A health technology assessment of transient elastography in adult liver disease

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CRD summary
This review concluded that non-invasive transient elastography was accurate for diagnosing the stage of fibrosis in patients with moderate fibrosis or cirrhosis. The evidence was extensive and the findings were generally consistent across studies. There was potential for review bias and uncertainty about variation, but the authors' conclusions reflect the evidence and their recommendations for further research seem reasonable.

Authors' objectives
To assess the clinical and cost-effectiveness of non-invasive ultrasound transient elastography to assess the stage of fibrosis in certain types of liver disease.

Searching
Eight databases, including PubMed, EMBASE, and DARE, were searched for publications between 2001 and June 2011 in English or French. Search terms were reported. Grey literature sources were searched.

Study selection
Eligible for inclusion were cohort studies assessing the safety and efficacy of non-invasive transient elastography to diagnose the stage of fibrosis in adults (over 18 years old). Patients had any of five types of chronic liver disease: hepatitis B, hepatitis C, non-alcoholic fatty liver disease, cholestatic liver disease, and complications after liver transplant. The accuracy of transient elastography had to be compared with that of liver biopsy, and liver histology had to be reported using METAVIR or a similar classification system. Studies had to report sensitivity and specificity or positive and negative predictive values, or sufficient data to calculate these measures. The outcomes of interest were the accuracy in differentiating between stages of fibrosis: mild (stage 1 or less), moderate (stage 2 or more), severe (stage 3 or more), and cirrhosis (stage 4); and complications. This scoring system did not accurately reflect the METAVIR system, but it was the system used by the authors.

The characteristics were only presented for just over half of the included studies. The mean patient age ranged from 35 to 68 years, and most of them were male.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
Study quality was assessed according to the 14-item QUADAS. The authors did not state how many reviewers assessed quality.

Data extraction
True and false positives, true and false negatives, sensitivities and specificities, and positive and negative predictive values were extracted to calculate summary estimates.

Two independent reviewers extracted the data. Discrepancies were resolved by consensus.

Methods of synthesis
A bivariate meta-analysis was used to jointly pool the sensitivity and specificity scores, and to estimate the area under the summary receiver operating characteristic curve. Diagnostic accuracy was defined as excellent (AUC 0.9 to 1.0), strong (0.8 to 0.9), good (0.7 to 0.8), sufficient (0.6 to 0.7), poor (0.5 to 0.6), or test not useful (<0.5). Positive and negative predictive values for each of the described studies were reported.

Statistical heterogeneity was assessed using I². Meta-regression was undertaken to assess any sources of heterogeneity. Sensitivity analyses were performed by type of liver disease. Publication bias was assessed in funnel plots and the Egger test.
Results of the review

Fifty-seven studies were included in the review; the total number of participants was unclear. Most studies were of high quality (range 10 to 14); 78% of studies scored the maximum 14. The results were not reported for one study.

The diagnostic accuracy of transient elastography was strong for detecting moderate fibrosis (stage 2 or more). The area under the curve was 0.88 (95% CI 0.84 to 0.90; 45 studies; sensitivity 80%, 95% CI 76 to 83; specificity 81%, 95% CI 77 to 85). Accuracy was excellent for severe fibrosis (stage 3 or more). The area under the curve was 0.92 (95% CI 0.89 to 0.94; 35 studies; sensitivity 84%, 95% CI 81 to 87; specificity 87%, 95% CI 83 to 90). Accuracy was excellent for cirrhosis (stage 4). The area under the curve was 0.94 (95% CI 0.91 to 0.96; 49 studies; sensitivity 86%, 95% CI 82 to 89; specificity 89%, 95% CI 87 to 91).

Subgroup analyses by type of liver disease and fibrosis stage showed that the accuracy for moderate fibrosis was generally strong for patients with hepatitis B, hepatitis C, non-alcoholic fatty liver disease, and liver transplant patients (AUC range 0.78 to 0.89). For severe fibrosis, it was strong for patients with hepatitis B (AUC 0.89) or hepatitis C (AUC 0.92). For cirrhosis, it was strong to excellent for patients with hepatitis B (AUC 0.86), hepatitis C (AUC 0.94), or non-alcoholic fatty liver disease (AUC 0.96); the results were fully reported. There was insufficient evidence to assess accuracy in patients with hepatitis A or cholestatic liver disease, and for severe fibrosis and cirrhosis in liver transplant patients. There was evidence of statistical heterogeneity across different disease categories and fibrosis stages.

There was some evidence that mean age and the percentage of failures had an impact on diagnostic accuracy; full results of the meta-regression were reported. There was no evidence of publication bias.

Cost information

All costs were reported in 2010 Canadian dollars (CAD). On average, liver biopsy cost an additional CAD 362 per procedure compared with transient elastography. The additional cost per correct diagnosis with liver biopsy, compared with transient elastography, ranged from CAD 1,427 to CAD 7,030 depending on the type of liver disease. Other results were reported.

Authors' conclusions

Transient elastography was accurate and cost-effective for diagnosing patients with moderate fibrosis or cirrhosis.

CRD commentary

The review question and supporting inclusion criteria were clearly stated. A comprehensive search of the literature was undertaken, but as the search was limited by language, language bias cannot be ruled out. Data extraction was performed by two people, but it was unclear whether this was true for study selection and quality assessment. The potential for reviewer error and bias cannot be ruled out. Study quality was assessed using appropriate criteria, which indicated that they were generally of high quality. Due to the nature of the studies, none were randomised controlled trials.

Patient and study details were brief, and were not provided at all for almost half the studies. It was therefore unclear what test thresholds were used and it was difficult to determine how similar or different the studies were. The authors explored the sources of heterogeneity to some extent. Appropriate methods were used to calculate summary receiver operating characteristic curves, and summary estimates for sensitivity and specificity. The authors acknowledged that most studies were of patients with hepatitis C, and the need for validation for other types of liver disease. They stated that quality assessment did not include intention-to-treat analysis, making it unclear whether some studies were biased.

The evidence was extensive and the findings were generally consistent across studies, suggesting that transient elastography has good diagnostic accuracy. There was potential for bias in the review and some uncertainty about variation across studies, which suggest an overestimation of the results, but the authors' conclusions reflect the evidence and their recommendations for further research seem reasonable.

Implications of the review for practice and research

Practice: The authors stated that transient elastography should be considered for the non-invasive assessment of liver fibrosis.
Research: The authors stated that further research was required to assess the accuracy of transient elastography in patients with hepatitis A and cholestatic liver disease, and in monitoring fibrosis progression.

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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.