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

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We would like to thank Dr Moodley and Dr Dhanda for their insightful editorial[x] on our study on collagen proportionate are (CPA) in patients with alcohol-related liver disease (ALD).[1]

The editorial discusses how our findings can be applied in clinical practice, given the increasing use of non-invasive tests (NITs) to diagnose ALD, which seem to be cost-effective in the broader ALD population.[2,3] We do not dispute that NITs will be used instead of liver biopsy in a significant proportion of patients with ALD. However, the prognostic value of the NITs is still unknown and liver biopsy should be considered to establish the diagnosis and assess the exact stage of disease in selected patients with moderately elevated or equivocal NIT results. In line with Moodley and Dhanda, we believe that CPA is useful in those selected patients.

While the use of liver biopsy is debatable in clinical practice to stage ALD, it is recommended in clinical studies.[4] Our study shows that CPA is the strongest histological surrogate marker for liver-related outcomes in ALD. Furthermore, CPA has several advantages compared to a categorical scoring system. First, the biological nature of liver fibrosis in ALD is a continuous spectrum, which can be captured by using the continuous scale of CPA in contrast to traditional categorical scoring systems.[5] Second, the use of categorical scoring systems to assess the severity of liver fibrosis in clinical trials has recently been heavily criticised due to the major inter-observer variability ($\kappa < 0.50$).[6] In contrast, CPA has an excellent inter-observer reliability ($\kappa = 0.91$).[7] Based on this, we believe that CPA is suitable as the primary histological outcome measurement in clinical studies of ALD. In a broader sense, given the prognostic significance of CPA, we argue that it should be routinely performed and reported in any patient who is having a liver biopsy for clinical or research purposes as it provides valuable additional information.

Finally, Moodley and Dhanda speculate on why our data show that alcohol abstinence improves overall mortality but not liver-related outcomes. We acknowledge that our data on alcohol use may be incomplete and therefore interpretation of these data must be taken with caution. However, it is anticipated that liver-related mortality accounts for only 15% of all alcohol-attributable deaths.[8] Given this, one would expect that alcohol abstinence has stronger impact on all-cause mortality compared to liver-related outcomes. Our interpretation is that the severity of fibrosis is an indicator of the hepatic susceptibility to alcohol, and this seems to be the strongest predictor of the progression rate in individuals with alcohol misuse.

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