

detecting mild steatosis.⁷ Yet, it seems highly unlikely that missing out on some individuals with only mild steatosis resulted in a complete distortion of associations. Last, the FAST score was mentioned; this is a composite of liver stiffness, CAP and AST (aspartate aminotransferase) that has been used to predict the presence of NASH-fibrosis.⁸ This score is likely to encounter the same issues as liver stiffness alone and might not discriminate between venous congestion and NASH-fibrosis. Because of the important role attributed to liver stiffness in this algorithm, validation of the diagnostic accuracy of the FAST score is required in populations at risk of venous congestion.

In conclusion, we believe that the potential issues mentioned by Tsai *et al.* have not had any impact on our conclusion that atrial fibrillation was associated with liver stiffness and not with fatty liver disease. However, additional studies are warranted to investigate the exact impact of the association between atrial fibrillation and fatty liver disease on current elastography-based risk stratification algorithms.

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Conflicts of interest

RdK is a speaker for Echosens, consultant for AbbVie and received grants from AbbVie, Gilead and Janssen. The remaining authors reported no relevant conflicts.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Writing of the manuscript: LvK and RdK. Critical review of the manuscript, approval of final version approval of submission: LvK, MK, and RdK.

Supplementary data

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HBsAg seroclearance and reduction in late recurrence of HBV-related HCC: Causality or co-existence?

To the Editor:

We read with great interest the recent article in *Journal of Hepatology* by Yoo *et al.*¹ Among 2,520 patients who were alive and recurrence free 2 years after curative resection for HBV-related early-stage (BCLC stage 0/A) hepatocellular carcinoma

(HCC), 891 (35.4%) patients developed late recurrence (>2 years after surgery) while 172 (6.8%) achieved HBsAg seroclearance during a median follow-up duration of 6.9 years after resection. Using univariate and multivariate analysis, the authors demonstrated that HBsAg seroclearance was independently associated with a significantly lower risk of late recurrence of HBV-related HCC. As the authors stated at the end of this paper, HBsAg seroclearance has a “beneficial impact” on reducing the

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risk of late recurrence for patients with HBV-related HCC. Although interesting, we have the following concerns about the inherent relationship between HBsAg seroclearance and late recurrence.

First, in this study, Yoo *et al.* did not give the details regarding the sequence of HBsAg seroclearance and late recurrence. During the median follow-up of 6.9 years, among 172 patients with HBsAg seroclearance, 36 (20.9%) patients developed late recurrence. It is very possible that some patients first developed late recurrence of HCC and then achieved HBsAg seroclearance in the real world. If so, it is inappropriate for a cohort study to use variables that occurred after the occurrence of the endpoint event. In our opinion, the ambiguous sequentiality between HBsAg seroclearance and late recurrence suggests that the causal relationship between them is really very weak.

Second, by inhibiting viral replication, antiviral therapy has been widely recognized as being associated with reduced post-operative recurrence, especially late recurrence of HBV-related HCC.^{2,3} Actually, HBsAg seroclearance is also one of the results of antiviral therapy, although the probability of its occurrence is still very low nowadays.^{4,5} That is to say, both HBsAg seroclearance and the reduction in late recurrence are the consequences of antiviral therapy, and these outcomes co-exist in patients treated with regular antiviral therapy during follow-up.

In conclusion, HBsAg seroclearance and no recurrence are optimal outcome events for patients undergoing curative liver resection for HBV-related HCC who receive antiviral therapy during the follow-up period. However, the effect of HBsAg seroclearance on the reduction of recurrence is still worthy of further mechanistic research.

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Conflicts of interest

The authors disclose no conflicts.

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Authors' contributions

Study concepts: Yong-Kang Diao, Qing-Yu Kong, Tian Yang; Manuscript preparation and editing: Yong-Kang Diao, Qing-Yu

Kong; Manuscript review: Tian Yang. All the authors reviewed the paper and approved the final version. Yong-Kang Diao and Qing-Yu Kong contributed equally to this work.

Supplementary data

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HBsAg seroclearance reduces the risk of late recurrence in HBV-related HCC

To the Editor:

We read with great interest the article published in the *Journal of Hepatology* by Yoo *et al.* and colleagues.¹ This study found that HBsAg loss was associated with a 38% lower risk of late recurrence of hepatocellular carcinoma (HCC) after curative liver resection compared with persistent HBsAg positivity.

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