EASD-EASO clinical practice guidelines for the management of non-alcoholic fatty liver disease. J Hepatol 2016;64:1388–1402. https://doi.org/10.1016/j.jhep.2015.11.004.
[3] **Choi J**, **Lee SR**, Choi EK, Ahn HJ, Kwon S, Park SH, et al. Non-alcoholic fatty liver disease and the risk of incident atrial fibrillation in young adults: a nationwide population-based cohort study. Front Cardiovasc Med 2022;9:832023. https://doi.org/10.3389/fcvm.2022.832023.
[4] European Association for the Study of the Liver. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. J Hepatol 2021;75:659–689. https://doi.org/10.1016/j.jhep.2021.05.025.
[5] Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA 1998;280:1690–1691. https://doi.org/10.1001/jama.280.19.1690.
[6] Long MT, Yin X, Larson MG, Ellinor PT, Lubitz SA, McManus DD, et al. Relations of liver fat with prevalent and incident atrial fibrillation in the framingham heart study. J Am Heart Assoc 2017;6:e005227. https://doi.org/10.1161/JAHA.116.005227.
[7] **Käräjämäki AJ**, **Pätsi OP**, Savolainen M, Kesäniemi YA, Huikuri H, Ukkola O. Non-alcoholic fatty liver disease as a predictor of atrial fibrillation in middle-aged population (OPERA study). PLoS One 2015;10:e0142937. https://doi.org/10.1371/journal.pone.0142937.
[8] Targher G, Valbusa F, Bonapace S, Bertolini L, Zenari L, Rodella S, et al. Non-alcoholic fatty liver disease is associated with an increased incidence of atrial fibrillation in patients with type 2 diabetes. PLoS One 2013;8:e57183. https://doi.org/10.1371/journal.pone.0057183.
[9] **Alon L**, **Corica B**, Raparelli V, Cangemi R, Basili S, Proietti M, et al. Risk of cardiovascular events in patients with non-alcoholic fatty liver disease: a systematic review and meta-analysis. Eur J Prev Cardiol 2022;29:938–946. https://doi.org/10.1093/eurjpc/zwab212.
[10] Gong H, Liu X, Cheng F. Relationship between non-alcoholic fatty liver disease and cardiac arrhythmia: a systematic review and meta-analysis. J Int Med Res 2021;49:3000605211047074. https://doi.org/10.1177/0300060521047074.

Accuracy of transient elastography in assessing fibrosis at diagnosis in individuals with autoimmune liver disease

To the Editor:

Recently, this *Journal* published a large, multi-center, longitudinal cohort study by Corpechot *et al.*, which validated the prognostic value of baseline liver stiffness (LS) by vibration-controlled transient elastography (VCTE) in individuals with primary biliary cholangitis (PBC). LS also improved the prognostic performance of established biochemical markers of treatment response.[1]

The study has directly supported the inclusion of baseline LS in prognostic tools developed for PBC. Interestingly, results from our meta-analysis regarding the diagnostic performance of LS for autoimmune liver disease (AILD) also provided indirect explanation for its prognostic role, considering baseline histological fibrosis is an independent predictor of disease progression and clinical outcomes in individuals with AILD.[2,3]

Of the 754 articles identified through the systematic search, a total of 44 studies published from 2006 to 2021 including 3,488 participants with AILD were finally enrolled. Taking liver biopsy as standard, we explored the diagnostic ability of 11 non-invasive markers of fibrosis in subgroups of individuals with autoimmune hepatitis (AIH) (n = 1,253), PBC (n = 1,734) and primary sclerosing cholangitis (PSC) (n = 501). Moreover, considering genetic and environmental factors can contribute to the development and progression of AILD, both Asian and European populations were covered in our study[4] (Table S1). Our results indicated that LS by transient elastography had a remarkable diagnostic performance compared to other non-invasive biomarkers of liver fibrosis (Table S2). Moreover, LS performed better for the diagnosis of PBC than AIH. LS had an excellent diagnostic accuracy in detecting liver fibrosis with summary area under ROC curves (AUROCs) of 0.94, 0.92 and 0.93 for significant fibrosis (SF), advanced fibrosis (AF) and cirrhosis, respectively, in individuals with PBC. While LS had a moderate to excellent accuracy with summary AUROCs of 0.83, 0.91 and 0.90 in individuals with AIH (Fig. 1). Liver histology predicts fibrosis progression and cirrhosis development in individuals with AILD; thus, the higher consistency between LS and liver histopathology in individuals with PBC can provide further support for Corpechot *et al.*'s findings.

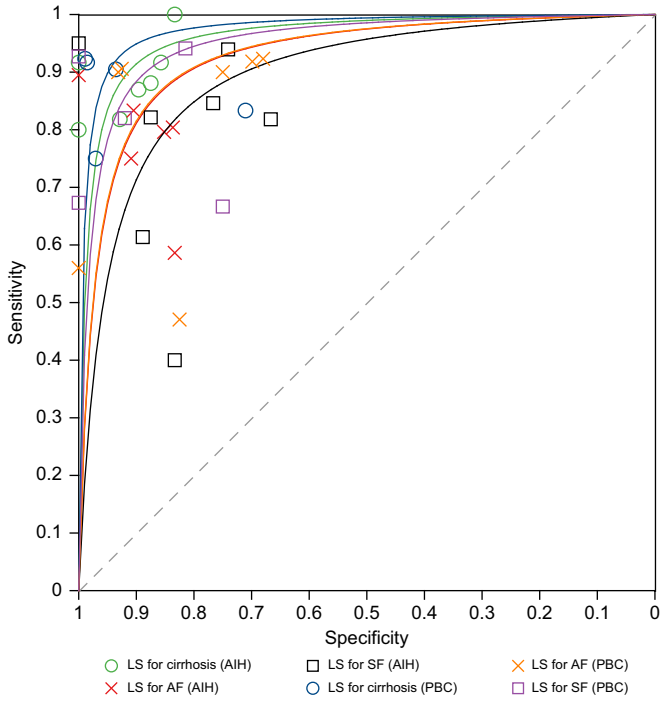

Fig. 1. Summary ROC plot of liver stiffness by transient elastography in detecting significant fibrosis, advanced fibrosis and cirrhosis in individuals with AIH and PBC. The summary sensitivity and specificity were calculated for each enrolled study and the summary ROC plot was produced in Review Manager (Revman 5.3 version). AF, advanced fibrosis; AIH, autoimmune hepatitis; LS, liver stiffness; PBC, primary biliary cholangitis; SF, significant fibrosis.

In conclusion, we agree with Corpechot *et al.* that VCTE is a reliable predictor of clinical outcomes in individuals with PBC and that LS should be incorporated into the prognostic markers to determine the state of disease progression. Still, the differential diagnostic efficiency of LS in our study provides a hint that the prognostic value of LS in individuals with PSC, AIH or PBC-AIH overlap syndrome warrants further investigation. More importantly, studies regarding dynamic changes of LS during the follow-up of individuals with AILD are needed to further validate its prognostic impact.

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Conflict of interest

All authors declare that no conflict of interest is associated with participation and contribution to this work.

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Authors' contributions

YS: data analysis and manuscript drafting. HC: data analysis and manuscript drafting. SDW: manuscript revision. WJ: study concept and manuscript revision.

Supplementary data

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References

[1] Corpechot C, Carrat F, Gaouar F, Chau F, Hirschfield G, Gulamhusein A, et al. Liver stiffness measurement by vibration-controlled transient elastography improves outcome prediction in primary biliary cholangitis. J Hepatol 2022;77:1545–1553. https://doi.org/10.1016/j.jhep.2022.06.017.
[2] Murillo Perez CF, Hirschfield GM, Corpechot C, Floreani A, Mayo MJ, van der Meer A, et al. Fibrosis stage is an independent predictor of outcome in primary biliary cholangitis despite biochemical treatment response. Aliment Pharmacol Ther 2019;50:1127–1136.
[3] Hartl J, Ehlken H, Sebode M, Peiseler M, Krech T, Zenouzi R, et al. Usefulness of biochemical remission and transient elastography in monitoring disease course in autoimmune hepatitis. J Hepatol 2018;68:754–763.
[4] Gulamhusein AF, Hirschfield GM. Primary biliary cholangitis: pathogenesis and therapeutic opportunities. Nat Rev Gastroenterol Hepatol 2020;17:93–110.

B vitamins for NASH: Use methylcobalamin, not cyanocobalamin

To the Editor:

Tripathi *et al.*[1] have elegantly shown how hyperhomocysteinemia aggravates non-alcoholic steatohepatitis (NASH). Their finding that treatment with folate and B12 reduced inflammation and improved hepatic histology suggests that folate and B12 will be important therapies for this condition. However, it is crucial to recognize that the form of B12 used should be methylcobalamin or hydroxycobalamin, not cyanocobalamin, particularly in patients with impaired kidney function, including the elderly.

It is now clear that folic acid and B12 reduce the risk of stroke; however, the benefit of B vitamins was obscured in the early trials by harm from cyanocobalamin among participants with renal failure.[2,3] In the Vitamin Intervention for Stroke Prevention (VISP) trial, there was no benefit of B vitamins in the entire study population.[4] However, in a subgroup from which patients with impaired kidney function (an estimated glomerular filtration rate [eGFR] <46 ml/min/1.72 m^2 – the 10^{th} percentile of eGFR in the study population), there was a 34% reduction of stroke/myocardial infarction over 2 years.[5]

A trial in patients with diabetic nephropathy randomized to placebo *vs*. folate 2.5 mg, B6 25 mg and cyanocobalamin 1,000 μg daily showed faster decline of renal function, and a doubling of cardiovascular events, with B vitamins.[6] All the events occurred among participants with GFR <50 ml/min/1.72 m^2.[7]