

We would like to thank Dr Ji and co-authors and Dr Cristoferi and co-authors for their interest in our study [1], that also provides us the opportunity to clarify several important points.

Dr Ji has tested the revised elastography thresholds we propose for the assessment of compensated advanced chronic liver disease in a cohort of 220 patients with MAFLD. More than half of these patients had co-existing HBV infection with an unknown treatment status, while 42% had traditional NAFLD. The authors demonstrated an excellent sensitivity of the low cut-off but a somewhat suboptimal specificity of the 12 KPa cut-off (81.5%). The term MAFLD is an umbrella term that potentially includes any cause of liver disease provided there is a co-existence of metabolic abnormalities. It would be very helpful if the authors have reported separately the diagnostic performance of the criteria in traditional NAFLD versus patients with HBV and metabolic abnormalities. It would also be crucial to report the treatment status of the patients with HBV. Our cohort included

values in patients with HBV [2]. Our hypothesis is that the suboptimal performance of the 12 KPa threshold is driven by the proportion of patients with treated HBV rather than the elusive diagnosis of MAFLD. To corroborate this, a recent cohort study from Hong Kong confirmed the diagnostic accuracy of our proposed revised criteria in patients with Chinese ethnicity and NAFLD [3].

Dr Cristoferi questions the need for dual cut-offs, and the use of the patients in the “grey zone” area for developing the model to classify such patients. We have previously shown that the use of currently available non-invasive tests at single cut-offs do not have sufficient diagnostic accuracy for the detection of cirrhosis, and this is also true for cACLD, as their diagnostic accuracy is even lower [4]. Moreover, there is not an established single Fibroscan cut-off, as most studies reported on post-hoc cut-offs that better suited their dataset [5]. The optional single cut-off for cACLD in our population was 9 KPa, but it would have a sensitivity and specificity of 80% which would be suboptimal for individualized decisions. We strongly believe that using the “grey zone” patients to develop the model for their

classification is the statistically correct way, as the model is applicable to this population rather than the whole study cohort.

In conclusion, we stand by and strongly support the use of dual cut-offs for cACLD in patients with NAFLD, ALD and untreated HBV and HCV at the thresholds reported in our paper.

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