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INVITED COMMENTARY

Combined liver-kidney transplantation: two for the price of one?

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In 1983, the first combined liver and kidney transplantation (CLKT) was performed by Margreiter *et al.* [1] and the first CLKT from a living related donor was carried out in Turkey in 1992 [2].

The indications for CLKT can be divided into three categories: (i) end-stage liver disease with chronic kidney failure, (ii) end-stage liver disease with acute kidney failure, and (iii) metabolic disorders [3]. CLKT is straightforward for patients with both end-stage liver and renal disease necessitating renal replacement therapy. However, it is less defined for patients with mild to moderate renal dysfunction and those with potentially reversible causes of acute renal failure including hepatorenal syndrome. It is challenging to accurately predict irreversibility or the possibility of progression of renal failure.

With the introduction of the Model for End-Stage Liver Disease (MELD) scoring system in 2002, which prioritizes renal dysfunction, a substantial increase in the number of CLKTs was observed especially in the US. This growing number of CLKT is not only a consequence of the MELD allocation system, but likely also because of changing practices in transplant centres [4]. Over the past 15 years, the number of CLKT performed in the US has increased from fewer than 150 per year to more than 700 in 2016. This comprises 9.3% of the total liver transplantations performed annually.

Concerns about the lack of clear rules for CLKT allocation have arisen as a consequence of the growing number of CLKT transplants [4,5]. Until 2017, there was no standard allocation policy for CLKT available in the US and each transplant centre had the freedom to decide eligibility on a case-by-case basis. However, in 2017 a UNOS allocation policy for CLKT was implemented, which defines medical eligibility criteria for CLKT and at the same time provides a safety-net by assigning priority for renal allograft allocation to liver transplant recipients with end-stage renal disease within 1 year after liver transplantation [6,7]. The implementation of a safety-net to allow accelerated access to kidney

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transplantation for liver transplant patients with persistent renal failure is an important component in fairer allocation of organs. Consequently, end-stage renal disease patients will have faster access to a donor kidney which is especially important considering the scarcity of donor organs. The median waiting time for a kidney only transplant in the US and UK is 4 and 3 years, respectively [8,9].

In Europe, national data on CLKT are lacking. In 2017, 45 CLKT were transplanted within the Eurotransplant region, which is 3% of the total liver transplantations [10]. Tinti *et al.* reported in this issue of Transplant International, the national UK experience on CLKT. From January 2001 to December 2013, 5912 (98%) patients receiving a liver transplant alone and 123 (2%) patients received a CLKT [11]. Their data show that the total number of CLKT performed in Europe (UK) did not increase over time, in contrast compared to situation in the US. In this study from Birmingham, they compared both a liver transplant alone and CLKT with respect to patient and graft survival after stratifying on pretransplant estimated glomerular filtration rate (eGFR) based on Chronic Kidney Disease KDIGO guidelines. Based on these national data, they conclude that CLKT is only beneficial for patients already on chronic renal replacement therapy, that is, in this group patient and graft survival was significantly higher when CLKT was undertaken compared to LT only. The authors subsequently suggest that CLKT is unnecessary in patients without RRT and interferes with appropriate utilization of kidney organs. CLKT is not superior to liver transplant alone regarding patient and graft survival or renal function in patients with KDIGO stages 3, 4 and 5. Striking is the similar or even worse kidney function after CLKT compared to liver transplant alone. Intuitively, one would expect a superior kidney function after CLKT compared to liver transplant alone with at best three functioning kidneys. The authors could not analyse this observation in more detail because of the study design. A possible explanation could be a more pronounced ischaemic/reperfusion damage when the kidney transplantation is performed right after the liver transplantation, when some of the recipients are haemodynamical instable and treated with vasopressors directly after liver transplantation. To avoid this situation, kidney transplantation could be postponed for 2–3 days. In the meantime, a kidney graft is placed on a hypothermic pulsatile perfusion machine [12,13]. This approach allows stabilization of the coagulopathy and haemodynamic status, before implantation of the kidney allograft. Consequently, the kidney graft is not compromised by hepatic reperfusion injury and elevated bilirubin levels, both of which damage renal tubules [14]. Ekser el al. compared the outcomes of simultaneous and delayed implantation of kidney grafts in CLKT. This study showed that delayed kidney transplantation in CLKT is associated with significantly improved kidney function with no DGF, and improved patient and graft survival [12]. These results are confirmed by Lunsford *et al.* [13] with significant better patient and graft survival after delayed implantation of the kidney.

Kidney after liver transplantation (KALT) is another alternative option, which is normally used for liver transplantation recipients who develop chronic renal failure because of calcineurin inhibitor-induced nephrotoxicity. The benefits of KALT in an earlier stage after liver transplantation are a lower perioperative morbidity and greater supply of kidneys (choice between deceased or living donor) [15]. Kitajama *et al.* [16] described 13 patients who underwent sequential liver transplantation and kidney transplantation even from single living donors. Kidney transplantation was performed between 1.7 and 47.0 months after the liver transplantation with excellent overall patient survival rate of 92.3% at 10 years and death-censored renal allograft survival rate of 100% at 10 years.

Combined liver and kidney transplantation has made a significant contribution for patients with dual-organ disease. Optimization of indication and selection of CLKT patients will reduce futile transplantation. Moreover, delaying kidney transplantation for 2–3 days will probably improve kidney function. It seems that stricter indications are needed to select those who benefit mostly from CLKT. The future will tell whether better stricter patient selection will lead to a more optimal use of donor organs and shorter waiting times for liver and kidney only transplantations, especially since alternative schemes for combining LT with KT are possible.

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Conflict of interest

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