from a prognostic point of view but also appear to be able to identify those patients likely to benefit from therapeutic intervention [9,10]. The prognostic utility of the presence of SIRS criteria has previously been described in ALD patients with ACLF [7]. This may in part explain the prognostic accuracy of the GAHS as white cell count is a principle component of both SIRS and GAHS.

In conclusion, it is unrealistic to suggest that biopsy is essential for the diagnosis and prognosis of patients with alcoholic hepatitis. Whilst biopsy may be necessary in cases of diagnostic uncertainty and for the characterisation of patients for research purposes, clinical criteria for diagnosis and identification of patients for treatment are readily available for the majority of patients with alcoholic hepatitis. The aim should be to assess such patients promptly on presentation rather than to rely upon strategies based upon histology which may delay assessment or be difficult to obtain outside specialist centres.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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Dermot Gleeson
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Reply to: "Is a liver biopsy necessary in alcoholic hepatitis?"

To the Editor:
We thank Drs. Forrest and Gleeson for their interest in our paper [1]. Their letter makes two points; one clinical and the other logistical, which will be addressed in turn.

Clinical

Our study describes the value of early liver biopsy (between days 1 and 7 from admission) in patients presenting with acute decompensation of cirrhosis. As correctly identified by Forrest and Gleeson, only biopsies taken *early* in the admission are valuable in interpreting the cause of decompensation. However, we beg to differ with them on the relative importance placed on hyperbilirubinaemia as a key feature of ASH versus other causes of decompensated alcoholic liver disease. Indeed, in the paper they cite by Katoonizadeh *et al.* [2], patients with acute-on-chronic liver failure (ACLF) presenting with hyperbilirubinaemia had most commonly sepsis with high SIRS, confirmed by ductular bilirubinostasis, which was also an independent prognostic factor. In our series, mean bilirubin values of 227 μmol/L in heavy drinkers with onset of jaundice less than 1 month from the acute admission fits with other studies addressing diagnostic criteria in ASH [3,4]. However, 50% of patients with high SIRS had no significant histological features of ASH using the grading system we describe and yet sepsis related mortality was higher in these patients with their biopsies showing significant cholestasis. Thus, high bilirubin cannot distinguish infection from the hepatic inflammation of ASH in decompensated cirrhosis and their respective management is completely different.

Louvet *et al.* show that in patients failing corticosteroid treatment of ASH, mortality from infection is high, suggesting that corticosteroids may promote increased infection in these patients and precipitate poor outcome [5]. It follows that the practice of clinical grading of AH in a decompensated alcoholic cirrhotic is likely to significantly underestimate infection, adversely impact on survival and inappropriately target anti-inflammatory therapies from those patients in most need, i.e. those with severe histological ASH. Thus, whilst desirable to make a rapid diagnosis of ASH to institute appropriate therapy, to commence therapy on clinical grounds may be more hazardous to the patient than availing objective biopsy confirmation. Additionally, most of the large French corticosteroid trials included patients after a liver biopsy to diagnose ASH. Therefore, to suggest use of corticosteroids without liver biopsy confirmation is not based on evidence.

In relation to use of widely published scoring systems such as modified DF, MELD and more recently GAHS [6,7], we agree that

they have utility in highlighting patients most at risk of having severe ASH. However, as acknowledged by Forrest and Gleeson for DF, all these scores draw upon criteria such as clotting time which are prone to significant variations between labs, whilst MELD and GAHS also employ measures of renal function, which in the context of advanced liver disease, are unreliable and change with clinical status (e.g. urea with fluid status, feeding and GI bleeding). The GAHS score perhaps has advantage over others by including white cell count thereby reflecting component of SIRS but as stated above, caution should be exercised when interpreting SIRS in a decompensated alcoholic, as this encompasses all patients with alcoholic liver disease and ACLF (including sepsis) and not just ASH, requiring quite different management. Furthermore, our data shows that not only is the area under receiver operator curves higher for the ASH histological score compared to DF or MELD, its specificity is markedly higher with predictive utility for defining 28-day mortality.

Logistical

Forrest and Gleeson correctly highlight the significant burden of alcoholic liver disease admissions in the UK. However, the number of purported alcoholic hepatitis cases is a small fraction of the admissions with alcoholic cirrhosis and indeed those with high SIRS scores [2]. Our own data over 3 years demonstrates that patients with a clinical presentation suggestive of ASH have a frequency of about two cases per month in a tertiary unit with specialist interest in this disease. The important point here is how to correctly identify 'true' severe alcoholic steatohepatitis (ASH) from those with advanced decompensated cirrhosis, as their early mortality remains significantly high (25–40%) despite optimal supportive management [8,9]. Appropriate identification and intervention in severe ASH will undoubtedly reduce mortality and warrants the necessary resource allocation as seen with conditions such as acute myocardial infarction and stroke, which are managed in non-tertiary centres, all of whom have access to interventional radiology and histopathology. The key question which our paper addresses, therefore, is how to most accurately identify ASH in the at-risk population and not to consider biopsy in most patients with alcoholic liver disease for which we agree with Forrest and Gleeson is not a useful application of resources.

In conclusion, whilst acknowledging the need for greater resource allocation to diagnose and expediently treat the growing population at risk of ASH in the UK, we believe our data clearly affirms the importance of liver biopsy to make a diagnosis of ASH and thus facilitate appropriate triage to therapy. The value added of liver biopsy in this setting is that it will also allow more reliable interpretation of data from clinical trials of new interventions by accurately defining the 'at risk' severe ASH population with the most to gain from intervention, whilst also clearly identifying patients who have other causes of liver disease.

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