Diagnostic accuracy of echocardiography for pulmonary hypertension: a systematic review and meta-analysis

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CRD summary
This review concluded that, given the limitations of echocardiography, diagnosis of pulmonary hypertension and the assessment of response to therapies required right heart catheterisation. These conclusions reflect the data presented, but should be interpreted cautiously given the possibility of missed studies and generation of pooled estimates from clinically and statistically heterogeneous data.

Authors' objectives
To assess the accuracy of echocardiography (tricuspid regurgitant jet method) for detection of pulmonary hypertension and determine the correlation of pulmonary pressures obtained by echocardiography with those obtained by right heart catheterisation.

Searching
MEDLINE, EMBASE, PapersFirst and The Cochrane Library were searched to February 2010. Search terms were reported. Searches were limited to studies in English. Bibliographies of retrieved articles were screened for additional studies.

Study selection
Studies of adult patients (more than 18 years) in whom right ventricular systolic pressure (RVSP) was measured by Doppler transthoracic echocardiography and calculated from the maximum tricuspid regurgitation jet velocity by using the modified Bernoulli equation (4v²) and adding right atrial pressure (RAP) were eligible for inclusion. RAP had to be estimated from jugular venous pressure (JVP), given a fixed value from 5mmHg to 10mmHg or estimated by measuring the inferior vena cava size and change with spontaneous respiration using echocardiography. Included studies had to measure systolic pulmonary arterial pressure (sPAP) by right heart catheterisation (reference standard) and perform echocardiography within three months of the right heart catheterisation.

Studies had to report data on the correlation between RVSP measured by echocardiography and sPAP measured by right heart catheterisation or sufficient data to populate 2x2 contingency tables (numbers of true positive, false negative, false positive and true negative test results).

Most of the included studies were published between 2000 and 2009, were performed in USA and were prospective in design. Mean age of study populations was 58 years. Mean percentage of male participants was 58%. Study populations varied and included participants with cardiac disease (various causes), lung disease (various causes), or mixed cardiac and lung disease.

Studies were independently assessed for inclusion by two reviewers. Disagreements were resolved by consensus or consultation with a third reviewer.

Assessment of study quality
The methodological quality of included studies was independently assessed by two reviewers using the 14-item QUADAS tool; any disagreements were resolved by consultation with a third reviewer.

Data extraction
Data were extracted on: mean values for sPAP by echocardiography and right heart catheterisation and correlation coefficient between these two measures; threshold values for determining pulmonary hypertension using echocardiography and right heart catheterisation; and 2x2 contingency data for echocardiography compared with right heart catheterisation. Sensitivity and specificity of echocardiography for pulmonary hypertension, with 95% confidence intervals (CIs), were calculated for each study.
The authors did not specify how many reviewers performed the data extraction.

**Methods of synthesis**

A summary correlation co-efficient, with 95% CIs, was calculated using a random-effects model.

Summary estimates of sensitivity and specificity, with 95% CIs, were calculated using a bivariate model. Overall positive and negative likelihood ratios were calculated from the summary estimates of sensitivity and specificity. Subgroup analyses were carried out for different study populations (pulmonary hypertension, transplant of heart, lung, or liver and heart failure).

Between-study heterogeneity was assessed using the $I^2$ statistic and explored using various sensitivity analyses. Publication bias was assessed using the Egger method and a funnel plot.

**Results of the review**

Twenty-nine studies with a total of 1,485 participants for whom echocardiography was possible were included in the review. Twenty-seven studies reported correlation coefficients for echocardiography versus right heart catheterisation and 12 studies reported sufficient data to calculate sensitivity and specificity. No study reported whether investigators who used the reference standard of right heart catheterisation were aware of the results of echocardiography and 24 studies did not report information on blinding of investigators performing the index test (echocardiography) to the results of right heart catheterisation. Five studies were considered to be at risk of spectrum bias because they recruited a selected patient group (patients with pulmonary hypertension). Eight studies were at risk of disease progression bias because the time interval between index test and reference standard was not reported (five studies) or was more than a month (three studies).

The summary correlation coefficient between echocardiography and right heart catheterisation-derived sPAP was 0.70 (95% CI 0.67 to 0.73). The $I^2$ statistic was 99% (95% CI 88 to 99) and indicated significant heterogeneity between the studies. Subgroup analyses gave summary correlation coefficients of 0.65 (95% CI 0.61 to 0.69; 12 studies) for studies with mean sPAP of 50mmHg or less and 0.71 (95% CI 0.65 to 0.77; eight studies) for studies with mean sPAP more than 50mmHg. Egger's test and an asymmetric funnel plot indicated significant publication bias.

The overall summary estimates of sensitivity was 83% (95% CI 73 to 90) and for specificity was 72% (95% CI 53 to 85). The summary positive likelihood ratio was 3.0 (95% CI 1.7 to 5.3) and the summary negative likelihood ratio was 0.24 (95% CI 0.14 to 0.39). $I^2$ was high (>80%) for both sensitivity and specificity and heterogeneity was not explained by threshold effect.

Sensitivity analyses did not reveal a significant source of heterogeneity for either the correlation coefficient analysis or the diagnostic accuracy analysis.

**Authors' conclusions**

The authors concluded that there was modest correlation between sPAP estimated from echocardiography compared with measured by right heart catheterisation for mild to moderate values of sPAP. Diagnostic accuracy for echocardiography for pulmonary hypertension with a sPAP threshold of 40mmHg was relatively modest.

**CRD commentary**

The review reported a clear research question and specified detailed inclusion criteria. Several sources were searched to identify relevant studies. The restriction to studies in English raised the possibility of language bias and means that relevant studies may have been omitted. The authors minimised the risk of error and bias during study selection and quality assessment; no such measures were reported for data extraction but it seemed likely that they were applied throughout the review. The methodological quality of included studies was assessed and reported in full and details of included study populations were provided. Appropriate methods were used to generate pooled estimates of test performance, although the validity of grouping these studies together was questionable given the apparent presence of significant heterogeneity not explained by threshold variation. Similarly, the validity of generating a pooled estimate of correlation was questionable, particularly given the apparently high degree of clinical and statistical heterogeneity.

The authors' cautious conclusions reflect the data presented, but should be interpreted cautiously given the possibility of missing studies and generation of pooled estimates from apparently clinically and statistically heterogeneous data.
Implications of the review for practice and research

**Practice:** The authors stated that when using echocardiography to measure pulmonary pressures, clinical context, prevalence of pulmonary hypertension in the patient population and other echocardiographic parameters of the right ventricle should be taken into consideration. They stated that limitations of echocardiography mean that diagnosis of pulmonary hypertension and assessment of response to therapies required right heart catheterisation.

**Research:** The authors did not specify any recommendations for future research.

**Funding**
Vancouver General Hospital and University of British Columbia, Canada.

**Bibliographic details**

**PubMedID**
21357375

**DOI**
10.1136/hrt.2010.212084

**Original Paper URL**
http://heart.bmj.com/content/97/8/612.abstract

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Aged; Cardiac Catheterization; Echocardiography, Doppler; Epidemiologic Methods; Humans; Hypertension, Pulmonary /diagnosis /ultrasonography; Middle Aged; Young Adult

**AccessionNumber**
12011002753

**Date bibliographic record published**
05/10/2011

**Date abstract record published**
16/05/2012

**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.