspicion of the disease.

### Methods

The objective was to assess the value of the D-dimer test to rule out AD (sensitivity) using a generally accepted cut-off value of <500 mg/l. We performed a retrospective analysis of all patients with AD at the University Hospital in Basel between January 2000 and October 2005, who had a D-dimer immunoassay (LiaTest®) available [11]. Diagnosis was confirmed by TEE, angiography, CT-scanning or histopathological findings.

The sensitivity of the D-dimer test was calculated and a potential association of time from symptom onset until collection of the D-dimer blood sample was assessed.

### Results

Twenty-five cases with confirmed AD and a D-dimer test were identified. The baseline characteristics are shown in table 1. Twenty-two patients had a true-positive and three patients had a false-negative D-dimer

Table 2
Recent studies evaluating D-dimers in AD.

test result (cut-off <500 mg/l), resulting in a sensitivity of 88.0% (70.0% to 95.8%). There was no association between the level of the D-dimer reading and time of symptom onset or the extent of dissection (figure 1).

We observed no particular characteristics in the three patients with a negative D-dimer test concerning age, gender, extent of dissection, outcome or histological features compared to the remaining cases.

# Discussion

In contrast to earlier studies reporting an excellent sensitivity of the D-dimer test in patients with AD (table 2), we found a substantial number of false negative test readings in our retrospective case-series. Twelve percent false-negative test readings using a <500 mg/l cut-off puts the usefulness of the D-dimer test to rule out AD in question. Until the results of large studies including consecutive series of patients with suspicion of AD and a rationale for an optimal cut-off value become available, we believe that D-dimer tests are not safe enough to rule out AD.

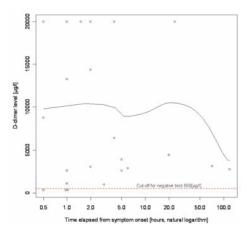
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Figure 1
Scatter plot with locally weighted regression line of time from symptom onset and level of D-dimer reading.



Baseline characteristics of 25 patients with AD.

Table 1

| Sex (male/female)                 | 22/3 (88/12%)            |  |  |  |
|-----------------------------------|--------------------------|--|--|--|
| Age (yr)                          | 62.7 (±15.4)             |  |  |  |
| Arterial Hypertension             | 18 (72%)                 |  |  |  |
| Smoking                           | 11 (44%)                 |  |  |  |
| Diabetes mellitus                 | 4 (16%)                  |  |  |  |
| Hypercholesterolaemia             | 7 (28%)                  |  |  |  |
| Marfan's Syndrome                 | 2 (8%)                   |  |  |  |
| Stanford type of dissection (A/B) | 20/5 (80/20%)            |  |  |  |
| Deaths (in-hospital)              | 8 (32%)                  |  |  |  |
| Cardiac tamponade                 | 6 (24%)                  |  |  |  |
| D-dimer level (median)            | 4420 μg/l<br>(300–20000) |  |  |  |
| Median time from symptom onset    | 2 hours<br>(0.5–120h)    |  |  |  |

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| Study                            | Number of patients | D-dimer neg. | Sensitivity | Cut-off<br>(µg/l) | Mean<br>(μg/l)        | D-dimer<br>assay                                   | Mortality | Design                       |
|----------------------------------|--------------------|--------------|-------------|-------------------|-----------------------|--|-----------|------------------------------|
| Weber et al. 2003 (1)            | 24                 | 0            | 100%        | 500               | 9400<br>(630–54700)   | Tina-quant assay<br>(Roche)                        | 42%       | pro- and<br>retrospective    |
| Perez et al. 2004 (2)            | 7                  | 0            | 100%        | 500               | n.a.                  | Semiquantitative latex agglutination assay         | n.a.      | retrospective<br>case series |
| Eggebrecht et al. 2004 (3)       | 16                 | 0            | 100%        | 500               | 2238<br>(632–6,419)   | Quantitative assay<br>D-Dimer Plus, (Dade Behring) | 50%       | pro- and<br>retrospective    |
| Hazui et al. 2005 (4)<br>(Roche) | 29                 | 2            | 93%         | 800               | n.a.                  | Latex agglutination,                               | n.a.      | pro- and<br>retrospective    |
| Akutsu et al. 2005 (5)           | 30                 | 0            | 100%        | 500               | 1800<br>(<100->4000)  | Rapid bedside assay<br>Cardiac reader (Roche)      | 13%       | prospective case control     |
| Ohlman et al. 2006 (6)           | 94                 | 1            | 99%         | 400               | 8610<br>(<300->20000) | Immunoassay<br>(Sta-LiaTest)                       | 23%       | retrospective<br>case series |
| Wiegand et al. 2007              | 25                 | 3            | 88%         | 500               | 4420<br>(<300->20000) | Immunoassay<br>(LiaTest®)                          | 32%       | retrospective<br>case series |