Annals of Hepatology 31 (2026) 102155

Contents lists available at ScienceDirect

Annals of Hepatology

journal homepage: www.elsevier.es/annalsofhepatology

Opinions

Beyond the association: towards an integrated hepato–renal approach

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ARTICLE INFO

Article History:
Received 30 October 2025
Accepted 2 November 2025
Available online 12 November 2025

Chronic liver disease (CLD) and chronic kidney disease (CKD) remain major global health challenges with profound effects on morbidity, mortality, and healthcare systems [1,2]. Traditionally considered distinct entities, they are increasingly recognized as interconnected within the broader cardio-metabolic continuum [3]. This emerging concept reflects overlapping risk factors, shared molecular pathways, and clinical observations that dysfunction in one organ increases susceptibility to disease in the other.

In this issue of *Annals of Hepatology*, He and colleagues provide compelling longitudinal evidence of a bidirectional association between CLD and CKD using data from the nationally representative CHARLS cohort (2011–2020) [4]. Among >9000 participants followed for nine years, baseline CLD nearly doubled the risk of subsequent CKD, while baseline CKD similarly increased the risk of developing CLD. These results reinforce the notion that liver and kidney diseases exist along a continuum of metabolic and inflammatory dysfunction, demanding integrated approaches to prevention and care.

The strength of this study lies in demonstrating true bidirectionality, bridging a gap left by earlier analyses that largely addressed unidirectional relationships. Prior meta-analyses established that metabolic dysfunction–associated steatotic liver disease strongly predicts CKD [5,6], while clinical cohorts in cirrhosis showed that renal impairment worsens liver-related outcomes [7]. However, the reported CKD prevalence (19.7%) warrants cautious interpretation, as it was based on a single estimate of glomerular filtration rate, without repeated measures, proteinuria assessment, or histologic confirmation—potentially overestimating the true burden compared to prior reviews [8]. Despite these limitations, the findings of He et al.[4] offer important insights and highlight the urgent need for prospective studies using standardized criteria to clarify the temporal and causal dynamics of this association.

The hepato–renal relationship extends far beyond statistical correlations—it is increasingly evident in daily clinical practice. In our center, we encountered a 39-year-old man with alcohol-associated cirrhosis and biopsy-proven IgA nephropathy who developed persistent hepatic encephalopathy (HE) resistant to standard therapy. Despite optimization of lactulose, rifaximin, and cautious use of L-ornithine L-aspartate under nephrology co-management, HE persisted. The patient's CKD (KDIGO G4A2) with recurrent metabolic acidosis and hyperkalemia further complicated management. An integrated evaluation by hepatology and nephrology ultimately led to simultaneous liver–kidney transplantation, resulting in full resolution of HE and renal dysfunction. This experience exemplifies the clinical reality that dual organ failure cannot be effectively managed within isolated specialties, underscoring the need for early coordinated decision-making between teams.

The coexistence of CLD and CKD magnifies disease burden, complicates pharmacologic strategies, and challenges traditional treatment paradigms [9]. Reduced renal clearance alters the pharmacokinetics of standard hepatologic therapies, while systemic inflammation, endothelial dysfunction, and altered gut–liver–kidney crosstalk accelerate multiorgan injury [10–12]. Recognizing these interactions should guide diagnostic and therapeutic strategies. Patients with CLD should undergo routine renal assessment—including estimated GFR, albuminuria, and markers of tubular injury—while those with CKD should be screened for hepatic steatosis and fibrosis [13].

Beyond individual care, structural integration between hepatology and nephrology is imperative. Shared clinical pathways can improve prognostication, optimize medication safety, and identify candidates for simultaneous transplantation. Although still underutilized, combined liver–kidney transplantation remains the only curative option for selected patients with advanced dual-organ dysfunction [14,15]. Development of joint guidelines and prospective registries would help refine selection criteria and long-term outcomes.

Mechanistic exploration of the gut–liver–kidney axis, systemic inflammation, oxidative stress, and metabolic signaling may yield targets for interventions with dual-organ benefits. Translational research should prioritize therapies that modulate shared pathways, such as SGLT2 inhibitors, renin–angiotensin system blockade, and microbiota-directed strategies. Furthermore, adopting cardio–renal–metabolic frameworks into hepatology could accelerate discovery of biomarkers and risk scores applicable across organ systems.

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https://doi.org/10.1016/j.aohep.2025.102155

The study by He et al. [4] and the clinical experience described herein converge on a single message: the liver and kidney seldom fail in isolation. Yet, clinical and research structures remain fragmented. The retrospective design and reliance on surrogate markers in the CHARLS analysis underscore the importance of future prospective validation across diverse populations. Nevertheless, the evidence presented supports an evolving paradigm that demands integration of hepatology into systemic disease management.

Moving forward, hepatology should explicitly embrace the concept of a hepato–renal–metabolic axis, aligning with modern approaches already transforming cardiovascular and endocrine medicine. Incorporating renal evaluation into hepatology practice—and hepatic assessment into nephrology—should become routine. Integrated co-management models, early cross-screening, and unified transplant strategies represent essential steps toward improving patient outcomes and redefining how chronic liver and kidney disease are perceived: not as parallel entities, but as interdependent components of a single systemic disorder.

Looking ahead, acknowledging the hepato–renal axis as a clinical and research priority will be essential to improving outcomes. A structured, integrated model is no longer optional but essential, ensuring coordinated management, early intervention, and optimized outcomes for patients with concurrent liver and kidney disease.

Declaration of interests

None.

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