de novo HBV infection under any type of antiviral prophylaxis (lamivudine or entecavir) in their study.[1]

In conclusion, the recommendation of this study[1] for universal use of high genetic barrier agents instead of lamivudine in HBsAg negative recipients of anti-HBc positive grafts is not based on strong data and certainly needs additional exploration in larger, ideally randomized, studies with careful evaluation of the risk of *de novo* HBV infection in all subgroups of such LT recipients. Until then, we believe that (in accordance with the current guidelines[3]), HBsAg-negative recipients of anti-HBc positive grafts can continue to receive prophylaxis with lamivudine, while both anti-HBc/anti-HBs positive recipients may need no anti-HBV prophylaxis at all.

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Conflict of interest

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Authors' contributions

Evangelos Cholongitas and George V. Papatheodoridis contributed equally in this paper

Supplementary data

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Reply to "Liver transplantation using hepatitis B core positive grafts: Which is the optimal antiviral prophylaxis?"

To the Editor:

We appreciate the interest and comments by Cholongitas and Papatheodoridis. *De novo* hepatitis B viral (HBV) infection was defined as HBV surface antigen (HBsAg) seropositivity and/or detectable HBV DNA in a non-HBV recipient. This is a widely adopted definition, and as all HBV naïve recipients were covered with antiviral therapy after receiving hepatitis B core antibody (anti-HBc) positive grafts in our study,[1] it would be highly unlikely for them to develop detectable HBV DNA. As the patients were on antiviral therapy, viral activity would be suppressed, and may explain the transient nature of HBsAg positivity in these patients. Moreover, in the histological study of patients with chronic HBV who remain HBsAg positive after transplantation on entecavir therapy, all stained negative for HBsAg.[2] We agree that the anti-HBc+/anti-HBs+ represents the lowest risk group. However, with the high number of anti-HBc+ grafts being used in our region, even a small percentage of *de novo* infection would be a significant risk. Previous studies have shown that using less potent agents with high resistance rates is associated with *de novo* infection and the development of resistance with longer follow-up.[3–5] Therefore, we would recommend adopting agents with better resistance profiles now that they are widely available.

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Are liver transplant centres critical for the critically ill patient with cirrhosis?

To the Editor:

We were very interested to read the study by Hernaez, Kramer and colleagues[1] in a recent issue of *Journal of Hepatology*, which examined the prevalence and outcomes of patients with acute-on-chronic liver failure (ACLF) using the US Department of Veterans Affairs database. The authors comprehensively describe the outcomes of 19,082 hospitalised patients with ACLF, compared to 53,234 patients with decompensated cirrhosis without ACLF, over a 10-year period. A key finding was that patients with ACLF admitted to liver transplant centres versus non-transplant centres had 20% and 19% lower odds of dying at 28 days and 90 days, respectively. However, it should be highlighted that firstly, the 28-day odds ratio had a confidence interval that crossed one (odds ratio 0.80, 95% CI 0.61–1.01); and secondly, that there was no difference in the unadjusted 28-day transplant-free mortality between transplant and non-transplant centres when stratifying by presence/absence of ACLF and ACLF grade, as illustrated in Fig. 3 of the manuscript.

We have previously published our experience in Australia and New Zealand, examining the outcomes of 17,044 critically ill cirrhotic patients admitted on a non-elective basis to intensive care units (ICUs) over a 16-year period in comparison to over 775,000 non-cirrhotic patients.[2] Although we were unable to classify patients by the CANONIC or NACSELD definitions of ACLF, we described a robust cohort of cirrhosis patients with SOFA (Sequential Organ Failure Assessment) defined organ failures with an overall transplant-free hospital mortality of 32.4%. We found that for patients with cirrhosis, there was no difference in unadjusted hospital mortality between liver transplant and non-transplant centres (34.2% and 32.1% respectively, $p = 0.06$). Furthermore, transplant centre status did not affect the adjusted annual decline in mortality ($p = 0.27$) or the interaction between the presence of cirrhosis and mortality ($p = 0.06$). We observed that specialist liver transplant ICUs treated patients with higher baseline illness severity scores and liver indices, but this did not affect mortality trends. Until recently, data have been relatively scant regarding liver transplant centre status and its influence on critically ill patients with cirrhosis, however our findings have been consistent with the existing literature.

Therefore, the question of whether liver transplant centre status is important lies within the definitions of ACLF used and the setting of care. As the authors acknowledge, the NACSELD definition of ACLF identifies a more unwell group of patients who would almost invariably need an ICU setting due to the level of organ support required. Using this definition would have excluded more than 4,500 participants in the Hernaez *et al.* study. Alternatively, in the CANONIC definition it could be assumed that many patients with ACLF-1 could be managed on the general ward (*e.g.*, single kidney failure, or liver failure with a creatinine value between 1.5–1.9 mg/dl).

Hence, the authors should clarify whether the NACSELD definition of ACLF or the setting of care (ward *vs.* ICU) alters the mortality benefit offered by liver transplant centres in their dataset. Secondly, clarification is needed regarding which measurable factors the authors believe influenced the mortality benefit in transplant centres in their cohort.

We speculate that some of the mortality benefit seen in the transplant centres may be attributable to more positive attitudes towards ICU admission candidacy and improvements in ward-based management rather than specific ICU management.