

## Critical Review Form Diagnostic Test

PGY-4

[Gorla R, Erbel R, Kahlert P, Tsagakakis K, Jakob H, Mahabadi AA, Schlosser T, Eggebrecht H, Bossone E, Jánosi RA. Accuracy of a diagnostic strategy combining aortic dissection detection risk score and D-dimer levels in patients with suspected acute aortic syndrome. Eur Heart J Acute Cardiovasc Care. 2015 Jul 16.](#)

**Objectives:** To validate the diagnostic performance of "a novel diagnostic algorithm combining the aortic dissection detection (ADD) risk score with D-dimer (D-d) level assessment in order to detect AAS rapidly in patients presenting with chest pain." (p. 2)

**Methods:** In this retrospective study, conducted at a single institution in Essen, Germany between January 2011 and May 2014, patients admitted to the emergency department (ED) with chest pain who had an available D-dimer level at presentation were included. All patients had an ADD risk score calculated retrospectively using a standard data entry form. A score  $\leq 1$  was defined as 'low probability,' and an ADD score  $> 1$  was defined as 'high probability.' D-dimer testing was by microparticle-enhanced immunoassay. Acute aortic syndrome (AAS) included aortic dissection, intramural hematoma, and penetrating aortic ulcer.

A total of 376 patients were included in the evaluation, with a mean age of 63.1 years. Of these, 61.4% were male. AAS was diagnosed in 85 (22.6%) patients, with an in-hospital mortality of 15.3%. An AAD score of 0 was found in 189 (50.3%) patients, a score  $\leq 1$  was found in 319 (84.8%), and a score  $> 1$  was found in 57 (15.2%).

Guide		Comments
<b>I.</b>	<b>Are the results valid?</b>	
<b>A.</b>	<b>Did clinicians face diagnostic uncertainty?</b>	Uncertain. The authors only included patients with chest pain and a D-dimer level sent on presentation, but the final diagnosis on these patients was uncertain at the time the D-dimer was sent. It is unclear if data entry forms (from which the ADD score was calculated) were filled out by investigators blinded to final diagnosis.
<b>B.</b>	<b>Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group? (Confirmation Bias)</b>	Uncertain. While the authors report that only patients with chest pain and a D-dimer level were included, it is unclear if all patients underwent confirmatory imaging to confirm or exclude an AAS, and it is uncertain if radiologists interpreting confirmatory imaging were blinded to D-dimer results.
<b>C.</b>	<b>Did the results of the test being evaluated influence the decision to perform the gold</b>	Uncertain. While the authors report that only patients with chest pain and a D-dimer level were included, it is unclear if all patients underwent confirmatory imaging

	<b>standard? (Ascertainment Bias)</b>	to confirm or exclude an AAS. It is possible that D-dimer results influenced the decision to perform confirmatory testing.																									
<b>II.</b>	<b>What are the results?</b>																										
<b>A.</b>	<b>What likelihood ratios were associated with the range of possible test results?</b>	<p>The diagnostic test characteristics for the ADD score, D-dimer, and combinations thereof are provided in the Table.</p> <p>Table. Diagnostic test characteristics of ADD and D-dimer</p> <table border="1"> <thead> <tr> <th>Patients</th> <th>Sensitivity</th> <th>Specificity</th> <th>PPV</th> <th>NPV</th> </tr> </thead> <tbody> <tr> <td>ADD score 0</td> <td>98.8%</td> <td>64.6%</td> <td>44.9%</td> <td>99.5%</td> </tr> <tr> <td>D-dimer</td> <td>97.6%</td> <td>63.2%</td> <td>43.7%</td> <td>98.9%</td> </tr> <tr> <td>D-dimer + ADD score 0</td> <td>100%</td> <td>67.5%</td> <td>1.6%</td> <td>100%</td> </tr> <tr> <td>D-dimer + ADD score <math>\leq 1</math></td> <td>93.5%</td> <td>63.2%</td> <td>21.5%</td> <td>98.9%</td> </tr> </tbody> </table>	Patients	Sensitivity	Specificity	PPV	NPV	ADD score 0	98.8%	64.6%	44.9%	99.5%	D-dimer	97.6%	63.2%	43.7%	98.9%	D-dimer + ADD score 0	100%	67.5%	1.6%	100%	D-dimer + ADD score $\leq 1$	93.5%	63.2%	21.5%	98.9%
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<b>III.</b>	<b>How can I apply the results to patient care?</b>																										
<b>A.</b>	<b>Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?</b>	Yes. The D-dimer is a well-validated lab test that is used widely in multiple settings. Its utility in some disease process, such as thromboembolic disease, has been well-established. The ADD score, while more subjective, has also been validated in multiple settings.																									
<b>B.</b>	<b>Are the results applicable to the patients in my practice?</b>	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.																									
<b>C.</b>	<b>Will the results change my management strategy?</b>	No. This was a retrospective study conducted at a single center. Only patients with a D-dimer level were included, and it is unclear who made the decision to order D-dimer levels, and what basis was used to make																									

		this decision. Further prospective studies should seek to determine the safety of a rule-out protocol involving a low-risk ADD score and negative D-dimer prior to widespread use of such a protocol.
<b>D.</b>	<b>Will patients be better off as a result of the test?</b>	Uncertain. Again, further prospective testing will be needed to verify the safety of this approach. If such testing is safe, resulting in a post-test probability below the test threshold for imaging, then we have the potential to reduce unnecessary radiation exposure, IV contrast exposure, and potential overdiagnosis of clinically irrelevant incidental disease.

**Limitatons:**

1. It is not specifically mentioned if the data entry forms were filled out by investigators blinded to D-dimer results or final diagnosis.
2. This was a retrospective study in which only patients with a D-dimer checked at presentation were included (selection bias).
3. The ADD score was calculated retrospectively using information available in the medical record, and when data was not available, the default was to mark the data as negative. This could potentially result in spuriously low ADD score results.
4. While the authors evaluate a means to assess [pre-test probability](#) via the ADD score, they do not provide a calculation of the [test threshold \(Pauker and Kassirer 1980\)](#) necessary to determine which patients may be appropriately ruled out with D-dimer testing alone.

**Bottom Line:**

**This study provides promising data to suggest that patients with an ADD score of 0 and a negative D-dimer are at very low risk of aortic dissection, with a negative LR of 0.0. Further prospective studies should seek to determine the safety of a rule-out protocol involving a low-risk ADD score and negative D-dimer, and should seek to clarify the test threshold below which confirmatory imaging is more likely to be harmful than beneficial, prior to widespread use of such a protocol.**