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Intraoperative Renal Biopsy During Liver Transplantation in Patients with Preexisting Acute Kidney Injury: Histopathological Associations with Postoperative Renal Replacement Therapy

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ABBREVIATIONS

AKI, acute kidney injury

ATI, acute tubular injury

CI, confidence interval

eGFR, estimated glomerular filtration rate

HRS, hepatorenal syndrome

IFTA, interstitial fibrosis and tubular atrophy

IQR, interquartile range

KDIGO, Kidney Disease: Improving Global Outcomes

LT, liver transplantation

MELD, Model for End-Stage Liver Disease

RRT, renal replacement therapy

SD, standard deviation

SLK, simultaneous liver-kidney transplantation

ABSTRACT

Background. Acute kidney injury (AKI) in decompensated cirrhosis is associated with poor outcomes after liver transplantation (LT), and creatinine-based tools poorly predict postoperative renal recovery. We evaluated whether histopathology on intraoperative renal biopsy is associated with renal replacement therapy (RRT) after LT.

Methods. In this retrospective single-center cohort study, 22 adults with decompensated cirrhosis and KDIGO-defined AKI underwent intraoperative renal biopsy during deceased-donor LT between October 2022 and June 2024. Two early deaths were retained in the safety cohort, leaving 20 patients for renal-outcome analysis. The primary endpoint was RRT within 90 days; prespecified histological predictors were acute tubular injury (ATI) score ≥2 and interstitial fibrosis and tubular atrophy (IFTA) >10%.

Results. Five of 20 patients (25.0%) initiated RRT within 90 days, and 3 remained RRT-dependent at day 90. RRT occurred in 5 of 9 patients with ATI ≥2 versus 0 of 11 with ATI <2 (risk difference, 55.6 percentage points; 95% CI, 16.8–81.1; $P = .008$) and in 4 of 7 with IFTA >10% versus 1 of 13 with IFTA ≤10% (risk difference, 49.5 percentage points; 95% CI, 8.4–77.2; $P = .031$). IFTA correlated strongly with time to renal function stabilization (Spearman $\rho = 0.907$; $P < .001$). No severe biopsy-related complications occurred, although transient hematuria was common. **No conventional preoperative clinical variable distinguished patients with and without subsequent RRT.**

Conclusions. Moderate-to-severe ATI and IFTA burden on intraoperative renal biopsy were associated with post-LT RRT requirement. Intraoperative biopsy was feasible in this high-risk population. These hypothesis-generating findings require validation in larger multicenter cohorts.

INTRODUCTION

Acute kidney injury (AKI) occurs in 20%–50% of patients with decompensated cirrhosis and strongly predicts mortality before and after liver transplantation (LT).[1,2] Serum creatinine and the Model for End-Stage Liver Disease (MELD) score poorly predict postoperative renal recovery,[3,4] partly because creatinine production in cirrhosis is confounded by reduced hepatic synthesis, malnutrition, and sarcopenia. A substantial subset of patients with pretransplant AKI progresses to persistent renal dysfunction or requires renal replacement therapy (RRT) after transplantation, and current tools cannot reliably identify these individuals.

The traditional dichotomy between hepatorenal syndrome (HRS), considered a purely functional disorder, and structural acute tubular necrosis has been increasingly challenged.[5] Urinary neutrophil gelatinase-associated lipocalin levels in HRS are intermediate between prerenal azotemia and tubular necrosis,[6] glomerular pathology has been identified in up to 77% of cirrhotic patients with AKI,[7] and cholemic tubular injury and bile cast nephropathy are common in jaundiced patients.[8,9] Functional and structural injury therefore appear to coexist along a continuum that clinical criteria cannot resolve.

Renal biopsy remains the reference standard for characterizing structural injury, but percutaneous biopsy is frequently contraindicated in LT candidates because of coagulopathy, thrombocytopenia, and ascites. Intraoperative renal biopsy, performed under direct vision with surgical hemostasis during the transplant operation, circumvents this constraint and was performed successfully in 21 LT recipients.[10] However, whether specific histological lesions on intraoperative biopsy are associated with postoperative RRT in patients with pretransplant AKI is unknown. We conducted this exploratory cohort study hypothesizing that higher acute tubular

injury (ATI) grades and greater interstitial fibrosis and tubular atrophy (IFTA) burden would be associated with RRT within 90 days.

MATERIALS AND METHODS

Study Design and Patients

This retrospective exploratory single-center cohort study was conducted at a tertiary LT center in northern China, and is reported in accordance with the STROBE guideline. Between October 2022 and June 2024, 109 consecutive adult deceased-donor LT recipients were screened. Inclusion criteria were age 18–70 years, decompensated cirrhosis, pretransplant AKI per KDIGO 2012 criteria,[11] and intraoperative biopsy yielding ≥5 glomeruli. Patients undergoing simultaneous liver-kidney transplantation (SLK), with RRT dependence >3 months, or without day-90 follow-up were excluded. Twenty-two patients underwent biopsy; 2 early posttransplant deaths preceded renal-outcome assessment and were retained in the safety cohort, leaving 20 patients for the primary analysis. MELD scores were calculated using the original 3-variable formula (serum creatinine, bilirubin, and international normalized ratio). The protocol was approved by the Ethics Committee of Tianjin First Central Hospital (approval No. 2020N151KY) and followed the Declaration of Helsinki. All patients provided written consent for the biopsy procedure; consent for retrospective analysis of deidentified data was waived.

Biopsy Procedure and Histopathology

To capture the pretransplant renal state and avoid confounding by caval clamping and the anhepatic phase, the biopsy was performed after mobilization of the native liver and before hepatectomy; a single cortical specimen was obtained from the outer third of the right renal upper pole using a 16-gauge Tru-Cut semiautomated needle, with immediate hemostasis by

bipolar electrocautery or 4–0 Prolene suture under direct vision. Paraffin sections were stained with hematoxylin-eosin, periodic acid–Schiff, Masson trichrome, and Jones silver, and immunofluorescence was performed for IgA, IgG, IgM, C3, C1q, fibrinogen, and albumin. Two renal pathologists blinded to clinical outcomes independently scored all specimens. Discordant ATI scores were resolved by joint review, and the consensus score was used for analysis; IFTA was estimated independently by each pathologist to the nearest 1%, and the mean of the 2 estimates was used for analysis. ATI was scored semiquantitatively from 0 to 3;[12] ATI ≥2 defined moderate-to-severe acute injury. IFTA was estimated as a continuous percentage of cortical area using the Banff 2022 classification as a reference framework,[13] with >10% prespecified as significant chronicity given evidence that even mild chronic changes carry prognostic weight.[14] Additional features recorded included global glomerulosclerosis, vascular changes, interstitial inflammation, pigment casts, thrombotic microangiopathy-like changes, immune complex deposition, and lesions specific to cirrhotic nephropathy (bile casts, IgA deposition, cholemic tubular injury, hepatic glomerulosclerosis).

Endpoints

The primary endpoint was initiation of RRT (hemodialysis, continuous RRT, or peritoneal dialysis) within 90 days after LT; persistent RRT dependence at day 90 was also recorded, and time to first RRT was summarized descriptively using Kaplan-Meier curves. The secondary endpoint was time to renal function stabilization, defined as 2 consecutive creatinine values ≥48 hours apart differing by <10% or <26.5 μmol/L in a patient no longer requiring RRT; stabilization after transient RRT was dated from RRT withdrawal. Biopsy-related adverse events were recorded prospectively in the 22-patient safety cohort.

Statistical Analysis

Continuous variables are presented as medians with IQR or means with SD, as appropriate. The 2 histological predictors (ATI ≥2 and IFTA >10%) and their thresholds were specified a priori on the basis of published evidence[12–14] rather than by data-driven selection; 90-day RRT incidence was compared using 2-sided Fisher exact tests, with risk differences reported with Newcombe 95% CIs[15] and Holm adjustment across the 2 comparisons; Firth-penalized logistic regression[16] served as a small-sample sensitivity analysis. Because no RRT events occurred in the ATI <2 group and only 5 events occurred overall, Cox regression was not used for primary inference.[17] Kaplan-Meier curves and log-rank tests were considered descriptive and were not adjusted for multiplicity. Associations with time to stabilization used Spearman correlation with bias-corrected accelerated bootstrap 95% CIs (2000 resamples), with Kendall tau-b as sensitivity analysis. Interobserver agreement was assessed using quadratic weighted kappa (ATI) and a 2-way random-effects single-measure intraclass correlation coefficient with absolute agreement (IFTA). A 2-sided $P < .05$ was considered significant. Analyses were performed using SPSS version 26.0 (IBM Corp, Armonk, NY) and R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria; logistf package). In addition, to contextualize the histological findings, baseline clinical variables were compared between patients with and without 90-day RRT using the Mann-Whitney U test for continuous variables and the Fisher exact test for categorical variables; this comparison was prespecified as descriptive and was not adjusted for multiplicity.

RESULTS

Patient Characteristics

Of 109 screened recipients, 22 underwent intraoperative biopsy; 2 died early (massive intraoperative hemorrhage on day 1 and intracerebral hemorrhage on day 4) before renal outcomes could be assessed, leaving 20 patients for the primary analysis; all 20 biopsy specimens were adequate, and no patient was lost to follow-up through day 90. Baseline characteristics are summarized in Table 1. The cohort was predominantly male (75.0%), with a median age of 58.5 years (IQR, 53.8–63.3) and a median MELD score of 12.0 (IQR, 9.8–14.3); 40.0% had Child-Pugh class C cirrhosis. Median serum creatinine was 151.8 μmol/L (IQR, 138.4–169.8), and the median estimated glomerular filtration rate (eGFR) was 37.5 mL/min/1.73 m^2 (IQR, 34.1–40.6). Fifteen patients (75.0%) had KDIGO stage 1 and 5 (25.0%) stage 2 AKI; none had stage 3 AKI or required preoperative RRT. Proteinuria ≥150 mg/d was present in 65.0% and microscopic hematuria in 35.0%. The most frequent clinical-etiological diagnosis was HRS-AKI (45.0%), followed by acute tubular necrosis (25.0%).

Histopathological Findings

Median core length was 14.0 mm (IQR, 13.0–14.3), with a median of 14.5 glomeruli (IQR, 12.8–16.3). ATI scores of 0, 1, 2, and 3 were observed in 4, 7, 6, and 3 patients, respectively; 9 (45.0%) had ATI ≥2. Median IFTA was 7.5% (IQR, 4.0–12.0); 7 patients (35.0%) had IFTA >10%. Global glomerulosclerosis, arteriosclerosis, pigment casts, thrombotic microangiopathy-like changes, and immune-complex deposition were observed in 8 (40.0%), 4 (20.0%), 4 (20.0%), 2 (10.0%), and 2 (10.0%) patients, respectively. Representative examples of acute tubular necrosis, interstitial fibrosis, and bile casts are shown in Figure 1. Interobserver agreement between the 2 pathologists was good (quadratic weighted $\kappa = 0.89$ for ATI, with exact agreement in 17 of 22 cases [77.3%]; intraclass correlation coefficient = 0.75 [95% CI, 0.48–0.89] for IFTA).

Renal Replacement Therapy Within 90 Days

Five patients (25.0%) initiated RRT at a median of 18 days (IQR, 6–30); 3 (15.0%) remained RRT-dependent at day 90, and 2 achieved stabilization on days 60 and 80 after RRT withdrawal. RRT occurred in 5 of 9 patients with ATI ≥2 versus 0 of 11 with ATI <2 (risk difference, 55.6 percentage points; Newcombe 95% CI, 16.8–81.1; Fisher exact $P = .008$; Holm-adjusted $P = .016$) and in 4 of 7 with IFTA >10% versus 1 of 13 with IFTA ≤10% (risk difference, 49.5 percentage points; 95% CI, 8.4–77.2; $P = .031$; Holm-adjusted $P = .031$). Firth-penalized sensitivity analyses were directionally consistent but imprecise (ATI ≥2: odds ratio, 28.1; 95% CI, 1.1–714.8; IFTA >10%: odds ratio, 10.7; 95% CI, 1.1–107.5). Kaplan-Meier estimates of 90-day RRT-free survival were 44.4% versus 100% by ATI stratum (log-rank $P = .0045$) and 42.9% versus 92.3% by IFTA stratum (log-rank $P = .0206$) (Figure 2A, B).

Comparison With Conventional Clinical Variables

No conventional preoperative clinical variable differed significantly between patients who initiated RRT within 90 days and those who did not (Table 2), including the MELD score (median, 15.0 [IQR, 12.0–17.0] vs 11.0 [IQR, 9.0–13.5]; P = .136), serum creatinine (P = .800), eGFR (P = .800), blood urea nitrogen (P = .800), KDIGO stage, Child-Pugh class, proteinuria, and microscopic hematuria (all P > .05). Baseline chronic kidney disease was numerically more frequent in the RRT group (2 of 5 vs 0 of 15; P = .053).

IFTA and Time to Renal Function Stabilization

Seventeen patients (85.0%) achieved stabilization at a median of 23 days (IQR, 14–30). IFTA correlated strongly with time to stabilization (Spearman $\rho = 0.907$; bootstrap 95% CI, 0.708–0.974; $P < .001$; Kendall tau-b = 0.774; $P < .001$). Patients with IFTA >10% stabilized

substantially later than those with IFTA ≤10% (median, 60 days [IQR, 60–75] versus 15 days [IQR, 11.8–23.3]; Mann-Whitney $P = .002$) (Figure 3).

Biopsy Safety and Feasibility

All 22 biopsies were technically successful, adding a median of 8 minutes (IQR, 6–10) to operative time. Immediate hemostasis was achieved in all cases (electrocautery alone in 18; additional suture ligation in 4), and no patient required transfusion for biopsy-related bleeding. No severe biopsy-related complications—defined as bleeding requiring transfusion or radiological/surgical intervention, perinephric hematoma, or arteriovenous fistula—occurred. Transient microscopic hematuria occurred in 15 patients (68.2%) and gross hematuria in 3 (13.6%), all resolving spontaneously within 72 hours. Both early deaths were adjudicated as unrelated to the biopsy procedure.

DISCUSSION

In this exploratory cohort of LT recipients with decompensated cirrhosis and pretransplant AKI, moderate-to-severe ATI and greater IFTA burden on intraoperative renal biopsy were associated with RRT within 90 days, and IFTA correlated strongly with delayed renal function stabilization. The risk differences were large, but confidence intervals were wide, events were few, and no multivariable model could be fitted; the findings should therefore be regarded as hypothesis-generating.

Notably, none of the conventional preoperative clinical variables—MELD score, serum creatinine, eGFR, KDIGO stage, or urinalysis findings—distinguished patients who subsequently required RRT from those who did not (Table 2). This descriptive comparison was underpowered and should be interpreted cautiously; however, it illustrates the well-recognized limitation of

creatinine-based assessment in cirrhosis: the 2 groups were clinically similar before transplantation yet histologically distinct. In this cohort, intraoperative biopsy captured prognostic information that was orthogonal to routinely available clinical parameters.

These data extend prior observations. Jin et al.[18] found IFTA to be common in LT recipients with chronic kidney disease, suggesting etiologies beyond calcineurin inhibitor nephrotoxicity, and Norén et al.10 successfully obtained intraoperative renal biopsies in 21 LT recipients. In the largest intraoperative biopsy series to date, reported to our knowledge only in abstract form (89 patients), Walls et al[19] found that IFTA >20% was associated with a composite of advanced chronic kidney disease or death. Our results suggest that even modest IFTA (>10%) may identify delayed recovery in patients with pretransplant AKI—a lower threshold than previously reported—although this cutoff was literature-derived rather than internally validated.

ATI ≥2 was associated with RRT, consistent with evidence from kidney transplantation that the magnitude of tubular damage, rather than regenerative activity, determines early functional outcomes.[20] Several caveats apply. ATI is morphologically nonspecific: the Banff 2022 report considers it too common and nonspecific to serve as a diagnostic feature in isolation,[13] perioperative insults (ischemia-reperfusion, hemodynamic instability, cholemic toxicity, calcineurin inhibitor exposure) produce indistinguishable morphology, and interobserver agreement for ATI scoring can be poor.[21] In the present study, interobserver agreement was good (weighted $\kappa = 0.89$), and consensus scoring by 2 blinded pathologists may have further improved reproducibility, but cannot eliminate this subjectivity.

The IFTA findings align with literature establishing IFTA as a dominant histological determinant of kidney disease progression[14] and with the acute-on-chronic paradigm, in which chronic changes erode the structural reserve available for recovery.[22] Preoperative biopsy studies have

linked >30% interstitial fibrosis or >40% global glomerulosclerosis to renal nonrecovery and are used to support SLK allocation,[23,24] but such biopsies precede transplantation by days to weeks, during which AKI may progress or partially reverse. Notably, patients in our cohort with IFTA of 10%–30% already showed markedly delayed stabilization, suggesting that current guideline thresholds[24] may underestimate the impact of mild-to-moderate chronicity on early posttransplant recovery.

No severe biopsy-related complications occurred in 22 procedures, consistent with previous intraoperative series[10,19] and comparing favorably with reported transfusion/complication rates of 4.5% for transjugular[25] and 4.3% for percutaneous biopsy.[26] Direct visualization enables precise cortical targeting and immediate surgical hemostasis without a separate invasive procedure—advantages particularly relevant in coagulopathic, thrombocytopenic patients. Nevertheless, the 13.6% incidence of transient gross hematuria indicates that minor bleeding is not negligible, and 22 procedures cannot exclude rare serious events.

The value of intraoperative biopsy does not lie in real-time SLK decision-making: routine histopathological processing requires several days and is incompatible with the operative window, and SLK candidacy must be determined preoperatively. Rather, its value lies in postoperative risk stratification—informing immunosuppression tailoring, nephrology follow-up intensity, and dialysis-access planning—and in providing a histological reference standard obtained at the exact time of transplantation, against which noninvasive predictors of chronicity can be calibrated for future pretransplant decision tools. Our finding that 45% of patients clinically diagnosed with HRS harbored chronic histological changes further supports a functional-structural continuum in cirrhotic AKI that may help explain heterogeneous responses to vasoconstrictor therapy.

This study has important limitations. The sample was small (20 patients, 5 events), precluding multivariable adjustment and rendering all associations exploratory. The IFTA threshold was literature-derived, without internal validation or exploration of alternative cutoffs, and the ATI score was not calibrated for the LT setting. Follow-up was limited to 90 days, precluding assessment of long-term renal outcomes. No non-biopsied comparator group and no preoperative biomarkers were available, so the incremental predictive value of histology over clinical assessment cannot be quantified. The stabilization correlation excluded the 3 patients with persistent RRT dependence at day 90. In addition, biopsy indication bias is possible: the decision to perform intraoperative biopsy was at the discretion of the surgical team, and biopsied patients may not be representative of all LT recipients with AKI. Finally, 2 early deaths in the safety cohort and the single-center design limit generalizability.

CONCLUSION

In conclusion, intraoperative renal biopsy was feasible in coagulopathic LT candidates with AKI, and moderate-to-severe ATI and IFTA burden were associated with 90-day RRT requirement. These hypothesis-generating observations support a functional-structural continuum model of cirrhotic AKI and justify validation in larger multicenter cohorts with biomarker comparison, competing-risk analysis, and longer follow-up before any clinical application.

DECLARATIONS

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Tianjin First Central Hospital (approval No. 2020N151KY) and was conducted in accordance with the Declaration of Helsinki.

All patients provided written informed consent for the intraoperative biopsy procedure; the requirement for additional consent for retrospective analysis of deidentified data was waived by the ethics committee.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding authors upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

N.H. drafted the manuscript and performed the statistical analysis. C.C. performed the intraoperative renal biopsies. Z.H. performed the histopathological scoring. J.S., Y.X.and G.L. performed the liver transplantation procedures and patient follow-up. J.L. performed renal function follow-up and managed renal replacement therapy. W.C. designed the study and interpreted the histopathological findings. W.J. designed the study and supervised quality control. All authors critically revised the manuscript for important intellectual content and approved the final version.

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REFERENCES

1. Patidar KR, Ma AT, Juanola A, et al; International Club of Ascites GLOBAL AKI team. Global epidemiology of acute kidney injury in hospitalised patients with decompensated cirrhosis: the International Club of Ascites GLOBAL AKI prospective, multicentre, cohort study. Lancet Gastroenterol Hepatol. 2025;10(5):418-430. doi:10.1016/S2468-1253(25)00006-8

2. Lekakis V, Wong F, Gkoufa A, et al. Mortality of acute kidney injury in cirrhosis: a systematic review and meta-analysis of over 5 million patients across different clinical settings. Aliment Pharmacol Ther. 2025;61(3):420-432. doi:10.1111/apt.18426

3. Nadim MK, Garcia-Tsao G. Acute kidney injury in patients with cirrhosis. N Engl J Med. 2023;388(8):733-745. doi:10.1056/NEJMra2215289

4. Lins PRG, Narciso RC, Ferraz LR, et al. Modelling kidney outcomes based on MELD eras - impact of MELD score in renal endpoints after liver transplantation. BMC Nephrol. 2022;23(1):294. doi:10.1186/s12882-022-02912-6

5. Jung CY, Chang JW. Hepatorenal syndrome: current concepts and future perspectives. Clin Mol Hepatol. 2023;29(4):891-908. doi:10.3350/cmh.2023.0024

6. Gambino C, Piano S, Stenico M, et al. Diagnostic and prognostic performance of urinary neutrophil gelatinase-associated lipocalin in patients with cirrhosis and acute kidney injury. Hepatology. 2023;77(5):1630-1638. doi:10.1002/hep.32799

7. Trawalé JM, Paradis V, Rautou PE, et al. The spectrum of renal lesions in patients with cirrhosis: a clinicopathological study. Liver Int. 2010;30(5):725-732. doi:10.1111/j.1478-3231.2009.02182.x

8. Bräsen JH, Mederacke YS, Schmitz J, et al. Cholemic nephropathy causes acute kidney injury and is accompanied by loss of aquaporin 2 in collecting ducts. Hepatology. 2019;69(5):2107-2119. doi:10.1002/hep.30499

9. van Slambrouck CM, Salem F, Meehan SM, et al. Bile cast nephropathy is a common pathologic finding for kidney injury associated with severe liver dysfunction. Kidney Int. 2013;84(1):192-197. doi:10.1038/ki.2013.78

10. Norén Å, Boi R, Pullerits R, et al. Proteomic analysis of human kidney biopsies unveils emerging acute kidney injury very early after liver graft reperfusion. J Transl Med. 2025;23(1):658. doi:10.1186/s12967-025-06695-w

11. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012;120(4):c179-c184. doi:10.1159/000339789

12. Kudose S, Hoshi M, Jain S, Gaut JP. Renal histopathologic findings associated with severity of clinical acute kidney injury. Am J Surg Pathol. 2018;42(5):625-635. doi:10.1097/PAS.0000000000001028

13. Naesens M, Roufosse C, Haas M, et al. The Banff 2022 Kidney Meeting Report: reappraisal of microvascular inflammation and the role of biopsy-based transcript diagnostics. Am J Transplant. 2024;24(3):338-349. doi:10.1016/j.ajt.2023.10.016

14. Srivastava A, Palsson R, Kaze AD, et al. The prognostic value of histopathologic lesions in native kidney biopsy specimens: results from the Boston Kidney Biopsy Cohort Study. J Am Soc Nephrol. 2018;29(8):2213-2224. doi:10.1681/ASN.2017121260

15. Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. Stat Med. 1998;17(8):873-890. doi:10.1002/(sici)1097-0258(19980430)17:8<873::aid-sim779>3.0.co;2-i

16. Firth D. Bias reduction of maximum likelihood estimates. Biometrika. 1993;80(1):27-38.

17. Peduzzi P, Concato J, Feinstein AR, Holford TR. Importance of events per independent variable in proportional hazards regression analysis. II. Accuracy and precision of regression estimates. J Clin Epidemiol. 1995;48(12):1503-1510. doi:10.1016/0895-4356(95)00048-8

18. Jin H, Wei Y, Qian Y, et al. Renal histopathological lesions after liver transplantation: what can we find besides calcineurin inhibitor-induced nephrotoxicity? BMC Nephrol. 2022;23(1):324. doi:10.1186/s12882-022-02952-y

19. Walls DO, Muraveika L, Palmer MB, Sawinski DL, Keating BJ, Abt PL. The use of native kidney biopsy to predict renal dysfunction following liver transplantation [abstract]. Am J Transplant. 2019;19(suppl 3):S145.

20. Pieters TT, Falke LL, Nguyen TQ, et al. Histological characteristics of acute tubular injury during delayed graft function predict renal function after renal transplantation. Physiol Rep. 2019;7(5):e14000. doi:10.14814/phy2.14000

21. Liapis H, Gaut JP, Klein C, et al; Banff Working Group. Banff histopathological consensus criteria for preimplantation kidney biopsies. Am J Transplant. 2017;17(1):140-150. doi:10.1111/ajt.13929

22. Venkatachalam MA, Griffin KA, Lan R, Geng H, Saikumar P, Bidani AK. Acute kidney injury: a springboard for progression in chronic kidney disease. Am J Physiol Renal Physiol. 2010;298(5):F1078-F1094. doi:10.1152/ajprenal.00017.2010

23. Wadei HM, Geiger XJ, Cortese C, et al. Kidney allocation to liver transplant candidates with renal failure of undetermined etiology: role of percutaneous renal biopsy. Am J Transplant. 2008;8(12):2618-2626. doi:10.1111/j.1600-6143.2008.02426.x

24. Charlton MR, Wall WJ, Ojo AO; International Liver Transplantation Society Expert Panel. Report of the first International Liver Transplantation Society expert panel consensus conference on renal insufficiency in liver transplantation. Liver Transpl. 2009;15(11):S1-S34. doi:10.1002/lt.21877

25. St Jeor JD, Reisenauer CJ, Andrews JC, et al. Transjugular renal biopsy bleeding risk and diagnostic yield: a systematic review. J Vasc Interv Radiol. 2020;31(12):2106-2112. doi:10.1016/j.jvir.2020.07.016

26. Palsson R, Short SAP, Kibbelaar ZA, et al. Bleeding complications after percutaneous native kidney biopsy: results from the Boston Kidney Biopsy Cohort. Kidney Int Rep. 2020;5(4):511-518. doi:10.1016/j.ekir.2020.01.012

TABLES

Table 1. Baseline characteristics of liver transplant recipients with cirrhosis and acute kidney injury

Characteristic	Value (N = 20)
Male sex, n (%)	15 (75.0)
Age, y, median (IQR)	58.5 (53.8–63.3)
BMI, kg/m², mean ± SD	23.1 ± 1.6
Child-Pugh class C, n (%)	8 (40.0)
MELD score, median (IQR)	12.0 (9.8–14.3)
Serum creatinine, μmol/L, median (IQR)	151.8 (138.4–169.8)
Blood urea nitrogen, mmol/L, median (IQR)	9.0 (8.3–9.8)
eGFR, mL/min/1.73 m², median (IQR)	37.5 (34.1–40.6)
Preoperative RRT, n (%)	0 (0.0)
KDIGO stage 1 / 2 / 3, n	15 / 5 / 0
Proteinuria ≥150 mg/d, n (%)	13 (65.0)
Microscopic hematuria, n (%)	7 (35.0)
Etiology of liver disease	
HBV/HCV, n (%)	12 (60.0)
Alcohol-related, n (%)	3 (15.0)
Autoimmune, n (%)	3 (15.0)
Other, n (%)	2 (10.0)
Hepatocellular carcinoma, n (%)	7 (35.0)
Clinical-etiological diagnosis	
Hepatorenal syndrome-AKI, n (%)	9 (45.0)
Acute tubular necrosis, n (%)	5 (25.0)
Acute-on-chronic kidney disease, n (%)	2 (10.0)
Other/uncertain, n (%)	4 (20.0)
Baseline chronic kidney disease, n (%)	2 (10.0)
Diabetes mellitus, n (%)	5 (25.0)

Abbreviation: AKI, acute kidney injury; BMI, body mass index; eGFR, estimated glomerular filtration rate; HBV, hepatitis B virus; HCV, hepatitis C virus; IQR, interquartile range; KDIGO, Kidney Disease: Improving Global Outcomes; MELD, Model for End-Stage Liver Disease; RRT, renal replacement therapy; SD, standard deviation.

Table 2. Comparison of preoperative clinical variables between patients with and without 90-day renal replacement therapy

Characteristic	RRT (n = 5)	No RRT (n = 15)	P value
Age, y, median (IQR)	53.0 (52.0–58.0)	59.0 (55.0–64.0)	0.080
BMI, kg/m², median (IQR)	24.2 (23.3–25.1)	22.8 (21.6–23.8)	0.197
MELD score, median (IQR)	15.0 (12.0–17.0)	11.0 (9.0–13.5)	0.136
Child-Pugh class C, n (%)	3 (60.0)	5 (33.3)	0.347
Serum creatinine, μmol/L, median (IQR)	154.9 (143.8–158.2)	148.6 (137.8–170.6)	0.800
eGFR, mL/min/1.73 m², median (IQR)	38.8 (37.9–39.7)	36.2 (33.9–40.6)	0.800
Blood urea nitrogen, mmol/L, median (IQR)	9.0 (8.6–9.3)	8.9 (8.2–9.9)	0.800
KDIGO stage 2, n (%)	0 (0.0)	5 (33.3)	0.266
Proteinuria ≥150 mg/d, n (%)	4 (80.0)	9 (60.0)	0.613
Microscopic hematuria, n (%)	2 (40.0)	5 (33.3)	1.000
Hepatocellular carcinoma, n (%)	1 (20.0)	6 (40.0)	0.613
Diabetes mellitus, n (%)	2 (40.0)	3 (20.0)	0.560
Baseline chronic kidney disease, n (%)	2 (40.0)	0 (0.0)	0.053
HRS-AKI as clinical-etiological diagnosis, n (%)	3 (60.0)	6 (40.0)	0.617

Note: Continuous variables were compared using the Mann-Whitney U test and categorical variables using the Fisher exact test; the comparison was descriptive and not adjusted for multiplicity. BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HRS, hepatorenal syndrome; IQR, interquartile range; KDIGO, Kidney Disease: Improving Global Outcomes; MELD, Model for End-Stage Liver Disease; RRT, renal replacement therapy.

FIGURE LEGENDS

Figure 1. Intraoperative native kidney biopsy during liver transplantation and representative histopathology. (A) Biopsy procedure and specimen adequacy: intraoperative view of the right renal upper pole exposed under direct vision after mobilization of the native liver (right); the retrieved cortical core on surgical gauze (top left, orange circle); a schematic of the biopsy site and tangential cortical trajectory targeting the outer third of the upper pole while avoiding the renal pelvis and calyces (bottom; capsule, cortex, and medulla indicated; inset shows the 16-gauge Tru-Cut needle core sample); and a whole-mount section of a representative biopsy core showing adequate cortical tissue (top; orange arrows indicate glomeruli; hematoxylin-eosin). (B) Acute tubular injury with tubular epithelial simplification and brush-border loss (arrows) (hematoxylin-eosin, original magnification ×200). (C) Interstitial fibrosis and tubular atrophy, with atrophic tubules embedded in fibrotic interstitium (arrows) (hematoxylin-eosin, ×200). (D) Intratubular bile pigment deposition (arrows) (hematoxylin-eosin, ×400).

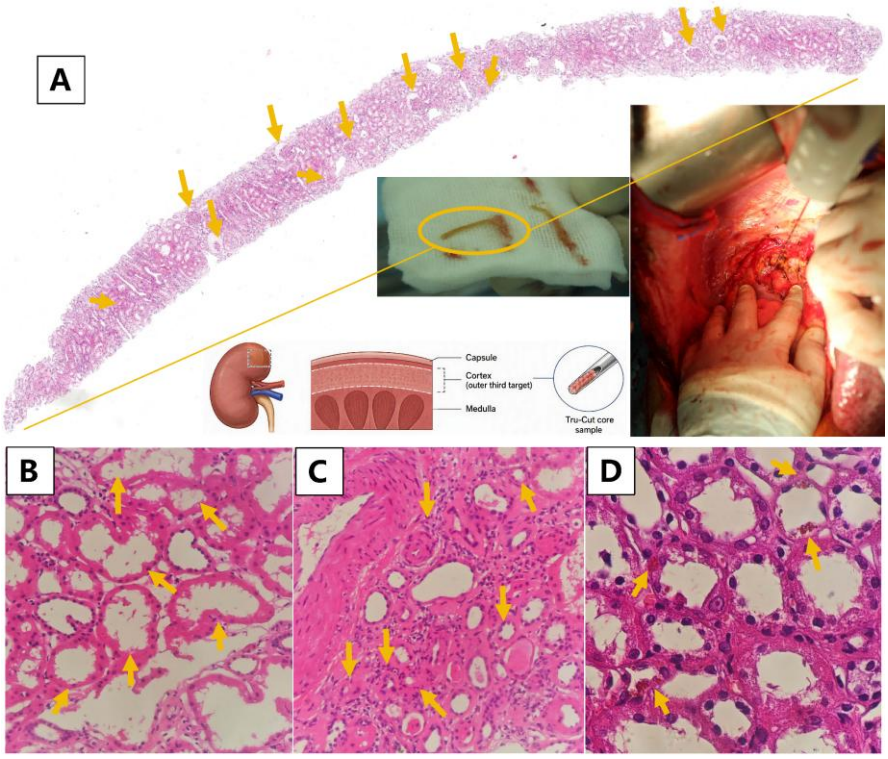


Figure 2. (A) Descriptive Kaplan-Meier curves of time to first renal replacement therapy (RRT) by acute tubular injury (ATI) score ≥2 (*n* = 9) versus <2 (*n* = 11); 90-day RRT-free estimates were 44.4% versus 100% (log-rank *P* = .0045). (B) Curves by interstitial fibrosis and tubular atrophy (IFTA) >10% (*n* = 7) versus ≤10% (*n* = 13); 90-day RRT-free estimates were 42.9% versus 92.3% (log-rank *P* = .0206). Curves are descriptive because the zero-event comparator precludes stable conventional hazard estimation.

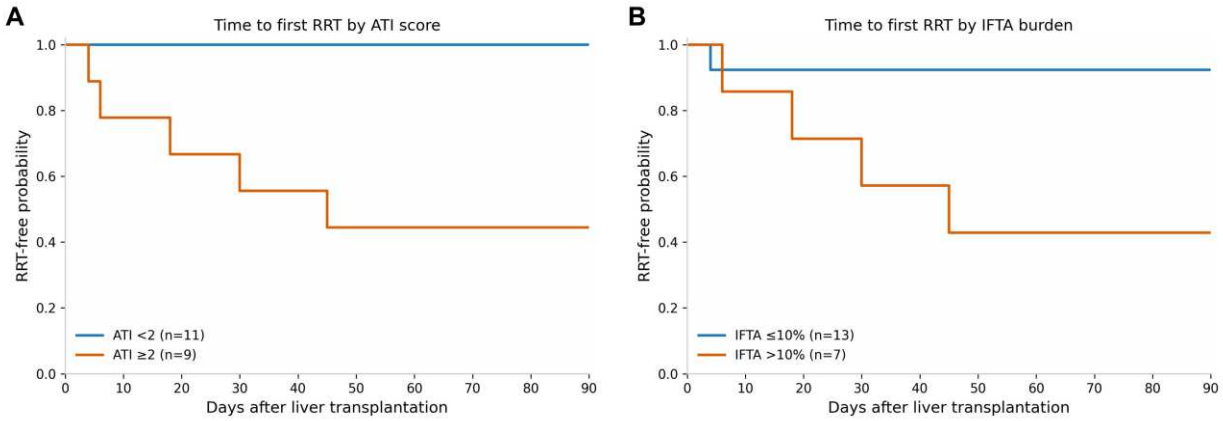


Figure 3. Scatter plot of IFTA proportion versus time to renal function stabilization among the 17 patients achieving stabilization within 90 days; squares denote patients requiring transient RRT. Spearman ρ = 0.907 (bootstrap 95% CI, 0.708–0.974; $P < .001$).

