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EDITORIAL

Liver and kidney function in refractory heart failure: The narrow gate to achieve post-transplant survival

KEYWORDS
Heart transplant;
Transplant benefit;
Equity;
Allocation

Summary Substantial evidence is underscoring the importance of a combined assessment of liver and kidney function in patients with refractory heart failure, to stratify early post- heart transplant risk: multi-organ dysfunction, while identifying sickest patients on the list is also associated with a high risk of post transplant complications. In this issue of the Journal, Dr. Lebray provides an analysis of combined kidney and liver function patients undergoing heart transplant, identifying potential boundaries for futility of transplantation, because of excessive post-operative risk. Further development of this concept may help to design prioritisation algorithms allocating the organ to HT candidates not only based on the risk of dying on the waiting list, but also on the chances to survive after transplant.

Impairment of liver and kidney function is a known marker of severity for advanced heart failure (HF) and a predictor of poor outcome in patients undergoing interventions such as heart transplant (HT) or mechanical circulatory support (MCS) [1]. Therefore, the assessment of extra-cardiac organ function is a crucial and double-edged task because on one hand, it may identify severely ill patients at greater need for HT or MCS; on the other hand, these patients are those less likely to survive after surgery. In this issue of the journal, Dr. Lebray et al. (predictive value of liver damage for severe early complications and survival after heart transplantation: a retrospective analysis) provide data supporting a strategy to help dissecting the dilemma between utility and futility in HT candidates with liver and kidney dysfunction.

The assessment of renal function is rather standardized and straightforward in clinical practice, relying on a single and simple laboratory parameter (serum creatinine), that provides a quite reliable information on the status of the kidneys in a large subset of patients, by itself, or factored in glomerular filtration rate (GFR) formulas. Regardless of potential limitation in the precision of true kidney function estimates, serum creatinine before HT is a major predictor of adverse outcome after HT, early and late after surgery [2].

Conversely, the measurement of hepatic function appears to be more complex and, probably, less frequently used in the everyday clinical practice. Indeed, several parameters can reflect liver function: bilirubin, AST, ALT, cholinesterase, INR, albumin and even serum cholesterol. However, medications may partially alter these parameters, most relevantly vitamin K antagonists (VKA), as well as coexistence of viral hepatitis or non-alcoholic fatty liver disease, complicating the perception and assessment of heart failure -driven liver impairment.

The model for end-stage liver disease (MELD) is the standard score to estimate liver function, developed to identify patients most likely to die on the waiting list and thus in need for higher priority for organ allocation in the setting of liver transplantation. In advanced HF as well, MELD score is a validated marker of illness severity. To overcome the effect of VKA, the MELD excluding INR (MELD-XI) score has been developed [3] and it has been validated to predict survival in patients with HF on medical therapy [1] and in patients with an LVAD [4].

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A recent analysis of UNOS data by Grimm et al. [5], involving more than 20,000 patients, has shown that pre-HT MELD-XI score can predict mortality at 1 month, 1 and 5 years after HT. Most of the effect, however, appeared to be related to early post-operative mortality, rather than to new-onset events occurring later after surgery.

Deo et al. [6], recently, analyzing about 35,000 HT recipients from UNOS Registry, found that patients having the highest quartile of MELD-XI score before HT were more likely to be in 1A status, on ECMO, IABP or VAD/TAH, and had a worse survival, with an higher risk of 30-day mortality, infections, stroke, dialysis, rejection and prolonged hospitalizations and a higher rate of graft failure and cerebrovascular disease in the long term, but not a specific effect on cardiovascular mortality. Because MELD-XI incorporates both renal and liver function, these studies support the concept that a combined assessment of function of the two organs is a marker of severity of heart failure with a significant impact on prognosis and may have more relevance than single parameters of organ function (i.e. creatinine or bilirubin alone).

The study from Lebray et al. adds further body of evidence to the relevance of combined liver and kidney function assessment in HT candidates. By including 321 patients listed for transplant between 2004 and 2009, authors analyzed the impact of clinical, biochemical and hemodynamic parameters and their effect on 90-days post-HT mortality and severe complications post-HT (primary graft failure). While MELD or MELD-XI score were only partially available in their cohort, they included the assessment of clinical ascites in their algorithm: although it may not necessarily capture sensitively liver function, ascites in these patients is a strong marker of right heart failure, often associated with severe impairment of liver function. In addition, this study population is sicker than that reported by previous UNOS registry studies, with older donors than those available in North America, accounting for a markedly worse post-HT survival. Moreover, outcomes were also influenced by the allocation policy allowing prioritization of these sicker patients, who were also those with worse post-surgical outcomes.

Despite several weaknesses, including the analysis based on MELD and not on MELD-XI, thus not adjusted for for VKA effect, this study provides further components to the difficult evaluation of the balance between equity and futility in heart transplantation. In a context of organ shortage, the allocation should not only take into account prioritization of the sickest, but also of those with greater chance to survive after HT [7,8]. The availability of mechanical circulatory supports may partially help to overcome this impasse: the evaluation suggested by Lebray, may help to identify patients who could be stabilized by a mechanical device before being listed for transplant. As stated at the end of the article, this policy allowed a significant improvement of post-transplant survival after 2011. It would have been interesting if authors had reported more data substantiating this policy change, but nevertheless, this concept provides the basis to build up a model that needs testing in a multicenter fashion than can guide the allocation of the best resource to the most suitable patient.

In summary, in the latest years substantial evidence is underscoring the importance of a careful assessment in a combined fashion of liver and kidney function in patients with refractory heart failure, to stratify early post-HT risk. Further studies should be directed at assessing the role of dynamic changes in liver and kidney function on the waiting list and predicting transplant-related benefit, ultimately aiming to improving organ allocation algorithms. Ideally, these should prioritize HT candidates not only based on the risk of dying on the waiting list, but also on the chances to survive after transplant.

Disclosure of interest

The authors declare that they have no competing interest.

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Marco Masetti
Luciano Potena*
Advanced Heart Failure and Transplant Program, Bologna University Hospital, Bologna, Italy

*Corresponding author. Policlinico di Sant'Orsola, Padiglione 21, Via Massarenti, 9, 40138 Bologna, Italy.
E-mail address: luciano.potena2@unibo.it (L. Potena)

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