A meta-analysis of transient elastography for the detection of hepatic fibrosis

CRD summary
This review found that transient elastography appeared to be an important non-invasive method for the assessment of liver fibrosis, but further research is needed. Potential biases in the review process and lack of clarity of study design and quality means that the results of the review should be interpreted with caution; the reliability of the authors’ conclusion is unclear.

Authors’ objectives
To evaluate the use of transient elastography to assess liver stiffness measurement compared with liver biopsy for the diagnosis of liver fibrosis.

Searching
PubMed, Current Contents and the Cochrane Library were searched for relevant studies in English; search terms were reported but search dates were not. Google Scholar, textbooks, medical reports from the United Nations and the World Health Organisation were also searched. References of retrieved articles were checked to identify additional studies. Experts in the field were contacted.

Study selection
Primary studies that assessed the accuracy of transient elastography (index test) compared with liver biopsy (reference or gold standard) for the diagnosis of liver fibrosis were eligible for inclusion. Studies had to provide detailed descriptions of the patients. Eligible studies were required to report optimal cut-offs or cut-offs in stiffness values, and/or diagnostic accuracy data suitable for meta-analysis (sensitivity, specificity, positive and negative predictive values, and area under receiver operating characteristic curves). Studies that compared transient elastography with other non-invasive serum markers were also included.

All the included studies were conducted in large or regional hospitals. The enrolled patients presented with mixed aetiologies, including hepatitis B virus, hepatitis C virus and hepatitis C post-orthotopic liver transplantation, HIV, and non-alcoholic fatty liver disease. The mean body mass index of included patients ranged from 21 to over 30kg/m²; their mean age ranged from 42 to 63 years; most were men. Percutaneous liver biopsies were performed in most studies; transjugular liver biopsies were performed in some studies. Most of the studies correlated liver stiffness measurements and fibrosis staging by histopathology according to the five-step METAVIR scoring system (ranging from F0 to F4). Significant fibrosis corresponded to cut-off values (in kilopascals) of up to F2; liver cirrhosis corresponded to a cut-off value of F4.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
The authors did not state that they formally assessed methodological quality, but did report on consecutive enrolment of patients into studies and some limited detail on the blinding used in the studies.

Data extraction
Cut-off data and diagnostic accuracy data were extracted from the studies by one statistician. Where cut-off data were available, they were used to calculate mean liver stiffness values (in kilopascals) and 95% confidence intervals (CIs) for significant fibrosis (up to F2) and cirrhosis (F4). Where diagnostic accuracy data were provided, kilopascal scores along with sensitivities and specificities were calculated for significant fibrosis and cirrhosis.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
The results were summarised in a meta-analysis. Overall weighted mean kilopascal values for up to F2 and pooled sensitivity and specificity values with corresponding 95% confidence intervals (CI) were reported.

Results of the review
Twenty-two studies (n=4,760 patients) were included in the review. The median sample size was 97 patients (range 30 to 1,007). Nineteen studies enrolled patients consecutively, although in one further study, recruitment of patients took place from the cohort. The liver biopsies were obtained blinded to transient elastography, but the results of transient elastography were not explicitly reported to have been obtained blind to liver biopsies.

Diagnostic cut-off levels: The weighted mean kilopascal of significant liver fibrosis (up to F2) was 7.81 (95% CI 7.77 to 7.85; n=3,514 patients) and liver cirrhosis (F4) was 15.56 (95% CI 15.50 to 15.70; n=4,430 patients) in studies that reported cut-offs (22 studies).

Liver fibrosis diagnosis (up to F2): In 17 studies that provided diagnostic accuracy data of transient elastography, the pooled sensitivity of the kilopascal score for significant liver fibrosis was 71.9% (95% CI 71.4 to 72.4; n=3,066 patients) and the specificity of the score was 82.4% (95% CI 81.9 to 82.9; n=3,066 patients). The kilopascal score for significant fibrosis was 7.71 (95% CI 7.67 to 7.75).

Liver cirrhosis diagnosis (F4): In studies that evaluated diagnostic test data of liver stiffness measurements by transient elastography for liver cirrhosis, the sensitivity was 84.45% (95% CI 84.2 to 84.7; n=4,052 patients) and the specificity was 94.69 (95% CI 94.3 to 95.0; n=4,052 patients). The kilopascal score of 15.08 (95% CI 15.0 to 15.10).

Authors' conclusions
Transient elastography appeared to be an important non-invasive method for the assessment of liver fibrosis, but evaluation in prospective studies is necessary to further increase the sensitivity of this diagnostic test and establish the clinical utility of this intervention.

CRD commentary
The review addressed a broad question. Criteria for the inclusion of studies were stipulated. The restriction of the review to studies published only in English meant that there was a risk of language bias; no search dates were reported. The authors did not report steps to minimise errors and biases at any point of the review process.

The design and quality of the included studies was not clear. Although the authors stated that data were available on predictive values and receiver-operator curves, these results were not presented in the review. The methods used to combine studies were not clearly reported. It was not clear whether pooling of the studies was appropriate. There were no examinations of statistical heterogeneity across the results.

Potential biases arising from the review process and missing information on diagnostic test results means that the results of the review should be interpreted with caution; the reliability of the authors' conclusion remains unclear.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further evaluation of transient elastography is required in prospective studies because the sensitivity and specificity of the test is not high enough for routine use on practice. Future studies should focus on large numbers of well-defined patients with variable body mass, including patients with non-viral hepatitis and non-alcoholic steatohepatitis.

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