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Original Article
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Outcomes of Highly Urgent ABO-Incompatible Living Donor Liver Transplantation in National Databases

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ABSTRACT

Background: Highly urgent adult living donor liver transplantation (HU-LDLT) is essential for patients with acute liver failure (ALF), acute-on-chronic liver failure (ACLF), and severe cirrhosis who are in life-threatening situations. The results of adult highly urgent ABO-incompatible (ABOi) living donor liver transplantation (LDLT) remain ambiguous when there is insufficient time to await a compatible organ. This study aimed to compare the results of adult ABOi HU-LDLT with those of adult ABO-compatible (ABOc) HU-LDLT utilizing data from the Korean Network for Organ Sharing (KONOS).
Methods: We conducted a retrospective study using KONOS data from 363 consecutive adult HU-LDLT patients between 2017 and 2021 in Korea.
Results: The incidence of ABOc-LDLTs and ABOi-LDLTs was 90.6% (n = 329) and 9.4% (n = 34), respectively. Hepatitis B virus infection and alcoholism are the main etiologies of adult HU-LDLT. The median waiting time was 1 day (range, 0–36 days) for ABOc LDLT patients and 3 days (range, 0–28 days) for ABOi LDLT patients. None of the patients developed antibody-mediated rejection during follow-up. The incidence of graft failure was 17.6% in ABOi LDLT patients and 7.6% in ABOc LDLT patients. However, the overall survival and graft survival rates in the ABOi LDLT patients were not different from those in the ABOc LDLT patients. ABOi LDLT was not associated with graft failure or death in multivariable analysis.

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Disclosure

The authors have no potential conflicts of interest to disclose.

Data Availability Statement

No additional data are available (access to the Korean Hospital to the Korean National Health Insurance Services (NHIS) database is restricted by law).

Author Contributions

Conceptualization: Kim J, Kim SJ. Data Curation: Kim J, Kim SJ, Kim SY, Park J, Hwang Y. Formal analysis: Kim J, Park B, Kim K. Funding acquisition: Kim J, Kim SJ, Jung DW. Investigation: Kim J, Kim SY, Park J, Hwang Y. Methodology: Kim J, Kim SJ, Park B, Kim K, Park J, Hwang Y. Project administration: Kim J, Choi YR, Hong G. Resource: Park JY, Han YS, Yi NJ. Software: Park B, Hong SH, Kim K. Supervision: Kim SY, Park J, Hwang Y, Jung DW. Validation: Park JY, Yi NJ, Jung DW. Visualization: Kim J. Writing-original draft: Kim J. Writing-review & editing: Kim J.

Conclusion: The present study supports ABOi-LDLTs as a feasible and safe treatment for highly urgent patients.

Keywords: Living Donors; Liver Failure; Donor Selection; Acute-on-Chronic Liver Failure; End-Stage Liver Disease; Survival; Mortality; Complications; Hepatorenal Syndrome; Mechanical Ventilation

INTRODUCTION

Liver transplantation (LT) is the definitive therapeutic intervention for adult patients experiencing acute-on-chronic liver failure (ACLF), acute liver failure (ALF), or severe cirrhosis that does not respond to conventional management.[1-3] Patients with ALF, ACLF, or critical cirrhosis require LT as soon as possible, because rapidly deteriorating liver failure can be fatal.[1,4]

Highly urgent deceased donor liver transplantation (DDLT) or living donor liver transplantation (LDLT) can be considered for patients with ALF, ACLF, or critical cirrhosis, which have a very high allocation priority as high emergency levels. However, since we have about 500 deceased donors per year in Korea,[3,5] there are cases where there are no deceased donors in the country for 2–3 weeks. Therefore, highly urgent patients without potential living liver donors (LLDs) die while awaiting a matching liver graft. Highly urgent living donor liver transplantation (HU-LDLT) may be the only option to save dying patients because deceased organ donation is low in Korea. Rapid determination of LDLT eligibility is essential to save patients with ALF, ACLF, or critical cirrhosis. In Korea, suitable LLDs are restricted to intimate relatives. In particular, ABO-incompatible (ABOi) LLDs should not be employed in emergency situations because of some period for desensitization. However, when ABO-compatible (ABOc) LLDs are unavailable, ABOi LLDs are the only choice under such critical circumstances. Currently, ABOi LDLT in a non-urgent setting can be performed successfully with similar outcomes to ABOc LDLT by depleting B cells and reducing anti-blood type isoagglutinin.[6,7] However, ABOi-LDLT was initially considered a contraindication due to the high risk of antibody-mediated rejection (AMR). Desensitization protocols for ABOi HU-LDLT for ALF, ACLF, or critical cirrhotic patients are impractical because of time constraints. The outcomes of adult ABOi HU-LDLT have not been reported. In addition, no previous study has compared adult ABOc HU-LDLT and adult ABOi HU-LDLT.

The objective of our study was to evaluate the results of adult ABOi HU-LDLT with adult ABOc HU-LDLT.

METHODS

Study design

We conducted a retrospective analysis of the Korean Network for Organ Sharing (KONOS) data from consecutive adult HU-LDLT patients spanning 2017 to 2021. The patient roster, demographic information, and dates of death or LT were obtained from the KONOS. Data were consolidated based on the requested laboratory results from each participating institution. This study adheres to the Strengthening the Reporting of COhort, cross-sectional, and case-control Studies in Surgery criteria.[8] From 2017 to 2021, 363 adult living donor liver transplants were conducted emergently.

Data collection

We collected the following recipient clinical data from KONOS: sex, age, body mass index (BMI), liver disease progression, hepatitis B virus (HBV), hepatitis C virus (HCV), Alcohol-related liver disease, chronic kidney disease, re-transplantation, hepatic encephalopathy (HE), hepatorenal syndrome (HRS), Model for End-stage Liver Disease (MELD) scores, graft-to-recipient weight ratio, postoperative complications, post-transplant infectious complications, hospitalization, acute cellular rejection, cause of death, follow-up duration, graft failure, and death. We assessed categorical values reflecting patient severity, including the use of a ventilator, hemodialysis, and intensive care unit stay before transplantation. We also assessed the presence of HRS or the grade of HE. The ABO-incompatibility between the recipient and donor blood types and re-transplantation were also evaluated. The interval between the day the HU-LDLT application was received by the KONOS and the day of the actual transplantation was also evaluated. Additionally, we collected the donor data from KONOS: sex, age, BMI, history of hypertension, diabetes, or psychological disorder, relationship between donor and recipient, type of donor operation, postoperative complications after donor hepatectomy, hospitalization, and follow-up duration.

Administrative LDLT approval process in Korea

To obtain LDLT approval, the transplantation center must provide documentation regarding the states of both the donor and recipient, which includes a rationale statement, a consultation report, and identification. Upon receipt and examination of these documents, KONOS generally requires about 14 days to render a decision about approval or disapproval.

Making practical judgments on the urgent implementation of LDLT is complex, and assessing the justification based purely on test data or medical records is problematic. The existing liver transplant application system in Korea mandates that a governmental entity sanction a note for each patient, contingent upon individual evaluations conducted by a minimum of two independent liver transplant surgeons and/or hepatologists. The rationale for HU-LDLT was evaluated and classified by examining the physician's notes of each HU-LDLT applicant.

Definition

HU-LDLT is a procedure conducted on patients with ALF, ACLF, or severe liver failure who are at imminent risk of mortality without prompt LDLT, necessitating accelerated approval from KONOS.

ALF is defined as a condition in people without underlying liver disease, characterized by liver injury (evidenced by abnormal liver function tests), coagulopathy (international normalized ratio greater than 1.5), and HE.[4] ACLF is characterized by the acute exacerbation of chronic liver disease in patients, encompassing ascites, HE, infection, gastrointestinal hemorrhage, and bacterial infection, which are classified as decompensations by the European Association for the Study of the Liver-Chronic Liver Failure collaboration, with liver dysfunction indicated by blood bilirubin levels of ≥ 3 mg/dL.[1,9] HRS was delineated according to the International Club of Ascites.[10] HCV was simultaneously characterized by positive anti-HCV and positive HCV RNA.[11] HBV was characterized by a positive HBsAg or HBV DNA test, or HBeAg positivity for over 6 months prior to transplantation.[12] Chronic renal disease was characterized by an estimated glomerular filtration rate of less than 60 mL/min/1.73 m^2 one year prior to the application for LDLT in the KONOS. Alcohol-related liver disease was delineated in accordance with the guidelines established by the Korean Association for the

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Study of the Liver.[13] HE is a neuropsychiatric condition resulting from liver impairment, characterized by diverse neurological and behavioral disorders.[14] The severity of HE is categorized according to the West-Haven criteria.[14]

We collected MELD scores from three days prior to and on the day of application submission, as well as on the day of transplantation, to evaluate changes in the patient's health. The rate of change of the MELD score (ΔMELD, %) was defined as follows. The identical definition of "Δ" was utilized for the other factors as well.

$$\Delta\text{MELD (Percentage Change)} = \{(\text{MELD Score on the Day of LDLT Application} - \text{MELD Score 3 Days Prior to LDLT Application})/\text{MELD Score 3 Days Prior to LDLT Application}\} \times 100$$

Statistical analysis

Patient characteristics were reported as medians and ranges for continuous variables, and as frequencies and percentages for categorical categories. Categorical and continuous data were analyzed using the χ^2 test, Fisher's exact test, and Mann-Whitney *U* test. A logistic regression model was employed to ascertain the risk variables for mortality during the waiting time. Odds ratios (ORs) and 95% confidence intervals (CIs) were computed. Multivariable analysis incorporated all clinically relevant candidate risk variables into the model, with the final selection determined by statistical significance ($P < 0.05$) using backward variable selection. The results were deemed significant when 2-sided *P* values were ≤ 0.05 by backward variable selection. Statistical analyses were conducted using SAS analytic software (version 9.4; SAS Institute, Cary, NC, USA) and R software (version 4.2.2; R Foundation for Statistical Computing, Vienna, Austria).

Ethics statement

This study was approved by the Samsung Medical Center Ethics Committee (SMC-2023-11-038) and complied with the Declaration of Helsinki. The requirement for written informed consent for this retrospective study was waived by the Internal Review Board of the Samsung Medical Center.

RESULTS

Baseline characteristics of the recipients

The baseline characteristics of the adult HU-LDLTs patients are summarized in **Table 1**. The incidence of ABOc-LDLT and ABOi-LDLT was 90.6% (n = 329) and 9.4% (n = 34), respectively. HBV infection and alcoholism are the main etiologies of adult HU-LDLT. The incidence of re-transplantation as the cause of HU-LDLT in the ABOi-LDLT group was higher than that in the ABOc-LDLT group ($P = 0.012$). However, the proportion of patients with a high MELD score > 30 in the ABOi-LDLT group was lower than that in the ABOc-LDLT group ($P = 0.012$). The median waiting period was 1 day (range, 0–36 days) for ABOc-LDLT patients and 3 days (range, 0–28 days) for ABOi-LDLT patients. There were no significant differences in recipient characteristics between the 2 groups.

Characteristics of LLDs

There were no significant differences in sex, age, BMI, history of hypertension, diabetes mellitus, psychological disorders, donor and recipient relationships, or hospitalization

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Table 1. Comparison of recipients (N = 363) between adult emergency ABOc-LDLT patients and adult emergency ABOi-LDLT patients

Variables	ABOc LDLT (n = 329)	ABOi LDLT (n = 34)	*P* value
Sex (male)	191 (57.7)	20 (58.8)	0.900
Age, yr	53 (20–77)	52 (31–73)	0.474
BMI, kg/m^2	23.5 (18.1–39.9)	22.8 (17.3–31.9)	0.624
Liver disease progression			0.141
ALF	104 (31.9)	10 (29.4)	
ACLF	146 (44.8)	11 (32.4)	
Critical cirrhotic	78 (23.3)	13 (38.2)	
HBV	95 (28.7)	15 (44.1)	0.062
HCV	11 (3.7)	0 (0.0)	0.257
Alcoholic-related liver disease	129 (39.0)	12 (35.3)	0.716
Chronic kidney disease	6 (1.8)	0 (0.0)	0.428
Re-transplantation	6 (1.8)	3 (8.8)	0.012
HE			0.459
None	123 (37.3)	13 (38.2)	
Grade I or II	128 (38.8)	16 (47.1)	
Grade III or IV	79 (23.9)	5 (14.7)	
HRS	114 (34.4)	6 (17.6)	0.055
Pre-transplant ICU care	153 (46.2)	12 (35.3)	0.223
Pre-transplant ICU stay, days	3 (1–61)	6 (2–14)	0.128
Pre-transplant ventilator support	79 (23.9)	4 (11.8)	0.109
CRRT in pre-transplant	80 (24.2)	5 (14.7)	0.214
Ascites	226 (68.3)	21 (61.8)	0.439
MELD score	29 (8–40)	27 (14–40)	0.132
MELD score > 30	176 (54.5)	10 (31.3)	0.012
ΔMELD score[a] > 10%	59 (23.3)	5 (15.6)	0.326
Waiting time, days	1 (0–36)	3 (0–28)	0.105
GRWR	1.11 (0.63–2.61)	1.21 (0.80–2.56)	0.347

Characteristics were reported as medians and ranges for continuous variables, and as frequencies and percentages (%) for categorical categories.
ABOc = ABO-compatible, LDLT = living donor liver transplantation, ABOi = ABO-incompatible, BMI = body mass index, HBV = hepatitis B virus, HCV = hepatitis C virus, HE = hepatic encephalopathy, HRS = hepatorenal syndrome, ICU = intensive care unit, CRRT = continuous renal replacement therapy, MELD = Model for End-Stage Liver Disease, GRWR = graft-to-recipient weight ratio.
[a]ΔMELD (Change Rate, %) = {(MELD Score on the Day of LDLT Application − MELD Score on the 3 Days Before LDLT Application)/MELD Score on the 3 Days Before LDLT Application} × 100.

between the 2 groups. The incidence of laparoscopic and robotic donor hepatectomies in the ABOi-LDLT group was significantly higher than that in the ABOc-LDLT group. There were more postoperative complications in the ABO-LDLT group than those in the ABOc-LDLT group. However, severe complications, including Clavien-Dindo grade III, were more frequent in LLDs with ABOi-LDLTs than in those with ABOc-LDLTs (**Table 2**).

Recipient outcomes

Fifty percent of the patients encountered post-operative problems. The occurrences of viral, bacterial, and fungal infections were comparable between the two groups. The median follow-up period was 27.4 months (range, 0–69.3 months) for the ABOc-LDLT group and 37.7 months (range, 0–65.4 months) for the ABOi-LDLT group. No patients exhibited AMR during the follow-up period. The rates of graft failure and mortality were 17.6% and 23.5% in ABOi-LDLT patients, and 7.6% and 21.5% in ABOc-LDLT patients, respectively. The causes of mortality in the ABOc LDLT group comprised surgical complications (n = 17), graft failure (n = 7), infection (n = 19), malignancy (n = 5), and others (n = 21), while the ABOi LDLT group experienced infection (n = 3), malignancy (n = 2), and others (n = 3). Nonetheless, the overall survival and graft survival rates in the ABOi-LDLT cohort were comparable to those in the

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ABOc-LDLT cohort (**Fig. 1**). No substantial changes in recipient outcomes were seen between the 2 groups, with the exception of the graft failure rate (**Table 3**).

Table 2. Comparison of living liver donors (N = 363) between adult emergency ABOc-LDLT patients and adult emergency ABOi-LDLT patients

Variables	ABOc LDLT (n = 329)	ABOi LDLT (n = 34)	*P* value
Sex (male)	202 (61.0)	23 (67.6)	0.450
Age, yr	32 (17–67)	30 (17–63)	0.722
BMI, kg/m^2	23.5 (18.7–39.0)	23.8 (18.8–29.4)	0.831
Hypertension	16 (4.9)	0 (0.0)	0.188
Diabetes mellitus	5 (1.5)	0 (0.0)	0.469
Psychological disorder	2 (0.6)	1 (2.9)	0.153
Donor and recipient relationship			0.780
Offspring	167 (50.8)	18 (52.9)	
Parents	35 (10.6)	1 (2.9)	
Sibling	56 (17.0)	7 (20.6)	
Relatives	29 (8.8)	3 (8.8)	
Spouse	37 (11.2)	4 (11.8)	
Non-family	5 (1.5)	1 (2.9)	
Donor operation			< 0.001
Open	274 (83.3)	14 (41.2)	
Laparoscopic	48 (14.6)	9 (26.5)	
Robotic	7 (2.1)	11 (32.4)	
Postoperative complications	21 (6.4)	5 (15.2)	0.064
Clavien-Dindo grade III	10	0	0.011
Hospitalization	8 (5–98)	8 (5–17)	0.464
Follow-up duration, days	382 (10–2,024)	368 (7–1,516)	0.175

Characteristics were reported as medians and ranges for continuous variables, and as frequencies and percentages (%) for categorical categories.
ABOc = ABO-compatible, LDLT = living donor liver transplantation, ABOi = ABO-incompatible, BMI = body mass index.

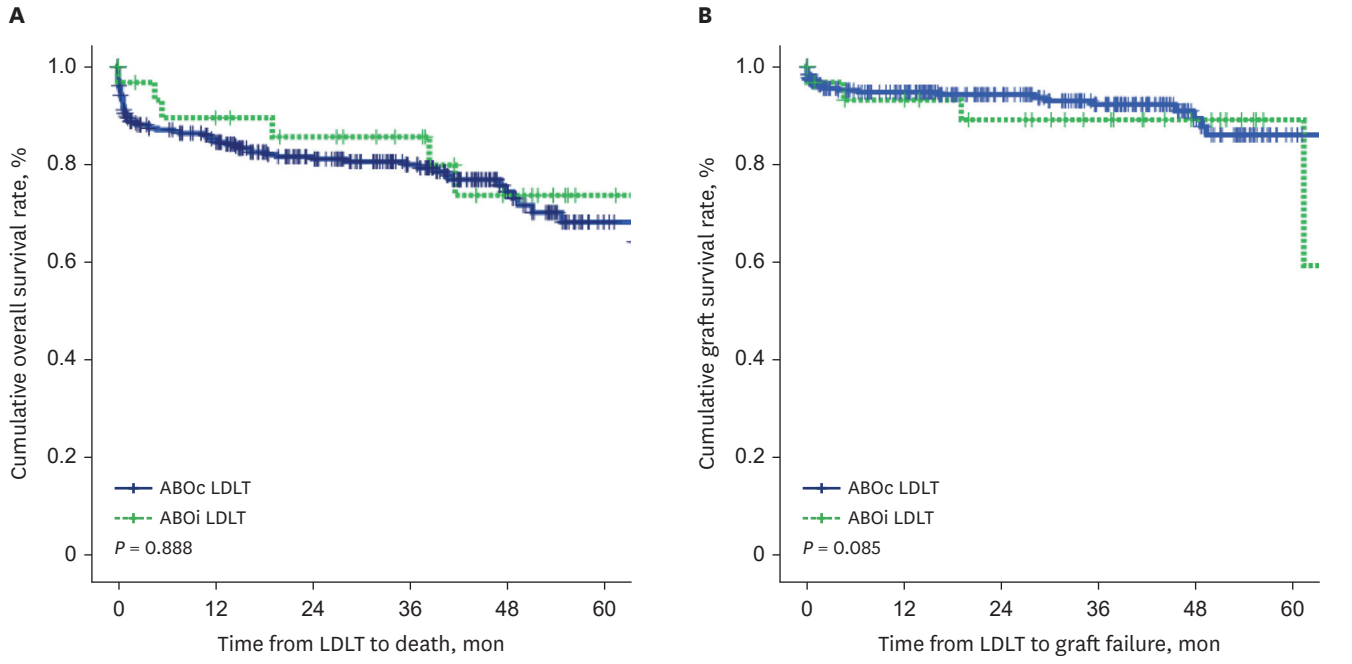

Fig. 1. Cumulative survival rates. (**A**) Overall survival. (**B**) Graft survival.
ABOc = ABO-compatible, ABOi = ABO-incompatible, LDLT = living donor liver transplantation.

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Table 3. Recipient outcomes between adult ABOc HU-LDLT patients and adult ABOi HU-LDLT patients

Outcomes	ABOc LDLT (n = 329)	ABOi LDLT (n = 34)	*P* value
Post-transplant ICU stay, days	7 (1–224)	5 (2–90)	0.179
Post-operative complications	210 (63.4)	19 (55.9)	0.457
Post-transplant infectious complications	150 (45.3)	12 (35.3)	0.263
Viral infection	56 (16.9)	6 (17.6)	0.914
Bacterial infection	112 (33.8)	9 (26.5)	0.385
Fungal infection	57 (17.2)	4 (11.8)	0.417
Hospitalization, days	25 (1–399)	24 (1–491)	0.462
In-hospital mortality	43 (13.0)	4 (11.8)	0.839
Acute cellular rejection	31 (9.4)	3 (8.8)	0.918

Characteristics were reported as medians and ranges for continuous variables, and as frequencies and percentages (%) for categorical categories.
ABOc = ABO-compatible, HU-LDLT = highly urgent living donor liver transplantation, ABOi = ABO-incompatible, LDLT = living donor liver transplantation, ICU = intensive care unit.

Risk factors for death and graft failure

Multivariable analysis indicated that chronic kidney disease, pre-transplant ventilator support, re-transplantation, and an elevated MELD score prior to HU-LDLT were significantly correlated with death. Moreover, HRS increased the likelihood of graft failure in the multivariable analysis (**Table 4**).

DISCUSSION

LT is the only effective treatment for patients with ALF, ACLF, or critical cirrhosis. In the absence of LT, these patients have poor outcomes. The high waitlist mortality has led to expanded donor selection to include LDLT.[15,16] Paucity of DDLT options in Korea results in the wide use of LDLT for ALF, ACLF, or critical cirrhosis, and excellent donor safety and recipient survival have been reported.[5,17,18] Currently, ABOi-LDLT can be performed successfully with similar outcomes to ABOc-LDLT by depleting B cells and reducing anti-blood type isoagglutinin.[6,7] However, ABOi HU-LDLT is not a standard procedure, and is usually considered the last option. ABOi-LDLT represents an immunological and logistical challenge in patients with ALF, ACLF, or critical cirrhosis. When ABOc LLDs are unavailable, ABOi LLDs are the only choice under such critical circumstances. Early reports of highly urgent ABOi-LT reported a high rate of complications due to infections, immunological graft loss, and other vascular complications.[19]

Our study describes 34 adult patients who underwent ABOi HU-LDLTs in Korea. Planning an ABOi-LDLT in the setting of ALF, ACLF, or critical cirrhosis is complicated by clinically worse medical status. The time interval between the decision to transplant and the LT procedure itself is short. Generally, B cells are depleted by rituximab 2–3 weeks before LT, followed by plasma exchange/plasmapheresis to reduce anti-blood-type isoagglutinin titers over the same 2–3 weeks.[20] However, it is dangerous for urgent patients with ALF, ACLF, or critical cirrhosis to wait for a liver graft for more than 2–3 weeks. In our study, the proportion of high MELD scores and re-transplantation in the ABOi-LDLT group indicated urgency; therefore, highly urgent ABOi-LDLT may be performed in such patients without suitable ABOc LLDs. Our study reported that the median time from the decision to transplant to HU-LDLT was one day in ABOc-LDLT patients and three days in ABOi-LDLT patients. ABOi-LDLT for highly urgent indications is feasible and can be performed with rapid desensitization over 2–3 days in experienced centers.[20] The extended waiting period for patients undergoing ABOi-LDLT in

Table 4. Risk factors for mortality and graft failure in the highly urgent LDLT patients

Variables	Patient mortality (n = 366, events = 80)				Graft failure (n = 366, events = 32)			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Male sex	1.00 (0.64–1.56)	0.996			0.90 (0.45–1.82)	0.774		
Age	1.01 (0.99–1.03)	0.229			1.02 (0.99–1.05)	0.212		
BMI	1.01 (0.96–1.06)	0.840			1.01 (0.94–1.10)	0.747		
HBV	1.19 (0.75–1.89)	0.469			1.06 (0.50–2.24)	0.882		
HCV	0.68 (0.17–2.77)	0.590			0.81 (0.11–5.95)	0.836		
Alcoholism	0.68 (0.42–1.09)	0.105			0.79 (0.38–1.65)	0.537		
Hypertension	1.14 (0.66–1.97)	0.638			1.27 (0.55–2.93)	0.581		
Diabetes	1.50 (0.92–2.46)	0.104			1.86 (0.88–3.95)	0.105		
Chronic kidney disease	4.38 (1.59–12.01)	0.004	3.88 (1.20–12.5)	0.024	1.24 (0.07–21.4)	0.882		
Albumin	0.68 (0.45–1.02)	0.061			1.02 (0.54–1.93)	0.942		
Total bilirubin	1.02 (1.00–1.03)	0.081			1.02 (0.99–1.05)	0.147		
INR	0.69 (0.50–0.94)	0.019			0.64 (0.38–1.06)	0.085		
Creatinine	1.16 (0.98–1.37)	0.080			1.09 (0.82–1.45)	0.565		
Ascites	0.85 (0.54–1.35)	0.499			0.89 (0.43–1.84)	0.745		
Reason for HU-LDLT								
ALF	Ref	1.000			Ref	1.000		
ACLF	0.76 (0.46–1.28)	0.303			1.27 (0.53–3.03)	0.591		
Critical ill cirrhotic	0.98 (0.56–1.71)	0.938			1.53 (0.60–3.87)	0.371		
Pre-transplant ICU care	1.33 (0.86–2.08)	0.200			0.68 (0.33–1.43)	0.311		
Pre-transplant ventilator care	1.70 (1.06–2.72)	0.029	1.82 (1.04–3.19)	0.037	0.68 (0.26–1.77)	0.429		
CRRT in pre-transplant	1.49 (0.92–2.42)	0.106			1.45 (0.67–3.14)	0.345		
HRS	1.36 (0.87–2.14)	0.177			2.24 (1.12–4.48)	0.023	4.33 (1.44–13.02)	0.009
HE								
Grade I or II	1.03 (0.63–1.69)	0.910			0.91 (0.44–1.88)	0.797		
Grade III or IV	1.00 (0.56–1.80)	0.993			0.33 (0.10–1.15)	0.082		
Child-Pugh class C	0.99 (0.14–7.17)	0.989			0.65 (0.03–12.3)	0.772		
MELD score	1.01 (0.99–1.04)	0.348			3.73 (0.85–16.2)	0.080		
ΔMELD score[a]	4.36 (1.78–10.67)	0.001	1.01 (1.00–1.03)	0.006	1.04 (0.99–1.09)	0.121		
ABO-incompatibility	1.00 (0.48–2.09)	0.995			2.04 (0.82–5.03)	0.123		
Re-transplantation	3.39 (1.37–8.38)	0.008	4.35 (1.56–12.2)	0.005	3.42 (0.81–14.4)	0.093		
Post-transplant ICU stay	1.01 (1.00–1.02)	0.003			1.01 (1.01–1.02)	0.001		
GRWR	2.17 (1.14–4.13)	0.019			0.92 (0.12–6.74)	0.932		

LDLT = living donor liver transplantation, HR = hazard ratio, CI = confidence interval, BMI = body mass index, HBV = hepatitis B virus, HCV = hepatitis C virus, INR = international normalized ratio, HU-LDLT = highly urgent living donor liver transplantation, ALF = acute liver failure, ACLF = acute-on-chronic liver failure, ICU = intensive care unit, CRRT = continuous renal replacement therapy, HRS = hepatorenal syndrome, HE = hepatic encephalopathy, MELD = Model for End-Stage Liver Disease, GRWR = graft-versus-weight ratio.

[a]ΔMELD (Change Rate, %) = {(Day of Application − 3 Days Before Application)/3 days Before Application} × 100.

our trial may have indicated the necessary desensitization procedures, which included rituximab prophylaxis and multiple total plasma exchanges. Overcoming the ABO barrier within a limited timeframe to execute ABOi-LDLT for ALF, ACLF, or severe cirrhosis is challenging. Preoperative ABO antibody titers must consistently be evaluated under complete plasma exchange methods. The dangers of both over- and under-immunosuppression must be judiciously managed, and adjunct operations like splenectomy should be meticulously evaluated. Prolonged administration of antifungal medicines and extended cytomegalovirus prophylaxis should be contemplated for patients undergoing severely urgent ABOi-LDLT.

ABOi-LDLT is challenging to strike a balance between infection and desensitization. Our findings indicated that approximately 35% of patients who had ABOi-LDLT encountered infectious problems, encompassing viral, bacterial, or fungal infections. The median period of hospitalization was 24 days; hence, the infectious complications were well managed without additional issues. The occurrences of postoperative and infectious complications in the ABOi-LDLT group were comparable to those in the ABOc-LDLT group.

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Mendes et al.[19] reported the survival of 5 of 10 patients who underwent highly urgent ABOi-LT, including 4 with their original grafts. One patient underwent retransplantation at 9 months.[19] Major complications included infections (3 deaths), rejection (including 3 cases of AMR), and biliary issues.[19] AMR-related graft loss is a major consideration in ABOi-LDLT.[20] However, none of the patients in the present study developed AMR after the ABOi-LDLT. Concerning long-term outcomes, overall survival and graft survival in ABOi-LDLT patients were comparable to those in ABOc-LDLT patients during emergencies. Our study examined the cause of mortality, but did not evaluate the precise type of cancer. The subsequent stage should involve identifying cancer incidence following ABOi-LDLT. Enhancing donor accessibility and minimizing waiting periods are essential for optimizing patient outcomes. Therefore, a rapid decision-making process is required because of the narrow transplantation window for patients with multi-organ failure.

The incidence of laparoscopic or robotic donor hepatectomy was significantly higher in the ABOi-LDLT group than that in the ABOc-LDLT group. ABOi HU-LDLT is commonly conducted in high-volume clinics, where minimally invasive donor hepatectomies are more prevalent compared to low-volume centers. Our research possesses multiple limitations. Initially, our study conducted a retrospective analysis of HU-LDLT cases utilizing KONOS data, which resulted in selection bias. Thus, the data did not include desensitization protocols, isoagglutinin titers, detailed surgical procedures, and post-transplant management. We lack information regarding blood type in both donor and recipient, rituximab prophylaxis, the frequency of complete plasma exchange, local graft infusion therapy, graft type, blood loss, blood transfusion volumes, immunosuppressants, and diffuse bile duct problems. Second, the restricted number of HU-LDLTs and the brief follow-up duration constrained statistical power. Third, the acquisition of critically urgent LDLT may be affected not only by the patient's health but also by the willingness of the donor or family and the circumstances of the transplantation center, factors that are challenging to quantify. Fourth, the etiology of liver failure (especially whether the patient had ALF, ACLF, or critical cirrhosis) was not precisely evaluated or analyzed within each subgroup.

In conclusion, this study demonstrates that ABOi-LDLT is a viable and secure treatment for urgent instances of ALF, ACLF, or serious cirrhosis.

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