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NAFLD: non-invasive tests or biopsies

K Simpson
Consultant in Hepatology, Centre for Liver & Digestive Disorders, Royal Infirmary of Edinburgh, Edinburgh, UK

TITLE Non-invasive markers of fibrosis in non-alcoholic fatty liver disease: validating the European Liver Fibrosis Panel and exploring simple markers

AUTHORS Guha IN, Parkes J, Roderick P et al.

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Correspondence to ***KJ Simpson, Centre for Liver & Digestive Disorders, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh EH16 4SA, UK***

tel. ***+44 (0)131 242 1621***
fax. ***+44 (0)131 242 1633***
e-mail ***k.simpson@ed.ac.uk***

SUMMARY

Non-alcoholic fatty liver disease (NAFLD) is a major cause of liver disease. It is important to identify NAFLD patients with hepatic fibrosis, who may benefit from current or future therapies, and those with cirrhosis for whom cancer surveillance, variceal prophylaxis or transplantation may be important. Currently, these patients can only be identified with confidence by liver biopsy, but biopsy is hazardous, subject to sampling error and impractical for screening large numbers of patients.

This study of 192 patients with NAFLD, who had had liver biopsies, aimed to test the ability of non-invasive markers to detect fibrosis of varying severity. The tests used were the original European liver fibrosis (OELF) test (age, tissue matrix metalloprotein inhibitor, hyaluronic acid and amino-terminal peptide of procollagen), the enhanced liver fibrosis (ELF) test (omitting age) and a panel of simple markers (age, body mass index, diabetes mellitus, impaired fasting glucose, aspartate aminotransferase (AST) / alanine aminotransferase (ALT) ratio, platelets and albumin).

The OELF and ELF tests performed similarly, and the analysis was done using the simpler ELF test. This test had an area under the curve of 0.90 for identifying severe fibrosis, 0.82 for moderate fibrosis and 0.76 for no fibrosis. Adding simple markers increased the test performance to 0.98, 0.93 and 0.84 respectively. Using the ELF alone to identify severe fibrosis would have avoided liver biopsy in 86% of patients (76% correctly), to identify moderate fibrosis would have avoided biopsy in 62% (52% correctly) and to identify any fibrosis would have avoided biopsy in 48% (38% correctly).

The authors conclude that while non-invasive tests will never replace liver biopsy, the ELF test with or without simple markers can identify those among the many patients with possible NAFLD who have early fibrosis, and those with severe fibrosis who require careful surveillance.

COMMENT

Non-alcoholic fatty liver disease is in all respects an enormous problem affecting the Western world and is becoming more prevalent in cultures previously considered to have low risk, such as the Far East. Non-invasive assessment of liver fibrosis would avoid the hazards of liver biopsy, remove the problem of sampling error and allow appropriate targeting of therapy and screening for complications such as oesophageal varices and hepatoma.

This paper suggests that the measurement of circulating markers can effectively identify severe fibrosis and avoid the need for liver biopsy in the majority of patients with NAFLD. The components (tissue inhibitor of matrix metalloproteinase 1, hyaluronic acid and amminoterminal peptide of pro-collagen III) of the ELF test required analysis by a central reference laboratory. However, the ELF test performed better than a scoring system derived from more routinely available data, such as age, AST/ALT ratio, platelets and albumin, and a combination of both systems produced the best results.

These data do not address whether the temporal progression of liver fibrosis is associated with worsening ELF tests, nor can they be directly translated to other causes of liver cirrhosis. However, earlier reports of ELF testing suggest that the discrimination of advanced fibrosis may be better in alcoholic liver disease and less good in hepatitis C, and provide prognostic utility in primary biliary cirrhosis. These studies herald a future in which the serial assessment of liver fibrosis is as widespread and easily available as the measurement of disease activity/severity is today with conventional liver function tests, allowing for the better monitoring of current and novel therapy and targeting of surveillance for hepatoma and varices.