Expert Opinion

JOURNAL
OF HEPATOLOGY

Combined liver with other solid organ transplants: Promises, pitfalls and ethical dilemmas

Francesco Paolo Russo[1,2,*,†], **Sarwa Darwish Murad**[3,†], Anjana A. Pillai[4], Alexandra Shingina[5], Laura Donahoe[6], Anna Mrzljak[7], Yaron Avitzur[8], Patrizia Burra[1,2,*,‡], Nazia Selzner[9,‡]

Summary

In this expert opinion, we explore the growing practice of multi-organ transplantation (MOT) in which liver transplantation is combined with another solid organ transplantation, such as heart, lung or kidney transplantation. There is an increasing demand for MOT as a lifesaving treatment for patients with multi-organ failure, despite societal challenges like donor shortage and complex logistics. MOT recipients, when well-chosen, demonstrate favourable survival outcomes, although the procedures involve significant risks and require close coordination among specialised teams. Patient selection and resource allocation require careful ethical consideration to balance equity and utility. Ethical dilemmas arise regarding prioritisation, particularly when organs are allocated to one patient over several others. In this opinion paper, we emphasise the need for global standardisation of protocols and robust multidisciplinary care. Immunological advantages, advanced risk assessments, and novel technologies, such as machine perfusion, improve success rates. This opinion piece calls for harmonised policies to address disparities in organ allocation while maintaining equitable access and optimised outcomes.

Introduction

In recent years, improvements in post-transplant care have made it possible to consider transplant candidates with more complex medical conditions, leading to a rise in combined liver multi-organ transplantation (LiMOT) procedures, which include combined heart-liver (CHLT), liver-lung (CLLT), and liver-kidney (CLKT) transplants, even as organ scarcity remains a significant challenge. LiMOT practices present unique challenges that demand: 1. careful evaluation of infrastructure and resources; 2. standardisation of immunosuppression protocols; 3. comprehensive anti-microbial prophylaxis protocols; and 4. multidisciplinary collaboration and integrated post-operative care across organ systems. Once these systems are in place, survival rates are similar in carefully selected LiMOT recipients as in single organ transplant recipients, with the liver providing immune-protective benefits for other allografts.[1]

However, a delicate balance exists in organ allocation. Policy makers must weigh the benefits of utilising scarce resources for one patient against the potential to save multiple lives. This requires continuous evaluation of existing data and maintaining system equity and utility.

During the 2024 ILTS (International Liver Transplantation Society) Annual Congress, a multi-society joint symposium of ILTS together with the European Association for the Study of the Liver and American Association for the Study of Liver Diseases was held, themed around LiMOT. This symposium, which drew considerable attention, formed the basis of the current expert opinion paper in which we will examine the promises, pitfalls and ethical dilemmas associated with combined heart-liver, liver-lung and liver-kidney transplantation.

Combined heart-liver transplantation

The need for CHLT arises from the close physiological link between heart and liver diseases. Heart failure can cause liver damage through congestion and ischaemia, while liver dysfunction can exacerbate cardiac conditions. This interplay necessitates careful patient selection to identify those who would benefit most from a dual-organ transplant rather than an isolated heart or liver transplant.[2]

According to recent guidelines, CHLT is particularly indicated for patients with end-stage heart failure and significant liver complications, such as cardiac cirrhosis or hepatocellular carcinoma, which can arise in chronic right heart failure or congenital heart defect-related conditions like Fontan-associated liver disease. For these patients, a heart transplant alone may not suffice due to the risk of hepatic complications that could hinder recovery or even be life-threatening.[3,4] The most common indications for CHLT are summarised in Fig. 1 and a strategy to determine which patients could potentially benefit from CHLT as opposed to single organ transplantation is proposed in Fig. 2.

* Corresponding authors. Address: Gastroenterology and Multivisceral Transplant Unit, Azienda Ospedale- Università Padova; Department of Surgery, Oncology and Gastroenterology, Università degli Studi di Padova, Italy.
E-mail addresses: francescopaolo.russo@unipd.it (F.P. Russo), burra@unipd.it (P. Burra).
† These authors contributed equally
‡ These authors contributed equally
https://doi.org/10.1016/j.jhep.2025.04.027

Current CHLT evaluation practices remain notably heterogeneous, highlighting significant challenges in standardisation. The assessment of liver disease severity varies substantially between centres, with some relying heavily on biopsy findings while others prioritise imaging and non-invasive markers.[5,6] Patient selection criteria demonstrate marked variation between centres with MELD-XI (a modified model for end-stage liver disease score excluding international normalised ratio – as CHLT candidates are often on vitamin K antagonists) score cut-offs for listing ranging from 12 to 16 across institutions, and significant heterogeneity in portal hypertension assessment methods, with no consensus on optimal measurement techniques or cut-off values.[7]

Geographic variations in practice reflect local resources and expertise. European centres often favour *en bloc* procedures, while North American programmes typically prefer sequential transplantation, where both organs are implanted separately but during the same operation. Asian protocols emphasise living donation considerations, and resource-limited regions face unique allocation challenges that influence their approach to CHLT.

Outcomes following CHLT are generally favourable, with 5-year survival rates often exceeding 80%, similar to those for isolated heart transplants. These outcomes are likely a result of careful patient selection as well as the well-described liver-related immunoprotective effects in CHLT.

While CHLT can be performed either sequentially or *en bloc*, the sequential approach is typically preferred as it allows for patient stabilisation and benefits from recent advances in liver perfusion technology.[8] The liver's immunological privilege[9] in CHLT provides protection against heart allograft rejection, leading some centres to consider this approach for highly sensitised candidates, with a liver-first strategy showing particular benefit in these cases.

The path forward requires collaboration to establish evidence-based protocols while acknowledging regional resources and constraints. Success in standardisation would improve outcomes and ensure equitable access to this life-saving procedure across the globe. The development of these standards must carefully balance the need for consistency with the flexibility to accommodate regional variations in resources and expertise.

Key recommendations for combined heart-liver transplantation:

- Consider CHLT for end-stage heart failure with documented cirrhosis with portal hypertension or end-stage liver disease otherwise meeting criteria for liver transplantation (*e.g.* hepatocellular carcinoma).
- Use MELD-XI >14.1 as a cut-off for dual transplant consideration.
- Evaluate severity of liver disease and portal hypertension through imaging and biopsy.
- Combined heart-liver transplantation is preferred over staged approach.
- Consider liver-first approach for highly sensitised patients.

Combined liver-lung transplantation

CLLT is an option for patients with concomitant end-stage pulmonary and hepatic disease, in which failure of one organ precludes transplantation of the other. UNOS (United Network for Organ Sharing) data from 2006-2016 showed that, out of

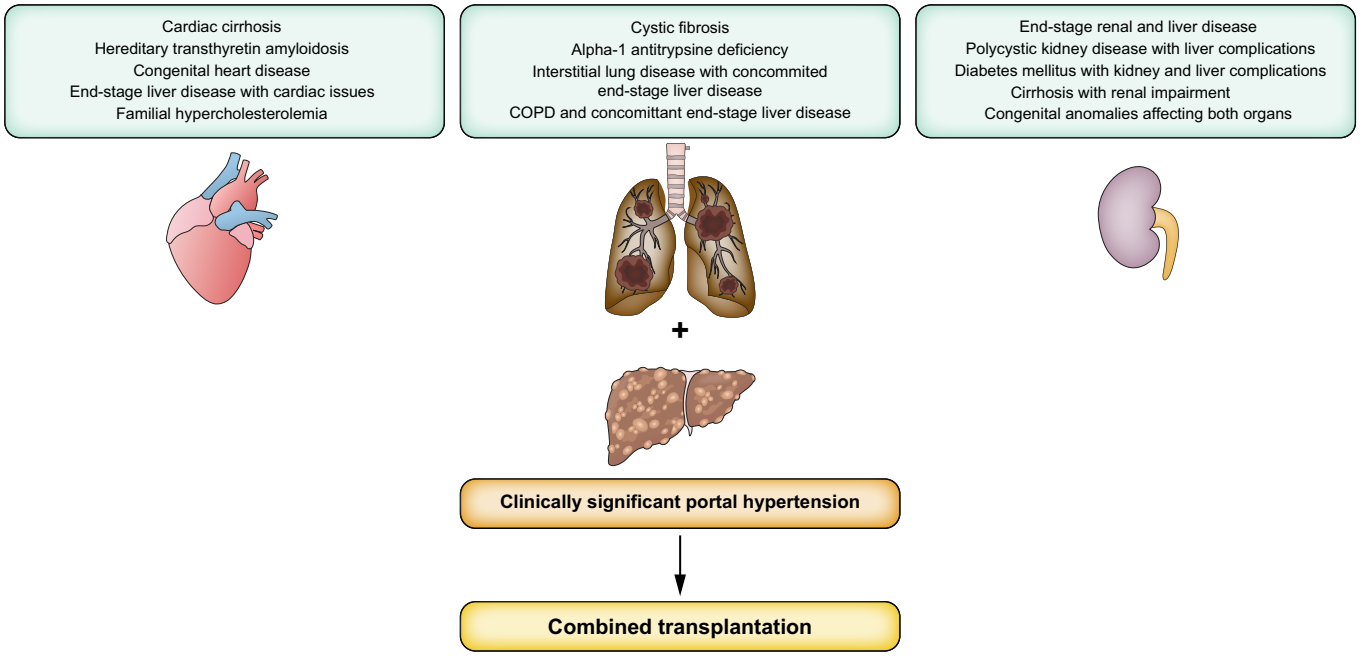

Fig. 1. Most common clinical indications for combined heart-liver, lung-liver and kidney-liver transplantation, in the setting of cirrhosis with clinically significant portal hypertension.

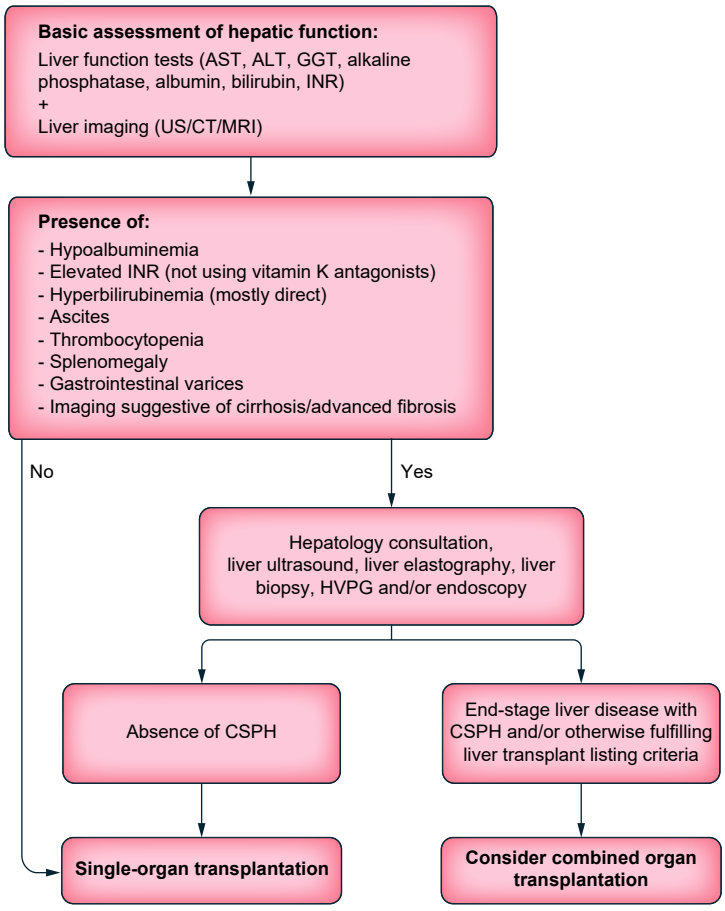

Fig. 2. Suggested algorithm to assess whether liver function warrants combined liver transplantation in candidates for heart, lung or kidney transplantation. ALT, alanine aminotransferase; AST, aspartate aminotransferase; CSPH, clinically significant portal hypertension; GGT, gamma-glutamyltransferase; INR, international normalised ratio; HVPG, hepatic venous pressure gradient.

23,513 patients listed for lung transplant, only 110 (0.4%) were listed for CLLT, of whom 35 died or were removed from the waiting list (32%) and merely 40 (36%) eventually underwent CLLT.[10] Indeed, CLLT is performed in a few high-volume centres only, the largest of which reported 19 CLLTs over 12 years.[11] In fact, reported global practices appear limited to less than 10 centres worldwide, most of them located in North America and Western Europe. The allocation of CLLT is driven by the LAS (Lung Allocation Score) and patients receive waitlist priority over single organ transplantation candidates.

The primary driver of CLLT is the pulmonary disease, with the most common indication being cystic fibrosis, followed by interstitial lung disease, chronic obstructive pulmonary disease, including alpha-1 antitrypsin deficiency, and pulmonary vascular disease[12] (Fig. 1). Over time, the number of transplants for cystic fibrosis is declining because of effective therapy, while the number for interstitial lung disease is increasing.

The two most common pulmonary conditions in end-stage liver disease, *i.e.* hepatopulmonary syndrome and portopulmonary hypertension, rarely warrant CLLT, as they usually improve upon liver-only transplantation. Indeed, liver-only transplantation resolves hepatopulmonary syndrome in 95% of cases after 6-12 months, while in rare cases, CLLT can be considered for portopulmonary hypertension when liver-only transplant is contraindicated (*i.e.* mean pulmonary artery pressure >45 mmHg despite targeted therapy for pulmonary arterial hypertension).[13,14]

The decision to perform CLLT as opposed to lung-only transplant is largely based on the severity of the underlying liver disease (Fig. 2). In CLLT surgery, the lungs are usually implanted first, due to the severity of the pulmonary disease, although *ex vivo* lung perfusion nowadays enables a liver-first approach.[15] Previously, all CLLTs were performed on cardiopulmonary bypass, while increasingly extracorporeal membrane oxygenation is being used, which lowers operative risks. However, perioperative mortality is still as high as 15%, highlighting the complex nature of CLLT and the need for experienced teams.[15]

CLLT survival rates vary considerably in the small case-series reported to date, ranging from 50-100% at 1 year and 49-100% at 5 years, with improvements in more recent eras. CLLT is associated with inferior survival compared to liver-only transplant and similar survival to lung-only transplant, although in children and patients with cystic fibrosis, survival is similar for CLLT and liver-only transplant.[16] In a recent propensity-score matched analysis investigating whether recipients of CLLT actually needed the liver, CLLT recipients were compared

to lung-only recipients with equal LAS and MELD-IX score. While waitlist mortality (hazard ratio 3.2) and transplant ratio (odds ratio 0.255) indicated higher waitlist removal in CLLT, no survival advantage of CLLT over lung-only transplant was found.[17,18] These data question the benefit and ethical principles of equity when allocating two organs to one recipient, while at the same time CLLT provides a transplant benefit for patients otherwise not eligible for single organ transplantation. Therefore, as in other LiMOT, careful patient selection is key in CLLT.

Key recommendations for combined liver-lung transplantation:

- CLLT is a rare procedure performed in a few high-volume centres in North America and Europe.
- Indications for CLLT are changing over time and should be reserved for those patients with simultaneous liver and lung failure, in whom failure of one organ precludes lifesaving single organ transplantation of the other.
- Outcomes after CLLT are comparable to lung-only, but worse than liver-only transplantation.
- Patient selection is key to ensure equitable access to transplant while at the same time providing a lifesaving option for those otherwise not eligible for transplantation.

Combined liver-kidney transplantation

Renal dysfunction in end-stage liver disease is not just a complication; it is a decisive factor in the trajectory of patient outcomes, pre- and post-transplant.[19,20] Despite advances in understanding the pathophysiology of end-stage liver disease and its renal implications, there remains a considerable gap in standardised global criteria for CLKT eligibility.[21]

In contrast to CHLT and CLLT, the indication for CLKT is usually driven by the kidney disease in patients with known liver disease, or a multisystem disease affecting both organs at the same time (Fig. 1); although, in rare cases, liver disease is discovered during the evaluation for kidney transplantation (Fig. 2). Here, the ethical considerations are different, since the liver allocation system is based on MELD, which incorporates kidney function, potentially favouring patients on the liver waitlist at the expense of those on the kidney waitlist. To this end, in the US, the Organ Procurement and Transplantation Network (OPTN) defined strict criteria for liver-kidney transplant candidates based on chronic kidney disease (CKD), acute kidney injury and rare metabolic disorders. Candidates who do not meet these criteria still have a "safety net" to access a deceased donor kidney transplant if their glomerular filtration rate is low (≤20 ml/min) or if they are dialysis-dependent between 60 days and 1 year after liver-only transplantation.[22] The access to CLKT is promoted in cases where the severity of the disease (*e.g.* primary hyperoxaluria type 1 or polycystic disease) is not accurately reflected by the MELD score through standard exceptions which are nationally defined. In Europe, Eurotransplant applies the MELD-based allocation system.[23] Other CLKT allocation policies across Europe also mostly rely on MELD-based allocation with an individualised approach. The high variability in regional policies, ranging from stringent OPTN standards to the more flexible but less standardised European guidelines, underscores the need for a harmonised approach that integrates both the complexity of renal pathology and patient individuality.[24]

This lack of uniformity, we believe, has significant implications that necessitate urgent re-evaluation and targeted strategic changes.

The growing body of evidence suggests that patients undergoing CLKT experience improved survival rates compared to those undergoing liver transplantation alone, especially in those with advanced CKD or extended dialysis durations.[25,26] It is also essential to recognise that the demographics of CLKT candidates are evolving, as recipients are becoming older and presenting with more severe illnesses and comorbidities, including a higher incidence of metabolic disorders. Furthermore, for haemodynamically unstable patients, the delayed kidney after liver transplant approach has been introduced. This method, combined with hypothermic machine perfusion, has demonstrated better outcomes compared to CLKT. The interpretation of CLKT as a dual-organ transplant that burdens the organ allocation system is another point of debate that could do with a shift in perspective. Instead, CLKT could be viewed as a strategic investment in reducing cumulative healthcare costs and improving long-term patient outcomes.[23] The immunological advantage that CLKT confers over kidney transplantation alone should not be underestimated.[25] This benefit not only enhances the recipient quality of life but also optimises organ utility by extending graft survival.

A vision for the future of CLKT should pivot from the current reactive model to a proactive, risk-based evaluation framework. This would mean expanding eligibility criteria beyond mere numerical thresholds to include comprehensive risk stratification models that integrate biochemical, imaging, and histopathological markers. Incorporating tools such as novel biomarkers indicative of early renal tubular damage or endothelial dysfunction could help clinicians better distinguish between transient acute or acute-on-chronic kidney injury and the progression to chronic, irreversible kidney damage.[27]

In conclusion, we believe the future of CLKT lies in fine-tuning of the eligibility criteria to include more precise biomarkers of irreversible *vs.* reversible kidney damage, and a rebalance of utility and equity, taking into consideration additional benefits besides graft and/or recipient survival. A collaborative international framework for CLKT policy development could bridge these gaps. Aligning transplant practices globally with evidence-based guidelines that emphasise personalised medicine will hopefully foster more equitable access and improve prognosis.

Key recommendations for combined liver-kidney transplantation:

- There is a considerable gap in standardised global criteria for CLKT eligibility.
- Indications for CLKT are changing: candidates are getting older and sicker, with higher likelihood of metabolic disorders and other comorbidities.
- CLKT improves survival rates when compared to liver transplantation alone, especially in those with advanced CKD or extended dialysis duration.
- For haemodynamically unstable patients, the delayed kidney after liver transplant approach may be considered.
- There is an immunological advantage of CLKT over kidney transplantation alone.
- A collaborative international framework for CLKT policy development is needed.

Ethical perspective

The prevalence of LiMOT has increased significantly over the past two decades, with more patients being listed for and undergoing combined transplants. CLKT, the most common multi-organ combination, has increased in the US from fewer than 150 cases in 2000 to more than 700 cases in 2016, accounting for 9.3% of the total liver transplants in that year.[28] Despite this increase, allocation policies for LiMOT remain largely inconsistent around the globe with each multi-organ combination having its own allocation policies and prioritisation. This variability can lead to LiMOT futility and inequity in organ accessibility, either in the rate of transplantation or in the waiting time for transplantation, for patients waiting for LiMOT or a single organ.

The ethical framework that can guide the allocation of LiMOT focuses on two ethical principles – equity and utility. The first implies that individuals who can derive similar benefit from an organ ought to have equivalent access to it through an equitable allocation system.[29] While utility suggests that an action is right if it promotes as much or more aggregate good than an alternative action.[30] In the transplant setting, utility translates to the maximal good of an organ in terms of organ and patient survival, improved quality of life, medical status and quality adjusted survival while avoiding futile transplants. The balance between equity and utility is critical for a just allocation to multi-organ and single organ recipients.

LiMOT is ethically justified when both transplanted grafts are lifesaving (*e.g.* lung-liver or heart-liver). However, transplant in the setting of CLKT where the kidney is not lifesaving in the immediate peri-transplant time, poses an ethical challenge, is less defensible and occasionally may be inappropriate. In a study from the US, recipients of LiMOT compared to 'next sequential kidney alone candidates' were more often white, had a shorter wait time, lower need for dialysis pre-transplant and received higher quality organs, but exhibited lower patient survival.[31] These findings highlight the potential impact of over-prioritisation of LiMOT *vs*. kidney transplant candidates, which can specifically disadvantage certain groups, such as highly sensitised and/or paediatric recipients. Furthermore, short and long-term outcomes should be weighed when allocating organs to recipients of combined grafts. LiMOT procedures are often considered higher risk as they are performed in sicker recipients in multi-organ failure, while recipient death naturally results in the loss of two scarce organs that two other recipients could have benefited from.

In an attempt to reduce these disparities and improve equity and utility between kidney LiMOT and isolated kidney transplant, OTPN defined in 2017 medical eligibility criteria for CLKT based on predefined kidney function criteria or specific metabolic diseases. In addition, to encourage avoidance of an unnecessary kidney transplant, an allocation priority was provided for isolated liver transplant recipients who did not recover their kidney function post-transplant.[28] A recent white paper by the ethics committee of OPTN/UNOS on LiMOT allocation policies and practice can help guide national and local policy development to further optimise equity, utility and organ use.[32]

Key recommendations and priority areas for field advancement in multi-organ transplantation:

- Allocation policies for LiMOT should achieve balanced equity and utility in multi-organ and single organ transplant recipients.
- Over-prioritisation of combined liver-kidney transplant candidates negatively impacts other kidney transplant candidates and should be avoided.
- LiMOT practices and policies need to be periodically reviewed to monitor potential impact on recipients in need of a single organ.
- National and/or regional policies for allocation of LiMOT are necessary to optimise equity and utility of grafts.
- Assessment protocols for severity of liver disease and portal hypertension need to be standardised.
- There is an unmet need for unified candidate selection criteria for combined organ transplantation as opposed to single organ transplantation.
- Data on long-term outcomes should be collected and reported.
- Cost-effectiveness studies are needed.

Discussion

Single organ transplantation has transformed the prognosis of patients with irreversible organ failure, offering renewed life where alternatives are limited. Over the past 20 years, LiMOT, including CHLT, CLLT, and CLKT procedures, has become more prevalent despite challenges such as donor shortages and complex management protocols. Notably, patients listed for CHLT and CLLT face higher waitlist mortality, underscoring the importance of LiMOT in certain

high-risk populations where isolated organ transplantation may not suffice.

Policymakers face ethical dilemmas when balancing the allocation of limited donor organs to a single *vs.* multiple recipients. Equitable distribution and maximising patient survival remain critical priorities. LiMOT requires precise selection criteria to identify patients who would benefit most. The integration of detailed risk assessments, advanced imaging, and histopathological evaluations is essential to distinguish between reversible and irreversible organ damage. Additionally, LiMOT recipients demand coordinated, multidisciplinary care involving specialised preoperative assessments, immunosuppressive management, and post-transplant monitoring across organ systems. Despite these complexities, carefully selected LiMOT recipients demonstrate comparable or even improved short- and long-term survival rates relative to single organ transplant recipients. The success of these procedures hinges on experienced transplant teams, standardised protocols, and robust communication among all stakeholders to ensure optimal outcomes and judicious use of scarce donor resources. There is an unmet need to share and align knowledge and practices of LiMOT across the globe through international cross-disciplinary collaborative initiatives, uniting transplant professionals (including the figure of transplant hepatologists), policymakers and patient representatives in a joint quest to minimise disparities in organ allocation while maintaining equitable access and optimised outcomes for these complex patients.

Affiliations

[1]*Gastroenterology and Multivisceral Transplant Unit, Azienda Ospedale- Università Padova, Italy;* [2]*Department of Surgery, Oncology and Gastroenterology, Università degli Studi di Padova, Italy;* [3]*Department of Gastroenterology and Hepatology, Erasmus MC Transplant Institute, Erasmus MC University Medical Center, Rotterdam, the Netherlands;* [4]*Division of Gastroenterology, Hepatology, and Nutrition, University of Chicago Medicine, Chicago, Illinois, USA;* [5]*Division of Gastroenterology, Department of Internal Medicine at University of Michigan Health, USA;* [6]*Division of Thoracic Surgery, Toronto General Hospital, University Health Network, Toronto, Ontario, Canada;* [7]*Department of Gastroenterology and Hepatology, University Hospital Center Zagreb, Zagreb, Croatia;* [8]*Division of Gastroenterology, Hepatology and Nutrition, SickKids Hospital, University of Toronto, Toronto, ON, Canada;* [9]*Ajmera Transplant Centre, HBP & Multi-Organ Transplant Program, University Health Network, Toronto, Ontario, Canada*

Abbreviations

CHLT, combined heart-liver transplantation; CKD, chronic kidney disease; CKLT, combined kidney-liver transplantation; CLLT, combined lung-liver transplantation; LiMOT, liver multi-organ transplantation; MELD, model for end-stage liver disease; MELD-XI, MELD excluding international normalised ratio; MOT, multi-organ transplantation; OPTN, Organ Procurement and Transplantation Network.

Financial support

The authors did not receive any financial support to produce this manuscript.

Conflict of interest

The authors of this manuscript have no conflicts of interest to disclose.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

FPR, SDM, PB and NS were involved in the concept, design, and writing the manuscript; AAP, AS, LD, AM, and YA were involved in writing the manuscript. All authors were involve in revision an approval of the final draft of the manuscript.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2025.04.027.

References

Author names in bold designate shared co-first authorship

[1] Zhang IW, Lurje I, Lurje G, et al. Combined organ transplantation in patients with advanced liver disease. Semin Liver Dis 2024 Aug;44(3):369–382. https://doi.org/10.1055/s-0044-1788674. Epub 2024 Jul 25. PMID: 39053507; PMCID: PMC11449526.

[2] Zhao K, Mclean RC, Hoteit MA, et al. Combined heart and liver transplant: indication, patient selection, and allocation policy. Clin Liver Dis (Hoboken) 2019 Jul 2;13(6):170–175. https://doi.org/10.1002/cld.812. PMID: 31316764; PMCID: PMC6605737.

[3] Lewis MJ, Reardon LC, Aboulhosn J, et al. Clinical outcomes of adult fontan-associated liver disease and combined heart-liver transplantation. J Am Coll Cardiol 2023 Jun 6;81(22):2149–2160. https://doi.org/10.1016/j.jacc.2023.03.421. PMID: 37257950.

[4] Kittleson MM, Sharma K, Brennan DC, et al. American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology, Council on the Kidney in Cardiovascular Disease, Council on Cardiovascular Surgery and Anesthesia, Council on Cardiovascular and Stroke Nursing, Council on Quality of Care and Outcomes Research, Council on Lifelong Congenital Heart Disease and Heart Health in the Young Dual-organ transplantation: indications, evaluation, and outcomes for heart-kidney and heart-liver transplantation: a scientific statement from the American heart association. Circulation 2023 Aug 15;148(7):622–636. https://doi.org/10.1161/CIR.0000000000001155. Epub 2023 Jul 13. Erratum in: Circulation. 2023 Aug 15;148(7):e6. doi: 10.1161/CIR.0000000000001175. PMID: 37439224.

[5] Shingina A, Chadha R, Lim N, et al. Combined heart-liver transplantation practices survey in North America: evaluation and organ listing practices. Liver Transpl 2023 Jun 1;29(6):591–597. https://doi.org/10.1097/LVT.0000000000000079. Epub 2023 Feb 7. PMID: 36745932; PMCID: PMC10191975).

[6] Kobashigawa J, VanWagner LB, Hall S, et al. Consensus Conference participants Summary of a consensus conference on heart-liver transplantation. Am J Transpl 2024;24(3):380–390. https://doi.org/10.1016/j.ajt.2023.12.002. Epub 2023 Dec 9. PMID: 38072122.

[7] **Deo SV**, **Al-Kindi SG**, Altarabsheh SE, et al. Model for end-stage liver disease excluding international normalized ratio (MELD-XI) score predicts heart transplant outcomes: evidence from the registry of the United Network for Organ Sharing. J Heart Lung Transpl 2016 Feb;35(2):222–227. https://doi.org/10.1016/j.healun.2015.10.008. Epub 2015 Oct 9. PMID: 26527533.

[8] Rucker AJ, Anderson KL, Mulvihill MS, et al. Simultaneous versus sequential heart-liver transplantation: ideal strategies for organ allocation. Transpl Direct 2018 Dec 19;5(1):e415. https://doi.org/10.1097/TXD.0000000000000854. PMID: 30656213; PMCID: PMC6324910.

[9] Wong TW, Gandhi MJ, Daly RC, et al. Liver allograft provides immunoprotection for the cardiac allograft in combined heart-liver transplantation. Am J Transpl 2016 Dec;16(12):3522–3531. https://doi.org/10.1111/ajt.13870. Epub 2016 Jun 24. PMID: 27184686).

[10] Freischlag K, Ezekian B, Schroder PM, et al. A propensity-matched survival analysis: do simultaneous liver-lung transplant recipients need a liver? Transplantation 2019;103(8):1675–1682.

[11] Connor AA, Huang HJ, Mobley CM, et al. Progress in combined liver-lung transplantation at a single center. Transpl Direct 2023;9(5):e1482.

[12] Han JL, Beal EW, Mumtaz K, et al. Combined liver-lung transplantation: indications, outcomes, current experience and ethical Issues. Transpl Rev (Orlando) 2019;33(2):99–106.

[13] Raevens S, Boret M, Fallon MB. Hepatopulmonary syndrome. JHEP Rep 2022;4(9):100527.

[14] DuBrock HM. Portopulmonary hypertension: management and liver transplantation evaluation. Chest 2023;164(1):206–214.

[15] Machuca TN, Collaud S, Mercier O, et al. Outcomes of intraoperative extracorporeal membrane oxygenation versus cardiopulmonary bypass for lung transplantation. J Thorac Cardiovasc Surg 2015;149(4):1152–1157.

[16] Freischlag KW, Messina J, Ezekian B, et al. Single-center long-term analysis of combined liver-lung transplant outcomes. Transpl Direct 2018;4(5):e349.
[17] Desai CS, Gruessner A, Habib S, et al. Survival of cystic fibrosis patients undergoing liver and liver-lung transplantations. Transpl Proc 2013;45(1):290–292.
[18] Arnon R, Annunziato RA, Miloh T, et al. Liver and combined lung and liver transplantation for cystic fibrosis: analysis of the UNOS database. Pediatr Transpl 2011;15(3):254–264.
[19] **O'Leary JG**, **Levitsky J**, Wong F, et al. Protecting the kidney in liver transplant candidates: practice-based recommendations from the American Society of Transplantation Liver and Intestine Community of Practice. Am J Transpl 2016 Sep;16(9):2516–2531. https://doi.org/10.1111/ajt.13790.
[20] Morelli MC, Rendina M, La Manna G, et al., Italian Association for the Study of Liver, and the Italian Society of Nephrology. Position paper on liver and kidney diseases from the Italian association for the study of liver (AISF), in collaboration with the Italian society of nephrology (SIN). Dig Liver Dis 2021 Jun;53(Suppl 2):S49–S86. https://doi.org/10.1016/j.dld.2021.03.035.
[21] Singal AK, Ong S, Satapathy SK, et al. Simultaneous liver kidney transplantation. Transpl Int 2019 Apr;32(4):343–352. https://doi.org/10.1111/tri.13388.
[22] https://optn.transplant.hrsa.gov/media/1192/0815-12_slk_allocation.pdf.
[23] Eurotransplant. Liver Allocation system. Chapter 5. https://my.eurotransplant.org/wp-content/uploads/2024/08/H5-ELAS-MELD-August-2024.pdf.
[24] Cullaro G, Verna EC, Emond JC, et al. Early kidney allograft failure after simultaneous liver-kidney transplantation: evidence for utilization of the safety net? Transplantation 2021 Apr 1;105(4):816–823. https://doi.org/10.1097/TP.0000000000003310.
[25] Rana A, Robles S, Russo MJ, et al. The combined organ effect: protection against rejection? Ann Surg 2008 Nov;248(5):871–879. https://doi.org/10.1097/SLA.0b013e31817fc2b8. PMID: 18948817.
[26] Wong F, Leung W, Al Beshir M, et al. Outcomes of patients with cirrhosis and hepatorenal syndrome type 1 treated with liver transplantation. Liver Transpl 2015 Mar;21(3):300–307. https://doi.org/10.1002/lt.24049.
[27] Horvatits T, Pischke S, Proske VM, et al. Outcome and natural course of renal dysfunction in liver transplant recipients with severely impaired kidney function prior to transplantation. United Eur Gastroenterol J 2018 Feb;6(1):104–111. https://doi.org/10.1177/2050640617707089.
[28] Miles CD, Westphal S, Liapakis A, et al. Simultaneous liver-kidney transplantation: impact on liver transplant patients and the kidney transplant waiting list. Curr Transpl Rep 2018;5(1):1–6. https://doi.org/10.1007/s40472-018-0175-z. PMID: 29564203.
[29] Reese PP, Veatch RM, Abt PL, et al. Revisiting multi-organ transplantation in the setting of scarcity. Am J Transpl 2014 Jan;14(1):21–26. https://doi.org/10.1111/ajt.12557. PMID: 24354869.
[30] Cheng XS, Goldhaber-Fiebert J, Tan JC, et al. Defining a willingness-to-transplant threshold in an era of organ scarcity: simultaneous liver-kidney transplant as a case example. Transplantation 2020 Feb;104(2):387–394. https://doi.org/10.1097/TP.0000000000002788. PMID: 31107820.
[31] Westphal Scott G, Langewisch Eric D, Robinson Amanda M, et al. The impact of multi-organ transplant allocation priority on waitlisted kidney transplant candidates. Am J Transpl 2021 Jun;21(6):2161–2174. https://doi.org/10.1111/ajt.16390.
[32] OPTN/UNOS Ethics Committee. Organ Procurement and Transplantation Network. Ethical implications of multi-organ transplants, 2019. https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/ethical-implications-of-multi-organ-transplants/; 2019.

Keywords: multi-organ transplantation; combined heart-liver transplantation; combined lung-liver transplantation; combined kidney-liver transplantation; ethic.
Received 28 November 2024; received in revised form 14 April 2025; accepted 22 April 2025; available online 30 April 2025