



Diagnostic accuracy of non-invasive tests for advanced fibrosis in patients with NAFLD: an individual patient data meta-analysis

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ABSTRACT

Objective Liver biopsy is still needed for fibrosis staging in many patients with non-alcoholic fatty liver disease. The aims of this study were to evaluate the individual diagnostic performance of liver stiffness measurement by vibration controlled transient elastography (LSM-VCTE), Fibrosis-4 Index (FIB-4) and NAFLD (non-alcoholic fatty liver disease) Fibrosis Score (NFS) and to derive diagnostic strategies that could reduce the need for liver biopsies.

Design Individual patient data meta-analysis of studies evaluating LSM-VCTE against liver histology was conducted. FIB-4 and NFS were computed where possible. Sensitivity, specificity and area under the receiver operating curve (AUROC) were calculated. Biomarkers were assessed individually and in sequential combinations.

Results Data were included from 37 primary studies (n=5735; 45% women; median age: 54 years; median body mass index: 30 kg/m²; 33% had type 2 diabetes; 30% had advanced fibrosis). AUROCs of individual LSM-VCTE, FIB-4 and NFS for advanced fibrosis were 0.85, 0.76 and 0.73. Sequential combination of FIB-4 cut-offs (<1.3; ≥2.67) followed by LSM-VCTE cut-offs (<8.0; ≥10.0 kPa) to rule-in or rule-out advanced fibrosis had sensitivity and specificity (95% CI) of 66% (63–68) and 86% (84–87) with 33% needing a biopsy to establish a final diagnosis. FIB-4 cut-offs (<1.3; ≥3.48) followed by LSM cut-offs (<8.0; ≥20.0 kPa) to rule out advanced fibrosis or rule in cirrhosis had a sensitivity of 38% (37–39) and specificity of 90% (89–91) with 19% needing biopsy.

Significance of this study

What is already known on this subject?

- Patients with non-alcoholic fatty liver disease (NAFLD) and advanced fibrosis (F3–4) are at risk of disease progression and adverse clinical outcomes.
- Non-invasive tests with predefined cut-offs are used as screening biomarkers to identify those at low risk of advanced fibrosis who can be safely managed in primary care.
- Liver biopsy is still needed in secondary care to further identify those with cirrhosis who would benefit from surveillance for hepatocellular cancer and screening for oesophageal varices.

Conclusion Sequential combinations of markers with a lower cut-off to rule-out advanced fibrosis and a higher cut-off to rule-in cirrhosis can reduce the need for liver biopsies.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the hepatic manifestation of the metabolic syndrome with high prevalence worldwide.¹ Most patients remain asymptomatic for long periods of time (years/decades) with slowly progressive disease, but