Adenosine deaminase and tuberculous pericarditis: a systematic review with meta-analysis

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CRD summary
This review found that adenosine deaminase activity has clinical value as a diagnostic marker for tuberculous pericarditis. The authors' conclusions are supported by the data presented, but should be interpreted with some degree of caution given the limitations of the literature search, failure to appropriately assess study quality, and insufficient details of the included studies.

Authors' objectives
To determine the accuracy of adenosine deaminase (ADA) as a diagnostic marker of tuberculous pericarditis (TP) in patients with pericardial effusion (PE).

Searching
MEDLINE, LILACS and the Cochrane Library were searched from 1980 to August 2005; the search terms were reported. The bibliographies of included studies were screened. Only studies reported in the English language were included.

Study selection
Prospective studies that assessed ADA activity in PE in patients with TP, and that provided sufficient data to calculate the sensitivity and specificity, were eligible for inclusion. The method used to determine ADA activity had to be the same in all studies (it is unclear whether the methodology was specified a priori) and studies had to report data at a threshold of 40 U/L to define a positive ADA result. All studies used the Giusti methodology to measure ADA.

Inclusion criteria were not defined in terms of the reference standard. Diagnostic criteria for TP included Mycobacterium tuberculosis positive in PE or tissue culture, histopathological examination of pericardial with granulomas containing alcohol-acid resistant bacilli granulomas in pericardial tissue associated with active tuberculosis in another site, and clinical and/or laboratory evidence of TP that had clinical improvement after empirical treatment for tuberculosis. The control groups included patients with pericardial diseases with moderate to large PE, excluding those whose effusion was cardiac surgery related.

Two reviewers independently selected studies for inclusion in the review and any disagreements were resolved by consensus.

Assessment of study quality
The studies were assessed according to whether they included a consecutive or random sample, whether they included more than 10 patients with TB, the method used to measure ADA, and whether they used a case-control design.

The authors did not state how the validity assessment was performed.

Data extraction
The data were extracted as 2x2 tables of test performance. The sensitivity, specificity, positive and negative predictive values, and diagnostic odds ratios, together with 95% confidence intervals (CIs), were calculated for each study.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
A summary receiver operating characteristic curve was constructed. All reported accuracy measures were pooled, although details of the exact methods used were not reported. Publication bias was assessed using Egger's test.
Heterogeneity was assessed using the $\chi^2$ test.

**Results of the review**

Five studies (n=462) were included.

All studies enrolled consecutive patients and used a diagnostic cohort design; four included more than 10 patients with tuberculosis.

The sensitivity ranged from 83 to 100% and the pooled sensitivity was 88% (95% CI: 82, 91). There was no evidence of heterogeneity (p=0.108). The specificity ranged from 78 to 100% and the pooled specificity was 83% (95% CI: 78, 88). There was strong evidence of heterogeneity (p=0.004). There was no evidence of publication bias (p=0.1433).

**Authors' conclusions**

ADA activity has clinical value as a diagnostic maker for TP among other causes of PE.

**CRD commentary**

The review addressed a focused question with defined inclusion criteria. Inclusion criteria relating to the index test appear to have been very narrow, so potentially interesting studies might have been excluded from the review. The literature search was limited to three databases, no attempts were made to locate unpublished studies, and the review was restricted to English language studies. The possibility of publication bias was assessed but the method used to do so was not appropriate for diagnostic studies; the possibility of language and publication bias therefore remains. Appropriate steps were taken to minimise bias in the selection of studies, but it is unclear whether such steps were also taken for the extraction of data and quality assessment. Although a quality assessment was carried out and the results of this assessment reported, many important quality features were not considered and the quality of the primary studies is therefore unclear. The generalisability of the results is also unclear since very few details on the included studies were presented. The methods used to pool the studies were acceptable but the use of more robust methods, such as the bivariate method, would have been preferable. The authors' conclusions are supported by the data presented, but should be interpreted with some degree of caution given the limitations of the literature search, failure to appropriately assess study quality, and the lack of details of the included studies.

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

Practice: The authors stated that ADA is a simple and affordable test with enormous clinical value in the diagnosis of tuberculosis PEs.

Research: The authors stated that multicentre studies should be performed to establish more efficient criteria to differentiate pericardial tuberculosis from other pericardial diseases.

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