Systematic review and meta-analysis of the diagnostic accuracy of fibrosis marker panels in patients with HIV/hepatitis C coinfection

Shaheen AA, Myers RP

CRD summary
This review found that available fibrosis marker panels have acceptable performance for identifying significant fibrosis and cirrhosis in human immunodeficiency virus/hepatitis C virus coinfected patients, but were not yet adequate to replace liver biopsy. This was generally a well conducted review. The authors’ conclusions are likely to be reliable.

Authors’ objectives
To determine the accuracy of serum marker panels for predicting fibrosis in patients with human immunodeficiency virus (HIV) and hepatitis C virus (HCV) coinfection.

Searching
MEDLINE, EMBASE and The Cochrane Library were searched from 1997 to September 2006. Search terms were reported. References of relevant studies were screened. No language restrictions were applied.

Study selection
Studies that evaluated the accuracy of a panel of serum markers for the prediction of fibrosis in HIV/HCV coinfected patients that used liver biopsy as the reference standard were eligible for inclusion. Studies had to include more than 30 patients and report sufficient data to allow construction of a 2x2 table of test performance. Studies that included other liver diseases were eligible if data could be extracted separately for patients with HIV/HCV coinfection. The primary outcome was identification of significant fibrosis (defined as METAVIR stages F2-4 or Ishak stages F3-6). Prediction of cirrhosis was also considered.

Four studies assessed aspartate aminotransferase (AST)-platelet ratio index (APRI). Two studies assessed Forns’ index. FibroTest and SHASTA index were each assessed in single studies. Median patient age was 40 years. The proportion of males was 77%. Nearly all patients were on antiretroviral therapy. Median CD4 count was 429/mm$^3$.

Two reviewers independently assessed studies for inclusion. Disagreements were resolved through consensus.

Assessment of study quality
Two reviewers independently assessed study quality using QUADAS. Disagreements were resolved through consensus.

Data extraction
Two reviewers independently extracted data as 2x2 tables of test performance for each threshold reported in the study. Disagreements were resolved through consensus.

Methods of synthesis
Summary sensitivity and specificity together with 95% confidence intervals (CI) were estimated using the bivariate model for studies that reported on single tests at consistent thresholds. Summary receiver operating characteristic (SROC) curves were constructed using the methods of Moses et al. Summary diagnostic odds ratios (DORs) together with 95% CIs were estimated using DerSimonian and Laird random-effects models. Meta-regression was used to examine the impact of fibrosis measure, study quality, patient characteristics and reference standard on test performance. Publication bias was assessed using a regression-based test of funnel plot asymmetry.

Results of the review
Five studies were included in the review (n=574). Study quality was excellent: four studies scored 14 out of 14 and two scored 13 out of 14 on the QUADAS assessment.

Prediction of fibrosis (four studies): Prevalence of significant fibrosis was 51%. The summary diagnostic odds ratio
was 7.8 (95% CI 5.1 to 11.9; four studies) for prediction of significant fibrosis across all tests. There was no evidence of heterogeneity (p=0.68). Meta-regression found no significant association between any of the variables investigated and estimates of test accuracy. The summary diagnostic odds ratio for the APRI test was 6.8 (95% CI 3.8 to 12.1; three studies). There was no evidence of heterogeneity (p=0.79). At a threshold of 0.5, summary sensitivity and specificity for the APRI were 86% (95% CI 73% to 93%) and 41% (95% CI 34% to 48%). At the higher threshold of 1.5, summary sensitivity was 50% (95% CI 43% to 56%) and specificity was 92% (95% CI 87% to 95%).

Prevalence of cirrhosis: Prevalence of cirrhosis was 16%. Summary diagnostic odds ratio was 11.0 (95% CI 4.6 to 26.2; four studies) for cirrhosis. There was no evidence of statistical heterogeneity (p>0.2).

Authors’ conclusions
Available fibrosis marker panels had acceptable performance for identifying significant fibrosis and cirrhosis in HIV/HCV coinfected patients, but were not yet adequate to replace liver biopsy.

CRD commentary
The review addressed a focused question supported by clearly defined inclusion criteria. The literature search was adequate for published studies. No specific attempts were made to locate unpublished studies and so there was a possibility of publication bias. Although this was assessed in the review, methods used were not appropriate for diagnostic data. Study quality was assessed using appropriate criteria, but the results of the assessment were presented only as summary scores. However, these were very high and so this was less of a problem than if there had been greater variation across studies. Appropriate methods were used to pool data and the results were clearly presented. This was generally a well-conducted review. The authors’ conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that accuracy of fibrosis marker panels was not yet adequate to replace liver biopsy.

Research: The authors stated that additional studies in large cohorts were necessary to identify the optimal measure and generate more precise tools for future clinical use.

Bibliographic details

PubMedID
18215981

DOI
10.1310/hct0901-43

Original Paper URL
http://thomasland.metapress.com/content/23hl2931m1625p48/

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Biomarkers /blood; Female; HIV Infections /complications /virology; Hepatitis C /complications /virology; Humans; Liver Cirrhosis /diagnosis /virology; Male; Middle Aged

AccessionNumber
12008005811

Date bibliographic record published
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.