Open Access

Original Article

Frequency and Risk Factors of Biliary Complications after Living Donor Liver Transplant: A Case-Control Study

Mansoor Tariq Azim, Sohail Rashid, Muhammad Asad Saleem, Eisha Mansoor*, Hiba Zafar

Department of HPB & Liver Transplant, Pakistan Kidney and Liver Institute and Research Centre, Lahore Pakistan,
*Department of Community Medicine, Combined Military Hospital lahore/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To identify the frequency and risk factors of biliary complications in patients undergoing living donor liver transplantation (LDLT) at a single national referral center.
Study Design: Case-control study.
Place and Duration of Study: Pakistan Kidney and Liver Institute and Research Centre, Lahore Pakistan, from Mar to Nov 2024.
Methodology: Out of 500 patients who underwent LDLT, the ones who developed biliary complications (stricture, leak, or stones) were selected as cases (Group-A, n=125) while controls (Group-B, n=375) were the recipients who did not develop any biliary complications. Data on donor/recipient demographics, surgical details, and clinical variables was collected from the institutional electronic medical records. Chi square test was used to find association between the risk factors and biliary complications.
Results: Biliary complications occurred in 25% (n=125) of recipients. Anastomotic biliary stricture was the most common complication (100%), followed by stone formation (26.4%) and bile leak (3.4%). A statistically significant association was found between the number of ducts and frequency of biliary complications (OR= 1.7, 95%CI=1.14 - 2.56, *p*-value =0.01). Hence, the cases had 70% greater odds of having double ducts as compared to the controls.
Conclusion: In this study, 25% of LDLT recipients developed biliary complications, predominantly strictures. A statistically significant association was found between the number of ducts and biliary complications. These findings underscore the need for tailored surgical and postoperative strategies in patients with multiple bile ducts.

Keywords: Biliary Tract Disease, Liver, Living Donor Liver Transplantation, Post-Operative Complications.

How to Cite This Article: *Azim MT. Rashid S, Saleem MA, Mansoor E, Zafar H. Frequency and Risk Factors of Biliary Complications after Living Donor Liver Transplant: A Case-Control Study. Pak Armed Forces Med J 2026; 76(Suppl-8): S1307-S1312.*
DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-8.14191

INTRODUCTION

Complications after the liver transplantation are common, and are usually divided into anastomotic biliary strictures (ABS), non-anastomotic biliary strictures, and anastomotic biliary fistulas.[1,2] ABS, in particular, are normally witnessed in the first year of the transplant and contribute greatly to complications, between 13% and 36%.[3,4,5] Risk factors are diverse. Anastomotic strictures are more common after living donor liver transplantation (LDLT), as compared to deceased donation liver transplantation. This heterogeneity is, in part, explained by a lack of a standard definition of ABS and the difference in the populations of the patients used in different studies, such as the severity of the recipient, the type of graft, biliary reconstruction techniques, and the type of biliary stricture that is experienced.[6,7]

Correspondence: Dr Mansoor Tariq Azim, Department of HPB & Liver Transplant, PKLI and Research Centre, Lahore Pakistan
Received: 19 Nov 2025; revision received: 23 Jan 2026; accepted: 26 Jan 2026

Such complications may severely affect the future prognosis and cause graft failures and deaths. The complexity of the biliary system itself, as well as the complications of its manipulation during surgery in the course of transplantation, will also add to the risk of complications. Wachs *et al.,* first used duct-to-duct anastomosis (DDA) to perform LDLT but four weeks later ABS occurred prompting the change to Roux-en-Y HJ.[8] However, DDA may offer benefits, such as a shorter operating time, less sepsis, better enteric function, and subsequent complications that can be accessed easily via endoscopic means in the biliary tract. This has made DDA the biliary reconstruction of choice at most transplant centres. Lin *et al.,* have emphasised interesting conclusions.[9] The use of microsurgical methods to reconstruct the ducts resulted in a 2.5 times reduction in post-LDLT BAS rates, with only 2.5% of cases requiring any intervention.[9] Early detection and the use of preventative measures is very important in reducing complications.

We aimed to identify the frequency and risk factors of biliary complications in patients undergoing living donor liver transplantation (LDLT) at our setup.

METHODOLOGY

This case-control study was conducted at the Pakistan Kidney and Liver Institute and Research Centre (PKLIandRC), Lahore from March to November 2024. Approval for the study was obtained from the Institutional Ethical Review Committee (PKLI-IRB/AP/146; dated: 29th August 2023).

Inclusion Criteria: Adult patients of either gender who underwent primary living donor liver transplantation (LDLT) since the start of the program, with complete perioperative data and 1-year post-transplant follow-up (sufficient to assess biliary outcomes) were included.

Exclusion Criteria: Deceased donor liver transplantation, patients who died within 30 days of transplantation, prior to assessment of biliary complications, patients who underwent re-transplantation, and those who had incomplete or missing key clinical, surgical, or follow-up data were excluded.

A sample size of 499 patients was calculated using OpenEpi software, keeping a case to control ratio of 1:3 and a hypothetical proportion of controls with exposure at 10 and cases with exposure at 20.[3-5]

Out of 500 patients who underwent LDLT, the ones who developed biliary complications (stricture, leak, or stones) were selected as cases (Group-A, n=125) while controls (Group-B, n=375) were the recipients who did not develop any biliary complications (Figure-1). The data on required variables was obtained from the electronic medical record system of the hospital (SiSoft). Cases were considered as those LDLT-recipients who developed post-transplant biliary complications such as biliary stricture, bile leak, or biliary stones in the follow-up period. The LDLT recipients who, within the same duration, did not experience any biliary complications at the follow-up were used as controls. The controls were not directly matched to cases, but all of the eligible non-case patients were used as controls, in order to provide the maximum statistical power. Post–liver transplant biliary stricture was defined as narrowing of the bile duct after transplantation, detected on cholangiographic imaging and resulting in impaired bile drainage, with or without cholestatic liver functions. Biliary complications were identified based on clinical, biochemical, and radiological criteria. Patients presenting with deranged liver function tests suggestive of biliary obstruction were evaluated using ultrasound abdomen and magnetic resonance cholangiopancreatography (MRCP). Endoscopic retrograde cholangiopancreatography (ERCP) findings were used to confirm the diagnosis when indicated. Biliary complications were classified as: biliary stricture, bile leak, biliary stone formation. For analytic purposes, the presence or absence of any biliary complication constituted the primary outcome. The pre-specified variables which were evaluated as potential risk factors included; recipient age, gender, Hepatitis C virus (HCV) status, Hepatitis B virus (HBV) status, Antinuclear antibody (ANA) status, donor biliary duct anatomy (single vs multiple ducts), Model for End-Stage Liver Disease Sodium (MELD-Na) score, Child-Turcotte-Pugh (CTP) grade, operating surgeon, type of suture material used for biliary anastomosis, cold ischemia time (CIT), warm ischemia time (WIT). Exposure status for each variable was determined from perioperative records documented at the time of transplantation.

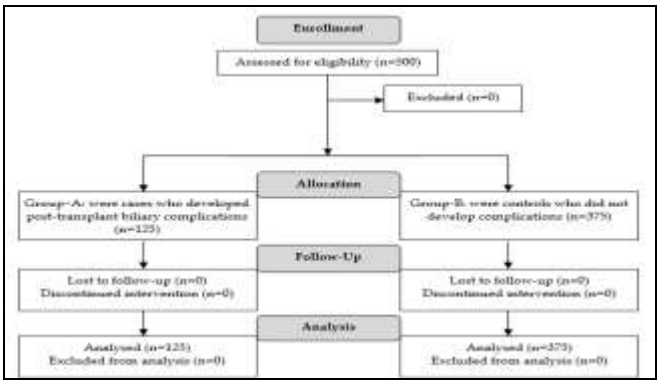

Figure-1: Patient Flow Diagram (n=500)

Data analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) version 26. Categorical variables were summarized as frequencies and percentages, while continuous variables were expressed as median and interquartile range (IQR) due to non-normal distribution, assessed using the Shapiro–Wilk test. Association between cases and controls were assessed using Chi-square test. Statistical significance was set at a *p*-value <0.05.

RESULTS

A total of 500 liver transplant surgeries were performed at PKLI Lahore in the study duration. The median (IQR) age of patients was 49(37-56) years. Male to female ratio was 3:1 with 382(76.4%) males and 118(23.6%) females.

Biliary complications were found to develop in 125(25%) of recipients (cases) whereas 375(75%) did not show any clinical evidence of biliary complication. A gradual reduction in the complication rates was observed as the program matured (Figure-2).

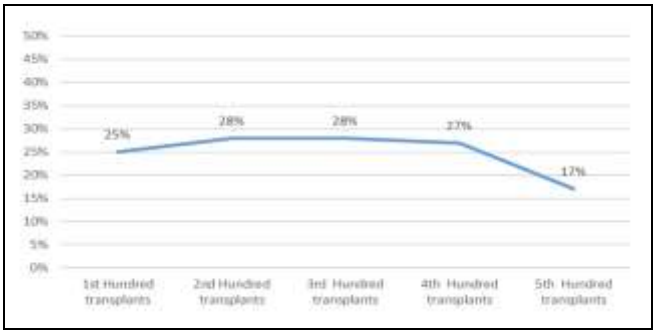

Figure-2: Biliary Complication Rate among Liver Transplant Surgeries (n=500)

ERCP was done for each of the 125 patients experiencing post-operative biliary complications. All were found to have a biliary stricture. Stones formed in 33(26.4%) while bile leak was observed in 17(3.4%) patients. Out of 125 patients who underwent ERCP, biliary obstruction was relieved in 57(45.6%) by the time this study was conducted and rest were under treatment. The average recovery time for these 57 patients was 10.13 months ranging from 2-28 months (Figure-3).

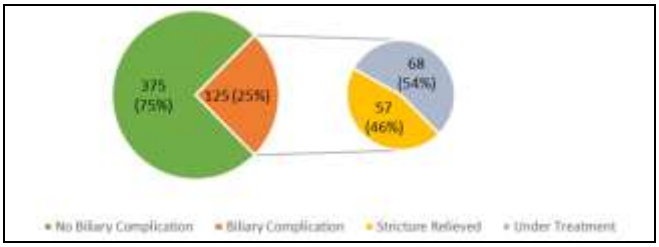

Figure-3 Outcome of Living Donor Liver Transplants with respect to Biliary Complications (n=500)

Risk factor analysis showed that HCV was positive in 258(51.6%) of cases while HBV in 75(15%). Twenty-six (5.2%) cases had a positive ANA. Polydioxanone suture (PDS) was used in 312(62.4%) cases and polypropylene in 185(37%). A total of 316(63.2%) cases had a single duct whereas double ducts were found in 184(36.8%) cases. The frequencies of patients with MELD score up to 15 was 179(35.8%), from 16-20 was 156(31.2%) and from 21 to 59 was 163(32.6%). According to CTP grade, 78(15.6%) were grade A, 243(48.6%) were grade B while 163(32.6%) were grade C. The median (IQR) CIT was 37 (26-48) minutes ranging from 4 to 650 whereas the median (IQR) WIT was 42(32-50) minutes ranging from 0 to 86.

A statistically significant association was found between the number of ducts and biliary complications (OR= 1.7, 95%CI=1.14-2.56, *p*-value =0.01). Hence, the cases had 70% greater odds of having double ducts as compared to controls. There was no statistically significant association between biliary complications and other studied variables, including gender, HCV status, HBV status, ANA status, surgeon, thread type, MELD score, and CTP grade (*p*-values >0.05) across groups, as shown in Table.

Table: Association of Biliary Complications with different variables (n=500)

Variable	Categories	Groups		OR	95% CI	*p*-value
		Group-A n (%)	Group-B n (%)			
Gender	Female	30(25.4)	88(74.6)	1.03	0.64-1.66	0.903
	Male	95(24.9)	287(75.1)			
HCV	Positive	70(27.1)	188(72.9)	1.26	0.83-1.92	0.256
	Negative	55(22.7)	187(73.3)			
HBV	Positive	16(21.3)	59(78.7)	0.79	0.43-1.42	0.426
	Negative	109(25.6)	316(74.4)			
ANA	Positive	7(26.9)	19(73.1)	0.80	0.46-1.39	0.776
	Negative	90(24.2)	282(75.8)			
Surgeon	A	2(11.1)	16(88.9)	0.79	0.45-1.39	0.347
	B	44(30.1)	102(69.9)			
	C	12(25.0)	36(75.0)			
	D	31(20.9)	117(79.1)			
	E	36(25.9)	103(74.1)			
Thread type	PDS	82(26.3)	230(73.7)	1.23	0.77-1.97	0.385
	Prolene	42(22.7)	143(77.3)			
Ducts	Double	58(31.5)	126(68.5)	1.7	1.14-2.56	0.01
	Single	67(21.2)	249(78.8)			
MELD score	A (up to 15)	46(25.7)	133(74.3)	0.51	0.28-0.94	0.094
	B (16-20)	47(30.1)	109(69.9)			
	C (21-59)	32(19.16)	131(80.4)			
CTP grade	A	19(24.4)	59(75.6)	1.68	0.98-2.98	0.719
	B	58(23.9)	185(76.1)			
	C	48(27.3)	128(72.7)			

**HCV: Hepatitis C virus, BHV: Hepatitis B virus, ANA: Anti-Nuclear Antibody, (MELD-NA): Model for End-Stage Liver Disease Sodium, CTP: Child-Turcotte-Pugh, CIT: Cold ischemia time, WIT: Warm ischemia time.*

DISCUSSION

ABS are seen in approximately 5% to 10% of patients during the initial 12 months following transplantation.[11] They are typically segmental, shorter, and confined to the anastomotic site. Bile leaks may enhance the likelihood of ABS development. ABS can emerge within 60 days post-LT because of factors like post-operative swelling, fibro-inflammatory response, and temporary ischemia. Strictures appearing within this timeframe usually respond well to 1-2 endoscopic dilation sessions and placement of plastic stents.[12] Conversely, AS developing after 3 months tend to have a more prolonged course and

often require extended endoscopic interventions for satisfactory outcomes. Endoscopic strategies for managing anastomotic strictures encompass techniques such as balloon dilation, passage dilation using a Soehendra biliary dilation catheter, insertion of plastic biliary stents, and self-expandable metal stents (SEMS). These procedures involve crossing the stricture with a guidewire, followed by dilation of the anastomosis using balloon dilators ranging from 4-10 mm and placement of plastic stents (7 Fr to 11.5 Fr). Soehendra dilators are particularly beneficial for severely stenosed anastomoses, offering dilation options from 4-10 Fr.[13] We observed that the most suitable treatment option was ERCP in our setup managing both bile leaks and strictures simultaneously. It's generally advisable to avoid balloon dilation in early strictures (<3 months) to minimize the risk of perforation or leaks. For many patients with AS, especially those presenting after 3 months post-LT, multiple endoscopic sessions (typically 3-5) are necessary to achieve long-term success. Notably, there's no standardized bile duct diameter that indicates a clinically significant bile duct stenosis.

In our study, we observed that positive ANA status was associated with an increased incidence of stricture formation but the results were not statistically significant. Jung *et al.,* in their study showed that immunological reactions are a potential risk factor for stricture formation.[14] Jung *et al.,* in their study, mentioned that although ANA is associated with the increased risks of stricture formation, however, the findings are not statistically significant, which correlates with our results.[15] In our study, we observed that HCV/HBV, CTD grade, age, CIT, and WIT were not significant risk factors to influence the rate of ABS formation. Moreover, neither the type of sutures used nor the surgeons involved significantly contributed to an increased risk of ABS. This may be attributed to the fact that all surgeries were performed by a cohesive team of surgeons from the same department, adhering to uniform surgical principles and possessing comparable levels of expertise and experience. Other studies concluded age and CIT are not significant risk factors for ABS, which correlates with our results.[16,17] One study reported that the risk of ABS formation was higher when patients were HCV positive and non-absorbable sutures were used during surgery, which doesn't align with the results of our study.[18] We found out that multiple ducts are associated with an increased incidence of ABS. Zear *et al.,* in their study concluded similar findings which synchronize with our results.[19] We concluded that the MELD score doesn't play a significant role in affecting the incidence of ABS. One analysis stated that the MELD score didn't impact the risk of post-transplant biliary complications.[20]

Recent evidence further supports our findings on the significance of biliary complications in LDLT. A meta-analysis comparing LDLT and deceased donor liver transplant (DDLT) confirmed that strictures and leaks remain more common after LDLT, though complication rates have declined in recent years with technical refinements.[21] Similarly, Foley *et al.,* reported stricture and leak rates of 20.6% and 11.4%, with multiple ducts and Roux-en-Y reconstruction as key risk factors, closely aligning with our results.[22] Long-term data also highlight the clinical impact of strictures, with poorer graft survival observed in patients who developed vascular compromise and bilomas.[23] Other large studies have identified multiple anastomoses, bile leak, and recipient age as additional predictors of stricture formation.[24]

By providing comprehensive data from a high-volume living donor liver transplantation (LDLT) center, this study adds to the existing medical literature and reflects real-world outcomes in a resource-constrained setting with minimal surgeon-related variability and standardized protocols. Unlike many previous studies, our analysis simultaneously evaluated immunological, anatomical, operative, and recipient-related factors allowing a more holistic assessment of risk factors for anastomotic biliary stricture formation. Importantly, our findings reinforce the significance of anatomical complexity—particularly multiple bile ducts—while also demonstrating that traditionally implicated variables such as cold ischemia time, warm ischemia time, age, viral hepatitis status, suture material, MELD score and surgeon variability may have less influence when surgeries are performed by a consistent and experienced transplant team following uniform surgical principles. Additionally, the study highlights the effectiveness of ERCP as a first-line therapeutic modality for managing biliary complications in LDLT, even in complex cases involving concurrent bile leaks and strictures.

In general, this study demonstrates that, in experienced centers, anastomotic biliary strictures following living donor liver transplantation are primarily caused by anatomical factors and the

severity of the recipient's disease. Early recognition and prompt endoscopic management, particularly with ERCP, allow effective treatment in most cases. Standardized surgical techniques, careful postoperative monitoring, and prompt intervention to improve graft and patient outcomes are backed up by these findings.

LIMITATION OF STUDY

This study has several limitations. As a single-center retrospective case-control study, the findings may have limited generalizability to other transplant centers with different patient populations, surgical expertise, and postoperative management protocols. The retrospective design also relies on the accuracy and completeness of electronic medical records, making it susceptible to information bias and missing data. Although we evaluated several donor- and recipient-related variables, other potentially important risk factors, such as variations in surgical technique, biliary anatomy, ischemia times, immunosuppressive regimens, surgeon experience, and long-term postoperative outcomes, were not comprehensively assessed and may have confounded the observed associations. Furthermore, the analysis was primarily based on univariate comparisons, and multivariable regression was not performed to adjust for potential confounders. Finally, the relatively short study period may not have captured biliary complications presenting later after transplantation, potentially underestimating their true frequency.

CONCLUSION

25% of patients who underwent LDLT developed biliary complications, out of which biliary stricture was the most common. The number of ducts was the significant risk factor for biliary complications.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MTA & SR: Data acquisition, data analysis, critical review, approval of the final version to be published.

MAS & EM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

HZ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Manay P, Seth A, Jackson K, Lentine KL, Schnitzler MA, Xiao H, et al. Biliary complications after liver transplantation in the United States: changing trends and economic implications. Transplantation 2023; 107(5): e127–e138. https://doi.org/10.1097/TP.0000000000004528
2. Miyagi S, Kawagishi N, Kashiwadate T. Relationship between bile duct reconstruction and complications in living donor liver transplantation. Transplant Proc 2016; 48(4): 1166–1169. https://doi.org/10.1016/j.transproceed.2015.10.073
3. Reichelt S, Semaan A, Lutz P, Kalff JC, van Beekum CJ, Manekeller S. Recipient warm ischemic time negatively influences biliary complications and graft survival: a single-center retrospective analysis. Front Gastroenterol 2025; 4: 1601741. https://doi.org/10.3389/fgstr.2025.1601741
4. Dogar AW, Ullah K, Shams-Ud-Din, Abbas SH, Hussain A, Ghaffar A, et al. Is a Preservation Solution for Living Donor Liver Transplantation Needed? Adding a New Chapter in LDLT! Transplant Direct 2022; 8(11): e1396. https://doi.org/10.1097/TXD.0000000000001396
5. Aujla UI, Syed IA, Malik AK, Ramzan M, Saeed A. Percutaneous Transhepatic Sphincterotome-Guided Management of Post-Living Donor Liver Transplant Biliary Anastomotic Stricture: An Innovative Approach. ACG Case Rep J 2024; 11(3): e01288. https://doi.org/10.14309/crj.0000000000001288
6. Nadeem MA, Awan AR, Rao AG, Ayyazuddin M, Salma UE, Laique S, et al. Role of antibiotic prophylaxis in liver transplant patients undergoing endoscopic retrograde cholangio-pancreatography: a systematic review and meta-analysis. EClinicalMedicine 2025; 89: 103560. https://doi.org/10.1016/j.eclinm.2025.103560
7. Georges P, Clerc C, Turco C. Post-transplantation cytomegalovirus infection interplays with the development of anastomotic biliary strictures after liver transplantation. Transpl Int 2022; 35: 10292. https://doi.org/10.3389/ti.2022.10292
8. Wachs ME, Bak TE, Karrer FM. Adult living donor liver transplantation using a right hepatic lobe. Transplantation 1998; 66(10): 1313–1316. https://doi.org/10.1097/00007890-199811270-00008
9. Lin TS, Chen CL, Concejero AM. Early and long-term results of routine microsurgical biliary reconstruction in living donor liver transplantation. Liver Transpl 2013; 19(2): 207–214. https://doi.org/10.1002/lt.23582
10. Chok KS, Lo CM. Biliary complications in right lobe living donor liver transplantation. Hepatol Int 2016; 10(4): 553–558. https://doi.org/10.1007/s12072-016-9710-0
11. Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health, Version 3.01. Updated April 2013 [cited 25th March 2024]. Available from: https://www.openepi.com
12. Magro B, Tacelli M, Mazzola A, Conti F, Celsa C. Biliary complications after liver transplantation: current perspectives and future strategies. Hepatobiliary Surg Nutr 2021; 10(1): 76–92. https://doi.org/10.21037/hbsn.2019.09.01
13. Akhter A, Pfau P, Benson M, Soni A, Gopal D. Endoscopic management of biliary strictures post-liver transplantation. World J Meta-Anal 2019; 7(4): 120–128. https://doi.org/10.13105/wjma.v7.i4.120
14. Inoue T, Ibusuki M, Kitano R. Severe biliary stricture dilation using the Soehendra stent retriever with a short-type balloon enteroscope in patients with surgically altered anatomies. J Gastrointest Surg 2019; 23(5): 953–958. https://doi.org/10.1007/s11605-018-3977-5

15. Jung DH, Ikegami T, Balci D, Bhangui P. Biliary reconstruction and complications in living donor liver transplantation. Int J Surg 2020; 82(Suppl): 138–144. https://doi.org/10.1016/j.ijsu.2020.04.069
16. Sakamoto A, Sakamoto K, Hikida T. Prolonged warm ischemia time in the recipient is associated with post-transplant biliary stricture following living donor liver transplantation. Surg Today 2024; 54(10): 1193–1200. https://doi.org/10.1007/s00595-024-02823-z
17. Zhu XH, Pan JP, Wu YF, Ding YT. Effects of warm ischemia time on biliary injury in rat liver transplantation. World J Gastroenterol 2012; 18(43): 6308–6314. https://doi.org/10.3748/wjg.v18.i43.6308
18. Loh J, Hashimoto K, Kwon CHD, Fujiki M, Modaresi EJ. Positive autoantibodies in living liver donors. World J Hepatol 2022; 14(9): 1757–1766. https://doi.org/10.4254/wjh.v14.i9.1757
19. Zear S, Stasiuk R, Zair L. Incidents and risk factors of biliary complications after orthotopic liver transplantation. Medicine 2021; 100(34): e26994. https://doi.org/10.1097/MD.0000000000026994
20. Kaldas FM, Korayem IM, Russell TA. Assessment of anastomotic biliary complications in adult patients undergoing high-acuity liver transplant. JAMA Surg 2019; 154(5): 431–439. https://doi.org/10.1001/jamasurg.2018.5527
21. Hassouneh R, Beran A, Rosenheck M. Risk factors for biliary strictures and leaks after living-donor liver transplantation: a systematic review and meta-analysis. J Gastrointest Surg 2024. https://doi.org/10.1016/j.gassur.2024.08.009
22. Foley DP, Fernandez LA, Leverson G. Biliary complications after liver transplantation from donation after cardiac death donors: an analysis of risk factors and long-term outcomes from a single center. Ann Surg 2011; 253(4): 817–825. https://doi.org/10.1097/SLA.0b013e3182104784
23. Artru F, Sacleux SC, Ursic-Bedoya J, Wandji LC, Lutu A, L'hermite S, et al. Long-term outcome following liver transplantation of patients with ACLF grade 3. J Hepatol 2025; 82(1): 62-71. https://doi.org/10.1016/j.jhep.2024.06.039
24. Gadour E. Lesson learnt from 60 years of liver transplantation: Advancements, challenges, and future directions. World J Transplant 2025; 15(1): 93253. https://doi.org/10.5500/wjt.v15.i1.93253