



# We need evidence-based futility thresholds to transplant grade-3 acute on chronic liver failure patients with poor respiratory, haemodynamic, and metabolic parameters

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Bernal and colleagues showed that liver transplantation (LT) in grade-3 acute on chronic liver failure patients (ACLF-3) was highly efficacious under the recently implemented British prioritisation policy.<sup>1</sup> An even greater effect was that the LT-free survival was null (survival benefit). After the pioneering articles<sup>2,3</sup> reporting the LT-feasibility in well-selected ACLF-3, Centres started listing and prioritising them according to the Model for End-stage Liver Disease sodium score. However, national or regional prioritisation rules remain undefined<sup>4</sup> and identification of delisting criteria when progression occurs is lacking.

In the literature, respiratory (by PaO<sub>2</sub>/FiO<sub>2</sub> ratio), haemodynamic (by number and dosage of vasopressors), and metabolic (by arterial lactate levels) failures have been reported as poor prognostic factors. Expert opinions suggested thresholds to separate patients considered eligible for LT from those considered too sick and, therefore, at unsustainable futility risk.<sup>5</sup> Nevertheless, the impact of evidence-based thresholds remains to be prospectively investigated.

Bernal and colleagues adopted general exclusion criteria, while the role of respiratory, haemodynamic, and metabolic failures seems to have not been considered *per se*.<sup>1</sup> Notably, PaO<sub>2</sub>/FiO<sub>2</sub>, number of vasopressors (given that dosages have not been reported), and lactate levels were not different compared to transplanted patients. The authors may have excluded severe cases according to general clinical conditions, perhaps also according to failure parameters.

We speculate whether the listing/prioritisation and de-prioritisation/de-listing pathways in the already listed

and newly listed candidates may be more appropriate. Notably, in the British experience, LT achieved a significantly better result than expected. Will these excellent results suggest enlarging the criteria for listing?

## Contributors

AWA had the original idea and wrote the first draft of this correspondence. MA, LC, FF, LDP, AF, and MI, discussed the problem and refined the draft. PB performed the critical revision of the final text for important intellectual content. All authors contributed to the writing and approved the final submitted version.

## Declaration of interests

PB has received lecture and consulting fees from Alpha Wasserman, Biotest, Chiesi Farmaceutici, IPSEN, Kedrion, Mayoly, Novartis, and has received consulting/advisory board fees from Astellas Pharma, Biotest, Gilead, Kedrion, MSD, Sandoz. The other authors declare that they have no competing interests regarding this manuscript.

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