Objectives: To evaluate “the diagnostic performance of D-dimer in acute AD [aortic dissection] in a population suspected of having the disease.” (p. 2702)

Methods: This multicenter, prospective trial was conducted at 14 centers in Europe, the US, and Japan. Patients in whom the treating clinician planned to perform an imaging test to evaluate for aortic dissection, with symptom onset within 24 hours of presentation, were eligible for enrollment. Data was collected using standardized clinical data report forms.

D-dimer levels for patients with confirmed aortic dissection were compared to patient cohorts with other final diagnoses. 2X2 contingency tables were created and used to calculate sensitivity, specificity, predictive values, and likelihood ratios.

A total of 220 patients were enrolled. Of these, 87 had radiographically proven acute aortic dissection and 133 had an alternative diagnosis (MI in 46 cases, angina 37, PE in 5 cases, other in 45 cases). Among the aortic dissection cases, 64 were type A and 23 were type B. Men comprised 61% of aortic dissection cases and 69% of non-aortic dissection cases.

Guide

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<td>I. Are the results valid?</td>
<td>Yes. Patients were only enrolled if the suspicion for aortic dissection was ”high enough to cause the evaluating physician to order an imaging test to identify the presence of AD [aortic dissection] on which the subjects were categorized.” (p. 2703)</td>
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<td>A. Did clinicians face diagnostic uncertainty?</td>
<td>Yes. Blood plasma was drawn on presentation, and only patients undergoing an imaging test to evaluate for aortic dissection were enrolled. The authors do not specify which imaging studies were considered to constitute confirmatory studies, and do not provide information on how many patients in each group underwent which confirmatory tests.</td>
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<td>B. Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group? (Confirmation Bias)</td>
<td>Uncertain. The authors mention that blood plasma was drawn on presentation, but do not specify whether clinicians were blinded to the results of D-</td>
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II. What are the results?

A. What likelihood ratios were associated with the range of possible test results?

- The area under the curve (AUC) for the receiver-operating characteristics curve for all patients was 0.84 (95% CI 0.78-0.89).

- Using a cut-off of 500 ng/mL, the sensitivity was 96.6% (95% CI 90.3-99.3%), specificity 46.6% (95% CI 37.9-55.5%). The positive predictive value was 37.6% and the negative predictive value was 97.6%. The positive likelihood ratio was 1.81, and the negative likelihood ratio was 0.07.

- When looking only at patients with symptom duration of 0 to 6 hours, similarly favorable rule-out properties were found, with a negative LR of 0.07. Diagnostic properties were also not significantly affected by aortic dissection type (A vs. B).

III. How can I apply the results to patient care?

A. Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?

Yes. This study utilized a commercially available, quantitative D-dimer immunoassay. This test has been shown to be highly reliable, is commonly used in the evaluation of thromboembolic disease, and is similar to the test used at our hospital.

B. Are the results applicable to the patients in my practice?

Yes. It is common to see patients in our emergency department in whom aortic dissection is included in the differential diagnosis, and in whom we would like to evaluate for dissection as the cause of the patient’s symptoms. We commonly perform advanced imaging (primarily CT aortic angiogram and MRI) in order to rule-out aortic dissection.

C. Will the results change my management strategy?

No. While the results of this study suggest that D-dimer has a low negative LR, and hence would result in a significant reduction in the probability of the disease if the test is negative, it would first be necessary to define the test threshold for advanced imaging for aortic dissection, and then to identify a low-risk population such that the post-test probability of a negative D-dimer is below this
Further studies will need to be performed to consistently identify such a low-risk population.

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<th>Will patients be better off as a result of the test?</th>
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<td>Uncertain. As noted above, further research will need to identify a low-risk subset of the population in whom the post-test probability of a negative D-dimer will be below the test threshold for confirmatory imaging studies prior to use of D-dimer to exclude aortic dissection.</td>
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**Limitations:**

1. The authors provide no information regarding cases eligible for inclusion but not enrolled (selection bias).

2. The authors do not specify what testing was considered adequate for confirmation of aortic dissection (CTA, MRI, TEE), and do not provide information regarding the number of patient who each type of imaging study performed.

3. It is unclear if clinicians were blinded to D-dimer test results, or if the results affected the decision to perform confirmatory testing (partial verification bias).

4. While the negative LR of D-dimer for aortic dissection is promising, the article does not discuss the role of pre-test probability or test threshold (Pauker and Kassirer 1980) necessary to determine which patients may be appropriately ruled out with D-dimer testing alone.

**Bottom Line:**

While this methodologically sound, prospective study demonstrated a low negative likelihood ratio for D-dimer in the evaluation of aortic dissection (0.07) a few issues remain. It was unclear in the article if radiologists and clinicians were blinded to D-dimer results, or if D-dimer results influenced the decision to proceed with confirmatory imaging studies. Additionally, the article does not address the importance of risk stratification, pre-test probability, and test thresholds in applying a screening test to rule out such a potentially lethal disease. Further research will need to validate a clinical decision rule to identify low-risk patients, such that the post-test probability of disease is below the test threshold for confirmatory imaging.