

Diagnostic accuracy of acoustic radiation force impulse elastography for the staging of hepatic fibrosis in non-alcoholic fatty liver disease: a systematic review and meta-analysis

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INTRODUCTION

- Non-alcoholic fatty liver disease (NAFLD) is becoming the most common chronic liver disease causing end-stage liver disease worldwide and is often associated with obesity, type 2 diabetes mellitus (T2DM) and dyslipidaemia¹.
- It is estimated to affect approximately one third of Western countries¹.
- There is an unmet need for non-invasive biomarkers to replace liver biopsy and ultrasound-based elastography techniques have shown promising results.

AIM

The aim of this systematic review and meta-analysis was to evaluate the diagnostic performance of acoustic radiation force impulse (ARFI) point shear wave elastography (pSWE) for staging hepatic fibrosis and diagnosing NASH in patients with NAFLD.

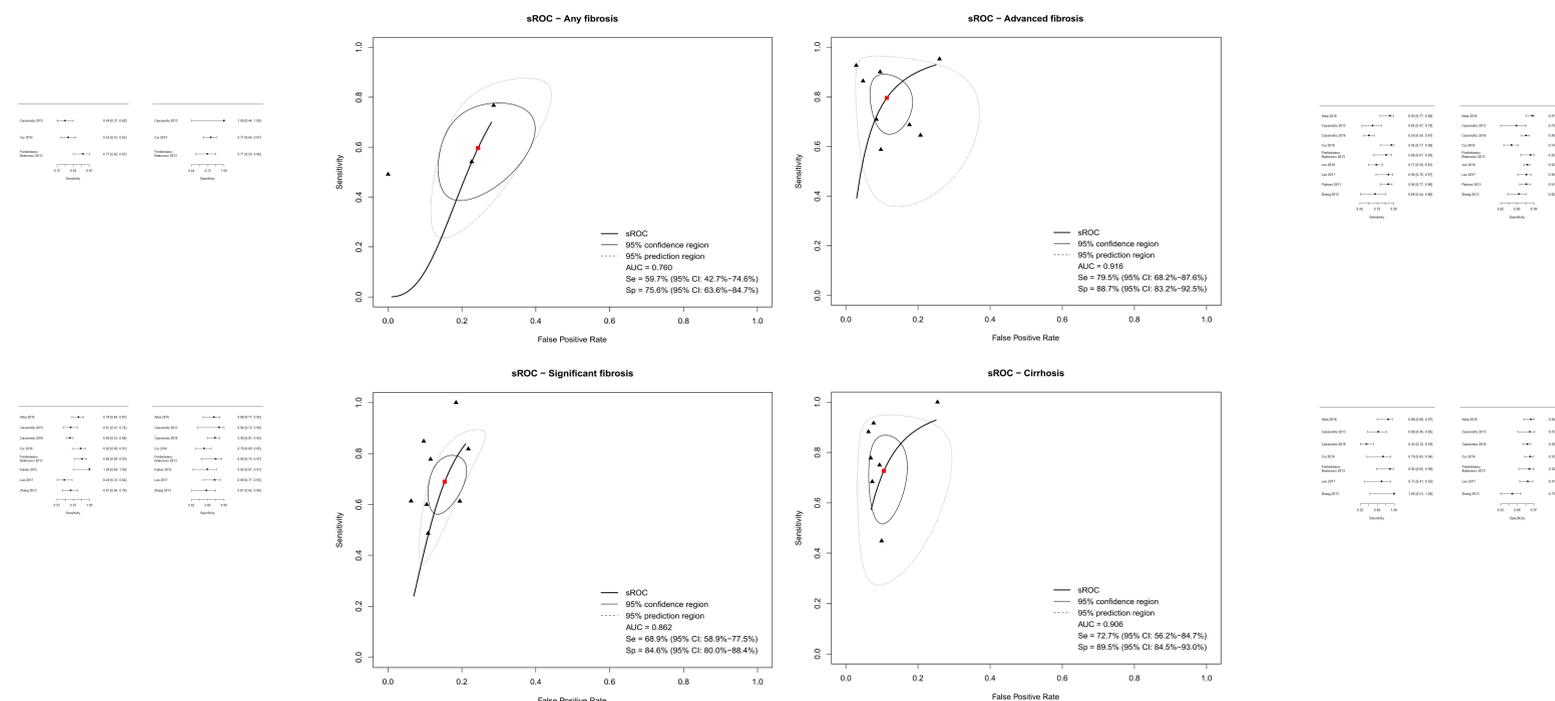
METHODS

- An electronic search of PubMed, EMBASE and Cochrane Library was conducted in March 2018 and updated in January 2019. Full-text papers and conference abstracts examining the diagnostic test accuracy of ARFI-pSWE were included.
- Studies reporting on adults with biopsy-proven NAFLD using the NASH CRN histological scoring system and ARFI-pSWE within 6 months of biopsy were included.
- Classification tables for diagnosing dichotomised fibrosis groups (any fibrosis – $\geq F1$, significant fibrosis – $\geq F2$, advanced fibrosis – $\geq F3$, cirrhosis – $F4$) were reconstructed for each study.

- Summary receiver operating characteristics curve (sROC), sensitivities, specificities, 95% confidence region, and 95% prediction region were produced using a bivariate logitnormal model.
- The minimum acceptable performance level was defined as **80% for both sensitivity and specificity**.
- Risk of bias was assessed using the QUADAS-2 tool.

RESULTS

- 10 studies (1326 patients (52% male, mean age range: 35-57) provided sufficient data for meta-analysis. 9 prospective, 9 single-centre studies.
- All studies were conducted in tertiary centres (2 France, 2 USA, 2 South Korea, 2 Germany, 1 Romania and 1 China).
- 4 studies reported the proportion of obese participants (mean prevalence 59%)
- 6 studies reported the proportion of patients with diabetes (mean prevalence 40%).
- Experienced radiologists performed ARFI using either Siemens Acuson S2000 or S3000
- The technical failure rate ranged from 0% to 21.5% (mean: 8%).
- 5 studies reported the length of the biopsy samples, 3 reported the quality criteria for biopsy specimen inclusion, 2 reported neither
- 4 studies reported the prevalence of NASH but none reported diagnostic performance to distinguish NASH from simple steatosis.
- All studies used the Youden index to obtain the optimal ARFI shear wave velocity to diagnose liver fibrosis stages.



Target condition	Number of patients	Mean prevalence, %	Number of studies	Cut-off range, kPa	Summary AUROC	Summary sensitivity, %	Summary specificity, %
F \geq 1	249	49	3	1.11 – 1.81	0.77	60	76
F \geq 2	641	58	6	1.17 – 1.81	0.89	77	90
F \geq 3	1170	29	8	1.34 – 4.24	0.93	81	89
F = 4	720	16	6	1.50 – 2.54	0.93	73	92

CONCLUSIONS

- In patients where liver stiffness can be successfully measured using ARFI, the test has **good diagnostic accuracy for fibrosis** in the context of cut-offs not being pre-specified.
- The use of ARFI-pSWE for the detection of **advanced fibrosis ($\geq F3$) reached our pre-defined minimum acceptable performance**.
- **Intention-to-diagnose analyses and validation of pre-specified cut-offs are lacking from the literature and these areas should be the focus of future studies.**

ACKNOWLEDGEMENTS

This study was conducted as part of a larger multicentre study named LITMUS (Liver Investigation: Testing Marker Utility in Steatohepatitis), which is funded by the European Union IMI2 scheme, to establish a defined set of non-invasive diagnostic biomarker(s) that will enable the detection and monitoring of fibrosis and NASH in NAFLD

REFERENCES

1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology* 2016;64:73-84.

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