Critical Review Form
Diagnostic Test

PGY-3

Nazerian P, Morello F, Vanni S, Bono A, Castelli M, Forno D, Gigli C, Soardo F, Carbone F, Lupia E, Grifoni S. Combined use of aortic dissection detection risk score and D-dimer in the diagnostic workup of suspected acute aortic dissection. Int J Cardiol. 2014 Jul 15;175(1):78-82.

Objectives: **"to evaluate the accuracy and the efficiency of a diagnostic strategy combining ADD [aortic dissection detection] risk score classification with D-dimer in a cohort of patients evaluated in the ED for suspected AD [aortic dissection]." (p. 78)**

Methods: **This retrospective diagnostic accuracy study was performed using a prospective registry of patients with suspected aortic dissection, collected at two emergency departments in Italy from January 1, 2008 to March 30, 2013. Eligibility for enrollment in the registry required the presence of a symptom concerning for aortic dissection (chest pain, back pain, abdominal pain, syncope, or symptoms of perfusion deficit), absence of an alternative diagnosis after evaluation by the attending physician, and clinical suspicion such that the attending physician ordered a CT aortic angiogram to exclude or confirm the diagnosis aortic dissection. Not all patients in the registry had a D-dimer, and only those who did were included in this analysis.**

The ADD score was calculated retrospectively by a team of physicians blinded to the final diagnosis. Any data not reported in the charts was defaulted to negative. D-dimer levels were performed using a latex agglutination test by technicians unaware of clinical data. CT aortic angiogram was performed and interpreted by radiologists not involved in the study. The final diagnosis was established by two independent physicians blinded to D-dimer level and ADD score.

A total of 1455 patients were evaluated for aortic dissection during the study period, of whom 1035 were enrolled in this study. Of these, 62.5% presented with chest pain, 33.6% presented with back pain, 19.3% presented with abdominal pain, 14.3% presented with syncope, and 12.9% presented with signs of a perfusion deficit. Aortic dissection was confirmed in 233 (22.5%) cases. The characteristics of registry patients who did not have a D-dimer level checked were similar to those included in the study.

<table>
<tr><th colspan="2">Guide</th><th>Comments</th></tr>
<tr><td>I.</td><td>Are the results valid?</td><td></td></tr>
<tr><td>A.</td><td>Did clinicians face diagnostic uncertainty?</td><td>Yes. Patients with suspected aortic dissection were prospectively enrolled in the registry, prior to knowledge of the results of imaging studies. It is unclear why some patients had D-dimer levels checked while others did not (clinician decision?).</td></tr>
<tr><td>B.</td><td>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>Somewhat. All patients underwent CT aortic angiogram to confirm or exclude aortic dissection, and all studies were read by radiologists not involved in the study. It is unclear if the radiologists were blinded to D-dimer results. ADD scores were calculated retrospectively by physicians blinded to final diagnosis.</td></tr>
<tr><td>C.</td><td>Did the results of the test being evaluated influence the decision to perform the gold standard?
(Ascertainment Bias)</td><td>Uncertain. The registry only included patients in whom CT aortic angiogram was ordered to evaluate for aortic dissection. It is unclear if all patients at the two emergency departments in whom aortic dissection was suspected underwent CT scanning, or if D-dimer alone was used to exclude aortic dissection in some low-risk patients.</td></tr>
<tr><td>II.</td><td>What are the results?</td><td></td></tr>
<tr><td>A.</td><td>What likelihood ratios were associated with the range of possible test results?</td><td>

AD prevalence based on ADD risk score is shown in Table 1.

Table. AD prevalence based on ADD score
<table>
<tr><td>ADD Score</td><td>AD prevalence</td></tr>
<tr><td>0</td><td>5.9%</td></tr>
<tr><td>1</td><td>26.2%</td></tr>
<tr><td>>1</td><td>39.5%</td></tr>
</table>

In the overall study population, D-dimer had a sensitivity of 98.3% (95% CI 95.7-99.5%), specificity of 35.9% (95% CI 32.6-39.3%), NPV of 98.6% (95% CI 96.5-99.6%), PPV of 30.8% (95% CI 27.5-34.3%), negative LR of 0.05 (95% CI 0.02-0.13), and positive LR of 1.53 (95% CI 1.45-1.62).

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</table>

		• There were no patients with an ADD risk score of 0 and a negative D-dimer who were found to have an aortic dissection. Two patients with an ADD score of 1 and a negative D-dimer were found to have an aortic dissection, and 2 patients with an ADD score > 1 and a negative D-dimer were found to have an aortic dissection.
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. Despite the fact that a latex agglutination test for D-dimer was used, as opposed to the immunofluorescent assay used in our institution, the results should still be applicable. These tests have both been shown to be highly reliable and are commonly used in the evaluation of thromboembolic disease.
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. This was a retrospective study conducted on a pre-existing registry of patients. Not all patients in the registry were included, as some did not have D-dimer levels checked. 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.
D.	**Will patients be better off as a result of the test?**	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. **This retrospective study included patients enrolled in a registry. Not all patients in the registry had a D-dimer, and only those who did were included in this analysis (selection bias).**

2. **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.**

3. **It is not explicitly stated that radiologists were blinded to D-dimer results, resulting in possible incorporation bias.**

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. 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.