Meta-analysis of usefulness of D-dimer to diagnose acute aortic dissection

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CRD summary
This review found that plasma D-dimer is a useful screening tool to identify subjects who do not have acute aortic dissection. The author's conclusions are reasonable but the small size of the evidence base and clinical diversity across studies mean that some caution is warranted when interpreting the results.

Authors' objectives
To investigate the utility of plasma D-dimer as a screening tool for acute aortic dissection.

Searching
MEDLINE and EMBASE were searched to 2009 for articles published in English. Search terms were presented. Editorial commentaries, reviews and reference lists were searched.

Study selection
Diagnostic studies of plasma D-dimer as a screening tool for acute aortic dissection were included. Studies had to include a control group without acute aortic dissection. Acute aortic dissection had to occur within two weeks of onset of symptoms and be confirmed using a standard imaging technique. Plasma D-dimer had to be measured using standardised assays. Studies had to present sufficient data to derive true positive and negative rates and false positive and negative rates.

The average age across studies ranged from 53 to 70 and 46% to 94% of the participants were men. Most studies were conducted in Europe or Japan. Computed tomography was used to diagnose acute aortic dissection in all studies; some studies also used other diagnostic methods. Plasma D-dimer was most commonly measured using latex agglutination or turbidimetric assays. Control groups included either healthy subjects or people with other disorders.

It was unclear how many reviewers assessed studies for inclusion.

Assessment of study quality
The QUADAS tool was used to assess study quality.

The authors did not state how many reviewers performed the assessment.

Data extraction
True positive, true negative, false positive and false negative rates were extracted using a 500ng/mL threshold to define a positive finding using plasma D-dimer. Supplemental data from previous reviews reporting that threshold were used if studies did not report data at the 500mg/mL threshold.

Two reviewers independently performed the data extraction.

Methods of synthesis
Sensitivity, specificity, positive and negative predictive values (PPV and NPV), and positive and negative likelihood ratios (LR+ and LR-) were calculated for each study and pooled across studies using DerSimonian-Laird random-effects meta-analyses to generate summary results with 95% confidence intervals (CI). Heterogeneity was assessed using Cochran’s Q test and I^2.

Results of the review
Seven studies were included, with 298 subjects with acute aortic dissection and 436 without (sample size range 16 to 94). Study quality appeared to be generally reasonable but none of the studies made it clear that plasma D-dimer assessments and acute aortic dissection diagnosis were performed blinded to the results of each other.

Pooled sensitivity was 97% (95% CI 94% to 99%; I^2=0%). Pooled specificity was 56% (95% CI 51% to 60%);
I²=82\%).

Pooled PPV was 60\% (95\% CI 55\% to 66\%; I²=39\%). Pooled NPV was 96\% (95\% CI 93\% to 98\%; I²=0\%).

Pooled LR+ was 2.43 (95\% CI 1.89 to 3.12; I²=78\%). Pooled LR- was 0.06 (95\% CI 0.03 to 0.12; I²=0\%).

**Authors’ conclusions**

Plasma D-dimer at a threshold of 500ng/mL is a useful screening tool to identify subjects who do not have acute aortic dissection and who are therefore unlikely to benefit from further aortic imaging.

**CRD commentary**

This diagnostic review addressed a relevant research question using appropriate inclusion criteria. A suitable search was performed but only studies published in English were included so some relevant studies may have been missed. Apart from the data extraction, it was unclear whether action was taken to avoid reviewer error and bias. Study quality was assessed and appeared to be moderate to good in most studies but it was not clear that tests were performed blind to patient characteristics. All studies were observational in nature and may have been affected by confounding or other biases.

Estimates of diagnostic performance were pooled in meta-analyses but the correlation between sensitivity and specificity, and between other measures was not accounted for and this may have produced misleading results. Only one threshold of plasma D-dimer (500ng/mL, based on its use in identifying pulmonary emboli rather than acute aortic dissection) was used; it was unclear whether other thresholds might give more favourable results. The number of participants was small. The considerable diversity in the clinical conditions across studies was reflected in high heterogeneity across studies in some analyses.

The results and the authors’ conclusions are reasonable given the evidence available but some caution is needed when interpreting the results due to the limited sample size and clinical diversity.

**Implications of the review for practice and research**

**Practice:** The authors suggested that use of plasma D-dimer may aid physicians when deciding whether to order additional diagnostic procedures to confirm diagnoses of acute aortic dissection.

**Research:** The authors recommended that further prospective studies were needed to investigate the usefulness of plasma D-dimer in different clinical settings.

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