Detection of heart transplant rejection in adults by echocardiographic diastolic indices: a systematic review of the literature
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CRD summary
This review concluded that current evidence does not support the use of echocardiography to predict allograft rejection in patients who have undergone heart transplants. Although the conclusions are supported by the data presented, they should be interpreted with extreme caution given the limitations of the search and the failure to investigate differences between the studies.

Authors' objectives
To review the accuracy of diastolic indices (DI) in predicting heart transplant rejection.

Searching
MEDLINE was searched from 1967 to July 2005 for publications in the English language. The keywords, which were reported, did not include a diagnostic filter. The reference lists of retrieved articles were screened to identify additional studies.

Study selection
Study designs of evaluations included in the review
Cross-sectional and cohort studies were eligible for inclusion.

Specific interventions included in the review
Studies that evaluated DI on echocardiography for diagnosing allograft rejection were eligible for inclusion. The DI evaluated by the included studies were: mitral inflow velocities (early and late diastolic wave peak velocity, pressure half time and isovolumetric relaxation time); velocity of propagation of left ventricular colour Doppler inflow; pulmonary vein Doppler flow (systolic wave peak velocity and early diastolic wave peak velocity); and tissue Doppler (early and late diastolic wave, and early diastolic wave peak velocity/early diastolic wave ratio).

The studies used different cut-off values to diagnose rejection.

Reference standard test against which the new test was compared
Studies that used biopsy results as the reference standard were eligible for inclusion. It appears that the reference standard in all the included studies was endomyocardial biopsy, although the reporting of this was not clear.

Participants included in the review
Studies in adults (age at least 19 years) who had undergone heart transplantation were eligible for inclusion. The participants had a mean age of 49 years and 76% were male.

Outcomes assessed in the review
The authors stated that studies had to report the correlation between echocardiography and biopsy to be included in the review. The primary outcomes reported in the review were the sensitivity, specificity, and positive and negative likelihood ratios (LRs).

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Studies were assessed for methodological quality according to the following criteria: presence of a reference standard;
independent, blind comparison with a standard; reference standard performed regardless of the result of the index test; sufficient details reported on the execution of the index test; presentation of LRs or information provided to calculate LRs; reproducibility of the test reported. The authors did not state how many reviewers performed the validity assessment.

Data extraction
Three reviewers independently extracted the data and resolved any disagreements through consensus. Where possible, the sensitivity, specificity, and positive and negative LRs were calculated for each DI investigated.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
Heterogeneity was not formally investigated. Differences between the studies were discussed in the text and the results were grouped according to DI investigated.

Results of the review
Nineteen studies were included. The sample size ranged from 7 to 264.

Thirteen studies included an independent blind comparison with a reference standard. All studies provided sufficient information on the methods used to measure the DI. Four studies presented data on reproducibility. None of the studies reported LRs but 11 studies reported sufficient data to calculate them.

The data reported below are only for those studies that provided sufficient information to calculate diagnostic accuracy. Limited results for other studies were reported in the paper.

Pressure half time (7 studies): the sensitivity ranged from 23 to 87% and the specificity from 76 to 98%. The variation did not appear to be related to threshold as there was considerable heterogeneity in the estimates, even between studies that used the same threshold.

Isovolumetric relaxation time (6 studies): the sensitivity ranged from 28 to 85% and the specificity from 79 to 98%. The variation did not appear to be related to threshold as there was considerable heterogeneity in the estimates, even between studies that used the same threshold.

Tissue Doppler late diastolic wave (2 studies): the sensitivity was 67% and 82%; the specificity was 49 and 53%.

Tissue Doppler early diastolic wave (2 studies): the sensitivity was 69% and 76%; the specificity was 59% and 88%.

Authors' conclusions
The evidence does not support the use of echocardiography to predict allograft rejection in patients who have undergone heart transplants.

CRD commentary
This review addressed a focused question but the inclusion criteria lacked clarity. The literature search was limited to one electronic database and was restricted to studies published in English. It is therefore likely that relevant studies have been missed and the review may be subject to language and publication bias. A quality assessment was carried out but this failed to address some important quality issues for test accuracy studies, and although the results of this were presented they were not considered in the synthesis of results. Details of the review process were incomplete, so it is not possible to determine whether appropriate steps were consistently taken to minimise bias.
Very limited details on the included studies were reported and, although this may have been due to limited reporting in the original studies, it is difficult to assess the generalisability of the results. The narrative synthesis might have been appropriate given the variation between the studies, but an investigation of the reasons for this heterogeneity would have improved this review. Although the conclusions are supported by the data presented, they should be interpreted with extreme caution given the limitations in the search and the failure to investigate heterogeneity between the studies.

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

Practice: The authors stated that the evidence currently available does not support the use of echocardiography to predict allograft rejection.

Research: The authors stated that there is a need for larger, high-quality studies in this area to evaluate newer DI such as tissue Doppler.

**Bibliographic details**


**PubMedID**

17000376

**DOI**

10.1016/j.echo.2006.04.029

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Adult; Blood Pressure; Diastole; Echocardiography /methods; Female; Graft Rejection /etiology /ultrasonography; Heart Transplantation /adverse effects /ultrasonography; Humans; Male; Prognosis; Severity of Illness Index; Stroke Volume; Treatment Outcome; Ventricular Dysfunction, Left /ultrasonography

**AccessionNumber**

12006007435

**Date bibliographic record published**

29/02/2008

**Date abstract record published**

29/02/2008

**Record Status**

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.