

Critical Appraisal Worksheet – Diagnosis
Eastern Virginia Medical School EM Journal Club

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Suzuki T, Distanto A, Zizza A, et al **Diagnosis of acute aortic dissection by D-dimer : the International Registry of Acute Aortic Dissection Substudy on Biomarkers (IRAD-Bio) experience.** Circulation. 2009 ;119 :2702-2707

Clinical Scenario:

65yo male presents to the ED with ‘tearing’ chest pain that radiated to the inter-scapular area that started acutely before coming to the ED. Pt has h/o HTN, DM, CAD. Pt denies diaphoresis, n/v, or other pain. You are concerned about the possibility of an acute thoracic dissection (TD) and wondered if a d-dimer would be helpful as a diagnostic test.

Are the Results Valid?*

<i>Questions</i>	<i>Comments</i>
Did all patients receive the diagnostic test being evaluated and a reference standard?	All patients were tested using the commercially available Triage D-Dimer test (made by Biosite). Only patients with high clinical suspicion for TD were included creating selection bias. The reference standard was not stated directly. It is assumed that reference standards were used by clinicians to elicit an accurate diagnosis though this was not stated (CT, MRI, TEE etc.). The authors do not specifically describe what their ‘gold standard’ test was for diagnosis of TA. It appears all patients underwent “diagnostic imaging” though this was not specifically described.
Was there an independent, blind comparison with a reference standard?	The reference standard in this investigation includes several tools however there was not one reference standard applied to all patients entered into the study.
Did the patient sample include an appropriate spectrum of patients to whom the diagnostic test will be applied in clinical practice?	Not really. Large disproportion of male patients. Patients were pre-selected as having a high PTP for TD. There were 220 pts enrolled from 14 centers in Europe, USA, and Japan. Pts were enrolled on the basis of clinician suspecting TD to the extent that they ordered imaging studies to confirm or deny diagnosis. Eighty-seven were diagnosed with TD, 133 were given other diagnosis. This is a prevalence of 39.5% in the population studied that far exceeds typical prevalence rates of TD of 0.3%. in pts presenting to the ED with chest pain. This large prevalence is also enhanced by inclusion of only pts suspected of having TD by clinician and not simply chest pain.
Did the results of the test being evaluated influence the decision to perform the reference standard?	Results of D-Dimer measurements were not made available to the treating physician and all patients underwent d-dimer as well as a definitive test to r/o TD. It is unclear if clinicians had access to performing D-dimer studies other than the Triage-D-dimer assay that was being tested.
Were the methods for performing the test described	Partially. Patients with onset of symptoms within 24 hours were tested using Triage D-Dimer test (made by Biosite). It appears patients were

in sufficient detail to permit replication?	enrolled in a consecutive fashion creating bias. No clinical rule was applied regarding pre-test probability and high 'suspicion' for TA was left to the discretion of the examiner.
What are the Results?*	
<i>Questions</i>	<i>Comments</i>
Are the sensitivity and specificity and/or likelihood ratios presented or data necessary for their calculation provided?	<p>Yes. A serum level of 500ng/ml (standard used for PE's) was adopted. Sensitivity/Specificity at (0-6hr)= 95.7(95%CI, 78.1 to 99.9)/ 61.3(95% CI, 42.2 to 78.2). Negative likelihood ratio 0.07. Cutoff level >1600 ng/ml @ (0-6hr). Positive likelihood ratio = 12.8.</p> <p>The level of 500ng/ml. Sensitivity/Specificity at (0-24hr)= 96.6(95%CI, 90.3 to 99.3)/ 46.6(95% CI, 37.9 to 55.5). Negative likelihood ratio 0.07. Positive likelihood ratio = 1.81.</p> <p>Also stats for pts with info regarding false lumen patency. (57 patients total, 46 patent, 11 not patent) P values too high, however suggest that false lumen patency associated with higher D-Dimer levels. Patent, mean=3477 ng/ml. Not patent, mean=2351 ng/ml.</p> <p>Average elevations in D-Dimer based on final diagnosis also presented: Acute TD type A 3310ng/ml(3213±1465), Acute AD type B 3902ng/ml(3574±1430), MI 694ng/ml(1459±1650), Angina 319ng/ml(760±974), PE 2765ng/ml(2452±1891), other 676ng/ml(1399±1511).</p>
How Can the Results Apply to Patient Care?*	
<i>Questions</i>	<i>Comments</i>
Will the reproducibility of the test result and its interpretation be satisfactory in my setting?	Yes. Study was reasonably well designed well and was in the setting of ED in 14 countries. Similar results to prior studies, meta-analyses.
Were the study patients similar on critical characteristics to my patients or those we want to generalize to?	<p>Yes. Our facility, NGH was one of the 14 hospital centers included in data collection. However was unable to determine how many patients were obtained from each site. If large number of patients were obtained from one location this could lead to under representation of other patient populations. Critical characteristics included high pre-test probability for all patients enrolled.</p> <p>Specific patient characteristics: 220 patients total, 145 male, 75 female. Median age was presented by final diagnosis: Type A TD(60.6yrs), Type B TD(60.2yrs), MI(65.2yrs), Angina Pectoris(61.7yrs), PE(50yrs), Other(62.2yrs).</p>
Will the results change my management?	Yes. Especially within the first six hours after onset of pain that is suspicious for TD a D-Dimer would be relevant screening test to order. Even over the first 24 hours a positive D-dimer for TD appears to be useful. At this time, algorithm that includes a validated clinical decision rule to determine PTP does not exist. The prevalence of TD is not as well known or studied as the prevalence for PE/DVT therefore NPV and PPV are less certain. It appears that d-dimer can be

	used as an adjunct in risk stratification of those suspected of having TD despite current availability of a validated pre-test prediction rule.
Will patients be better off as a result of the test?	Yes. If the D-Dimer can be employed to reduce unnecessary radiation exposure in those with low PTP who are being evaluated for chest pain. This may assist in reducing unnecessary diagnostic testing and additional radiation exposure.
Do the results of this study fit with other available evidence?	Yes, these results are consistent with other trials as well as two meta-analysis that suggest D-dimer may be a useful when considering the diagnosis of thoracic dissection.

Your Clinical Bottom Line:

This study illustrates that within the initial six hours after onset of symptoms suspicious to a clinician for TD, D-Dimer is a likely to be a useful diagnostic tool. The data also appears to extend to a 24 hour period as well. The result may help providers determine in these select patients that further imaging is unnecessary with D-Dimer less than 500ng/ml. However, further study is needed to broaden this recommendation to patients presenting with vague chest pain whose PTP for an acute dissection is very low.