Editorial: can quantitative fibrosis assessment be used to enhance prediction of outcomes in patients with alcohol-related liver disease?

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Can quantitative fibrosis assessment be used to enhance prediction of outcomes in patients with alcohol-related liver disease?

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Alcohol is a leading cause of morbidity and mortality globally.[1] In the UK, alcohol consumption remains high with a growing burden of alcohol-related liver disease (ALD) and poor outcomes in patients presenting to secondary care.[2] Strategies for early detection of advanced fibrosis in high-risk populations are recommended.[3] However, once fibrosis has developed, there are few predictors of long-term outcome. Histological parameters including fibrosis stage are important prognostic factors, but a reproducible and standardised ALD-specific scoring system is required that reduces the interobserver variation of existing scores.[4] Collagen proportionate area (CPA) is a semi-automated quantitative assessment of fibrosis with high inter- and intra-observer concordance.[5] CPA predicts decompensation and liver-related mortality in non-alcoholic fatty liver disease and hepatitis C related cirrhosis.[5,6] In patients with ALD, CPA correlates with liver stiffness measurement[7] and portal pressure[8] but has not previously been studied as a prognostic indicator.

Israelsen *et al* conducted a two-centre retrospective assessment of patient factors (including fibrosis stage and CPA) associated with clinical outcomes in patients with biopsy-proven ALD.[9] In the whole cohort, CPA and MELD independently predicted liver-related mortality. However, CPA was the only independent predictor of hepatic decompensation and liver-related death in patients with early or compensated ALD. Results were validated in an independent prospective cohort of patients with early ALD in whom transient elastography was concurrently performed. CPA strongly correlated with liver stiffness measurement and both predicted hepatic decompensation with equal but not additive predictive power.

It should be noted that this study is based upon liver histology from patients that would not routinely undergo liver biopsy. The authors acknowledge that the indications for biopsy were unknown and at the discretion of the treating physician. There were also considerable differences in patient characteristics between the two participating centres highlighting variations in local practice. So how can these findings best be applied to clinical practice? It is useful to know that CPA and liver stiffness measurement strongly correlate in patients with early or compensated ALD suggesting that non-invasive methods may suffice for prediction of liver-related outcomes. However, the strength of

CPA may lie in those with intermediate liver stiffness values. Transient elastography has lowest accuracy in patients with F2-F3 fibrosis[7] and is confounded by active alcohol use.[10] In such patients, biopsy with CPA assessment may more accurately stage fibrosis and provide additional prognostic information that can guide patient management.

Reduction in alcohol use remains the only strategy known to improve long-term outcomes in patients with ALD.[3] Yet abstinence did not independently predict liver-related outcomes in this study. This is most likely explained by incomplete alcohol consumption data due to the retrospective nature of the development cohorts. However, long-term abstinence from the point of biopsy onwards was clearly documented in a subset of patients and was a strong predictor of all-cause mortality at maximal follow-up (HR 0.50 [0-30-0.83]). One should not forget that however useful a predictor of clinical outcomes is, the most effective management is in tackling alcohol consumption.

References

1. GBD Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet.* 2018;392(10152):1015-1035.
2. Williams R, Aithal G, Alexander GJ, et al. Unacceptable failures: the final report of the Lancet Commission into liver disease in the UK. *Lancet.* 2020;395(10219):226-239.
3. European Association for the Study of the Liver. Electronic address eee, European Association for the Study of the L. EASL Clinical Practice Guidelines: Management of alcohol-related liver disease. *Journal of hepatology.* 2018;69(1):154-181.
4. Lackner C, Spindelboeck W, Haybaeck J, et al. Histological parameters and alcohol abstinence determine long-term prognosis in patients with alcoholic liver disease. *Journal of hepatology.* 2017;66(3):610-618.
5. Buzzetti E, Hall A, Ekstedt M, et al. Collagen proportionate area is an independent predictor of long-term outcome in patients with non-alcoholic fatty liver disease. *Alimentary pharmacology & therapeutics.* 2019;49(9):1214-1222.
6. Calvaruso V, Di Marco V, Bavetta MG, et al. Quantification of fibrosis by collagen proportionate area predicts hepatic decompensation in hepatitis C cirrhosis. *Alimentary pharmacology & therapeutics.* 2015;41(5):477-486.
7. Thiele M, Detlefsen S, Sevelsted Moller L, et al. Transient and 2-Dimensional Shear-Wave Elastography Provide Comparable Assessment of Alcoholic Liver Fibrosis and Cirrhosis. *Gastroenterology.* 2016;150(1):123-133.
8. Restellini S, Goossens N, Clement S, et al. Collagen proportionate area correlates to hepatic venous pressure gradient in non-abstinent cirrhotic patients with alcoholic liver disease. *World J Hepatol.* 2018;10(1):73-81.
9. Israelsen M, Guerrero Misas M, Koutsoumourakis A, et al. Collagen proportionate area predicts clinical outcomes in patients with alcohol-related liver disease. *Alimentary pharmacology & therapeutics.* 2020.
10. Moreno C, Mueller S, Szabo G. Non-invasive diagnosis and biomarkers in alcohol-related liver disease. *Journal of hepatology.* 2019;70(2):273-283.