

Lactate is important in determining prognosis in acute liver failure

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Identifying patients with acute liver failure (ALF) who will benefit from emergency liver transplantation (ELT) is not straightforward. Inaccurate selection carries major consequences. A patient who would have survived with medical management, incorrectly identified and transplanted will be subjected to unnecessary surgery, life-long immuno-suppression, and an increased risk of death. Additionally, a graft that could be utilised in another more appropriate candidate will be lost. The consequences of failure to identify a patient with ALF who would survive only with ELT are of equal magnitude as a potentially preventable death will result.

The transplantation selection criteria developed at Kings College Hospital (the KCC) are amongst the most commonly used, forming the basis for ELT registration in the United Kingdom and are in widespread international use [1,2]. Whilst their specificity is consistently reported to be at a high and clinically acceptable level, case series and meta-analysis suggest that sensitivity and negative predictive value are limited and may fail to identify a significant proportion of patients who will not survive without transplantation [3,4]. Furthermore, potential ELT recipients may be identified relatively late in their disease course such that the 'window of opportunity' for successful surgery is very short [5]. There is, thus, a need for supplemental early markers of poor prognosis to enhance the performance of the KCC, ideally being determined rapidly and easily with inclusion maintaining specificity and clinical simplicity but increasing sensitivity.

Arterial blood lactate measurement has many of these ideal features. It can be measured rapidly and accurately by point-of-care testing, and in the critically ill levels closely relates to severity of multiple organ failure. High arterial concentrations are near-universally associated with a poor prognosis [6]. In ALF, arterial blood lactate levels reflect both increased production from peripheral tissues and the injured liver and reduced clearance from the circulation as a consequence of impaired hepatic metabolic capacity. In this setting hyperlactataemia may indicate the severity of both the hepatic injury sustained and the accompanying multiple organ failure [7].

These features make lactate measurement particularly attractive as a selection criterion in paracetamol-induced ALF, where the duration of illness is short and multi-organ failure dominates

the clinical course [8]. In a mixed prospective/retrospective study of over 200 patients with paracetamol-induced ALF we found high blood lactate levels to be closely related to a fatal outcome. We suggested that the inclusion of specific threshold values into the KCC might improve test performance, increasing the speed of ELT candidate selection and sensitivity without a deleterious reduction in specificity [7].

Incorporation into decision-making protocols is of course dependent upon the results of external validation studies. A number have examined arterial blood lactate in ALF, finding high levels to be associated strongly and independently with death or transplantation in both paracetamol and non-paracetamol-induced disease [9–12]. Analysis of the performance of inclusion of the specific thresholds into the KCC for paracetamol-induced disease has been less consistent, with a report suggesting that early levels resulted in an increase in sensitivity in identifying non-survivors but at the expense of a critical reduction in specificity [10]. However, two other independent studies found that lactate measurements alone 12 h after admission to transplant centres had high predictive accuracy, with performance greater than the KCC alone [11,12].

Several factors may underly these observations, but of likely central importance is variability in the timing and degree of fluid resuscitation used to correct hypovolaemia at different centres. Improvements in systemic circulatory perfusion follow restoration of circulating volume. Clinical experience has shown that in parallel, substantial initial elevations in blood lactate may also correct rapidly. Persistent hyperlactatemia has consistently been shown to be of grave prognostic significance, emphasising the importance of serial monitoring [7,11].

What is the current place of blood lactate measurement in selection of potential transplant candidates? Decision-making on the basis of a single level at one point in time is not appropriate [8]. Whilst early blood lactate measurement provides a rapid initial indicator of the severity of disease and permits gross risk stratification, the greatest prognostic value will be gained from those patients in whom no correction of initially high levels occurs following volume resuscitation. In paracetamol-induced disease and in the context of coagulopathy and encephalopathy from acute liver injury, a sustained elevation of blood lactate should trigger consideration for transplant listing.

As ever, clinical judgement remains the key to listing decisions by the transplant team. Along with the psychosocial factors that must be considered, the decision-making process is a dynamic one that includes the continuous assessment of multiple clinical parameters [8,13]. Blood lactate measurement forms one useful component of the overall assessment of the patient with

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Abbreviations: ALF, acute liver failure; ELT, emergency liver transplantation; KCC, Kings College criteria.



ELSEVIER

Controversies in Hepatology

ALF and assists decision-making in relation to expected prognosis.

Conflicts of interest

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