



ABO blood type has no effect on hepatocellular carcinoma recurrence after living donor liver transplantation in the Korean Organ Transplantation Registry study: a case-control study

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Backgrounds: Hepatocellular carcinoma (HCC) recurrence after liver transplantation remains a significant concern. This study investigated the impact of ABO blood type on HCC recurrence and overall survival in individuals after living donor liver transplantation (LDLT) using data from the Korean Organ Transplantation Registry.

Materials and Methods: A retrospective analysis of 2380 LDLT patients from the KOTRY database (2014–2021) was conducted. Clinical outcomes were compared across ABO blood types using Kaplan–Meier survival and multivariate Cox regression analyses.

Results: ABO blood type did not significantly affect HCC recurrence or overall survival. Multivariate analysis demonstrated that only the Milan criteria were closely associated with HCC recurrence. Overall survival was dependent on the Milan criteria and ABO incompatibility in multivariable analysis. Patients beyond the Milan criteria with ABO-incompatibility had worse recurrence-free survival and overall survival compared with other groups.

Conclusions: ABO blood type does not predict HCC recurrence or overall survival. Clinical factors like beyond the Milan criteria and ABO-incompatibility remain critical in managing LDLT patients with HCC.

Keywords: ABO blood group system, hepatocellular carcinoma, living liver donors, survival

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Introduction

For patients with hepatocellular carcinoma (HCC), liver transplantation (LT) has the highest likelihood of achieving a cure relative to other therapeutic alternatives^[1,2]. However, recurrence of HCC occurs in some patients post-transplantation, which significantly affects patient survival despite active intervention for recurrent tumors. The Milan criteria are the primary standard that has been used to select LT candidates among HCC patients for over 20 years^[1,2]. Predicting the post-transplant prognosis in patients who have undergone LT for HCC poses a formidable challenge. Various factors that predict the risk of post-transplant HCC recurrence have been identified, including tumor size, tumor number, vascular invasion, tumor differentiation, and alpha-fetoprotein concentration^[1–3]. Therefore, a meticulous selection process is

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used to identify LT candidates to mitigate the risk of HCC recurrence.

The ABO blood group system is one of the earliest and most prevalent blood typing systems, comprising three carbohydrate antigens: A, B, and H^[4]. Recently, increasing evidence has revealed that ABO blood group type is associated with cardiovascular and pathophysiological processes in various diseases, such as tumors. Several studies have indicated that the ABO blood type may influence the risk of developing cancer^[5–7] and nonneoplastic disease^[8–11], and it may also represent a prognostic factor in some instances^[12,13]. Research has demonstrated the potential correlation of ABO blood type with malignancies, such as head and neck, gastric, skin, colorectal, ovarian, and pancreatic cancers^[15–7,14–20].

The prognostic significance of the ABO blood type has been assessed in patients with HCC^[21–23]. However, these studies have reported conflicting results. This inconsistency may be due to variations in the prevalence of ABO blood groups in various nations, regions, and ethnicities. Furthermore, the prognostic value of the ABO blood group after LT for HCC has only been assessed in two studies^[24,25]. Therefore, whether the ABO blood group may serve as an easy-to-use prognostic factor to improve the selection of LT candidates has not yet been established.

Due to the scarcity of deceased donor livers compared to the need for liver transplants, living donor liver transplantation (LDLT) has become a feasible alternative in Eastern Asia, including Korea, Japan, and China^[26,27]. The objective of this study was to assess the predictive significance of ABO blood type on HCC recurrence after LDLT using the Korean Organ Transplantation Registry (KOTRY) database.

Materials and methods

Data collection

The KOTRY database is a multi-center repository of LT data that have been prospectively gathered since 2014. Both donors and recipients are required to register with the KOTRY before transplantation. All registered patients were routinely followed at their outpatient clinic. This study was approved by the KOTRY, which is the only authorized national LT registry in South Korea. The study was initiated after obtaining approval from the ethics committee for each participating center, according to the Regulations on Human Organ Transplant and national legal requirements. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). All patients provided informed consent before registering in the database. Our study is reported in line with the STROCSS criteria^[28].

Patients

This study included adult patients registered in the KOTRY registry who underwent LDLT between 1 April 2014 and 31 December 2021. The exclusion criteria included retransplantation, multi-organ transplantation, and individuals younger than 20 years. Patients who underwent LT for reasons other than HCC were excluded. We initially selected 4570 adults who underwent LDLT. Of these cases, 2108 were excluded due to undergoing LT for reasons other than HCC. Of the remaining 2462 patients, 82 were removed due to poor follow-up data or

HIGHLIGHTS

- This study investigated the impact of ABO blood type on hepatocellular carcinoma (HCC) recurrence and overall survival after living donor liver transplantation (LDLT) using data from the Korean Organ Transplantation Registry.
- The results showed no significant association between ABO blood type and HCC recurrence or overall survival, with the Milan criteria and ABO incompatibility being the primary predictors of outcomes.
- The findings suggest that ABO blood type should not be considered a criterion for selecting LDLT candidates, emphasizing instead the importance of tumor biology and immunological compatibility.

inadequate information concerning HCC recurrence date or mortality date. Thus, the study finally included 2380 patients (Fig. 1). The general indications for LDLT in HCC patients were the Milan criteria. However, LDLT was performed even in cases of advanced HCC without extrahepatic metastasis if downstaging was successful. In addition, LDLT was performed for palliative treatment even in advanced HCC in end-stage liver disease patients, for whom other treatment options were not available.

Statistical analysis

Numerical variables were compared using means and standard deviations or medians and ranges according to normal distribution. Categorical variables are represented as counts and percentages. Continuous variables were examined using the analysis of variance test and the Kruskal–Wallis test. Recurrence-free survival (RFS) and overall survival (OS) rates based on ABO blood type were assessed using the Kaplan–Meier method and analyzed using the log-rank test. Two-tailed *P*-values below 0.05 were considered statistically significant. Statistical analysis was conducted using R software (R Foundation for Statistical Computing).

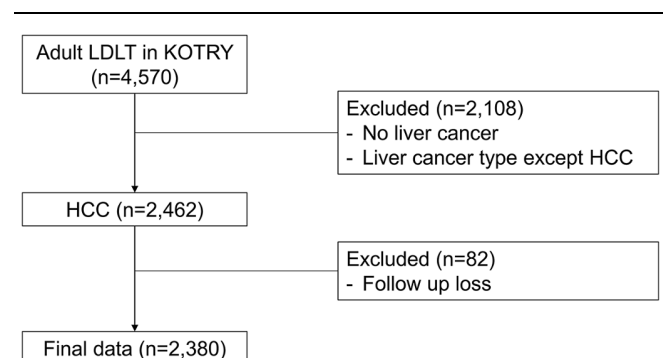


Figure 1. Patient population.

Table 1
Baseline characteristics of recipients according to ABO blood groups

	Group A (n = 864)	Group B (n = 629)	Group O (n = 627)	Group AB (n = 260)	P
Age (years)	56.9 ± 7.5	56.7 ± 7.4	57 ± 7.2	56.9 ± 7.8	0.921
Sex (male)	696 (80.6%)	521 (82.8%)	519 (82.8%)	219 (84.2%)	0.452
Height (cm)	166.6 ± 7.7	166.9 ± 7.7	166.8 ± 7.6	167 ± 6.8	0.830
Weight (kg)	68.2 ± 11.2	68.8 ± 11.4	67.9 ± 10.7	68 ± 10.6	0.542
BMI (kg/m ²)	24.5 ± 3.4	24.7 ± 3.6	24.4 ± 3.3	24.4 ± 3.3	0.413
Hypertension	212 (24.6%)	160 (25.4%)	153 (24.4%)	62 (23.8%)	0.956
Diabetes	247 (28.6%)	200 (31.8%)	178 (28.4%)	90 (34.6%)	0.158
Previous laparotomy	188 (21.8%)	148 (23.5%)	131 (20.9%)	64 (24.6%)	0.532
MELD score	11 [8, 14]	10 [8, 14]	11 [8, 14]	11 [8, 14]	0.305
Albumin (mg/dL)	3.4 [3.0, 3.9]	3.5 [3.0, 3.9]	3.5 [3.1, 3.8]	3.3 [2.9, 3.9]	0.117
Bilirubin (mg/dl)	1.10 [0.60, 2.00]	1.00 [0.60, 1.90]	1.06 [0.60, 1.70]	1.00 [0.70, 2.00]	0.742
INR	1.20 [1.08, 1.38]	1.17 [1.08, 1.39]	1.18 [1.07, 1.35]	1.19 [1.08, 1.40]	0.245
AFP (ng/mL)	6.6 [3.2, 24.5]	5.9 [3.2, 18.3]	5.6 [2.7, 22.2]	6.3 [3.1, 21.8]	0.317
PIVKA-II (mAU/mL)	29 [19, 72]	30 [19, 71]	29 [19, 71]	27 [19, 57]	0.640
HBsAg positive	611 (70.8%)	441 (70.6%)	465 (74.2%)	179 (68.8%)	0.315

AFP, alpha-fetoprotein; BMI, body mass index; HBsAg, hepatitis B surface antigen; INR, international normalized ratio; MELD, model for end-stage liver disease; PIVKA-II, protein induced by vitamin K absence II.

Results

Baseline characteristics

Table 1 summarizes the characteristics of the LT recipients included in this analysis, categorized by ABO blood group. No significant differences were detected among the groups regarding recipient age, sex, body mass index, model for end-stage liver disease (MELD) score, history of hypertension, diabetes, laparotomy, and tumor markers. The baseline characteristics of living liver donors and grafts are presented in Table 2. The mean age of living liver donors in Group A was significantly younger than that in Group B and Group AB. No other differences related to donors or grafts were observed.

Tumor characteristics

The tumor characteristics of the HCC patients classified by ABO blood type are presented in Table 3. The proportion of individuals beyond the Milan criteria was not significantly different among blood groups. More than 80% of patients received HCC

treatment before LT in all four groups. The median maximum tumor diameter was approximately 2 cm, and the median tumor number was approximately one in all groups. The presence of lymph node metastasis or portal vein thrombosis was very low, and there were no statistical differences among groups. Accordingly, AJCC staging was not different among groups.

HCC recurrence and OS

No differences in RFS and OS were observed in patients classified by blood group (Fig. 2). RFS and OS were not different in various blood types in the ABO-compatible group (Supplemental Digital Content Figure S1, available at: <http://links.lww.com/JS9/G691>) and the ABO-incompatible group (Supplemental Digital Content Figure S2, available at: <http://links.lww.com/JS9/G691>). In addition, RFS and OS in various blood types did not reach a significant level within the Milan criteria group (Supplemental Digital Content Figure S3 available at: <http://links.lww.com/JS9/G691>) and beyond the Milan criteria group (Supplemental Digital Content Figure S4, available

Table 2
Baseline characteristics of donors and grafts according to ABO blood groups

	Group A (n = 864)	Group B (n = 629)	Group O (n = 627)	Group AB (n = 260)	P
Age (years)	31.4 ± 10.3	33.6 ± 10.9	32.7 ± 11.3	33.2 ± 11.1	0.001
Height (cm)	169.3 ± 8.4	168.4 ± 8.5	169.2 ± 8.6	168.7 ± 9	0.142
Weight (kg)	68.1 ± 11.9	67.4 ± 11.9	68.1 ± 12.3	67.9 ± 12.4	0.733
BMI (kg/m ²)	23.6 ± 3.1	23.7 ± 3.1	23.7 ± 3.3	23.7 ± 3.1	0.985
Macrosteatosis (%)	2 [0, 5]	3 [1, 5]	1 [0, 5]	2 [0, 5]	0.605
WIT (min)	37 [29, 50]	37 [30, 47]	36 [28, 48]	38 [30, 50]	0.692
CIT (h)	1.5 [1.2, 2.0]	1.5 [1.2, 1.9]	1.5 [1.1, 1.9]	1.5 [1.2, 2.0]	0.150
Estimated graft volume (mL)	709 [662, 873]	760 [658, 861]	749 [653, 865]	740 [636, 851]	0.573
Proportion of estimated remnant liver volume	35 [33, 38]	36 [33, 38]	36 [33, 39]	36 [33, 39]	0.972
Actual graft weight (g)	710 [627, 813]	705 [623, 800]	715 [620, 809]	700 [590, 818]	0.358
GRWR	1.04 [0.90, 1.21]	1.02 [0.89, 1.21]	1.06 [0.89, 1.23]	1.02 [0.88, 1.23]	0.445

BMI, body mass index; CIT, cold ischemic time; GRWR, graft-to-recipient weight ratio; WIT, warm ischemic time.

Table 3
Tumor characteristics according to ABO blood groups

	Group A (n = 864)	Group B (n = 629)	Group O (n = 627)	Group AB (n = 260)	P
HCC					
Within MC	534 (75.9%)	391 (75.9%)	401 (78%)	163 (78.4%)	
Beyond MC	170 (24.1%)	124 (24.1%)	113 (22%)	45 (21.6%)	
History of HCC treatments before LT	702 (81.3%)	527 (83.9%)	527 (84.5%)	224 (86.5%)	0.169
Maximum tumor diameter (cm)	2.1 [1.4, 3.4]	2.1 [1.3, 3.4]	2.0 [1.3, 3.0]	2.2 [1.5, 3.3]	0.270
Tumor number	1 [1, 3]	1 [1, 3]	1 [1, 3]	1 [1, 3]	0.862
AJCC T stage					0.931
1. Tx	1 (0.3%)	0 (0%)	1 (0.4%)	0 (0%)	
2. T0	0 (0%)	0 (0%)	1 (0.4%)	0 (0%)	
3. T1a	87 (26.9%)	53 (22.6%)	53 (22.4%)	26 (28.6%)	
4. T1b	18 (5.6%)	9 (3.8%)	15 (6.3%)	3 (3.3%)	
5. T2	183 (56.5%)	146 (62.4%)	144 (60.8%)	55 (60.4%)	
6. T3	25 (7.7%)	18 (7.7%)	17 (7.2%)	4 (4.4%)	
7. T4	10 (3.1%)	8 (3.4%)	6 (2.5%)	3 (3.3%)	
Lymph node metastasis	7 (0.9%)	4 (0.7%)	3 (0.5%)	2 (0.8%)	0.862
Portal vein tumor thrombosis	24 (3%)	16 (2.8%)	17 (3%)	4 (1.7%)	0.721

AJCC, American Joint Commission on Cancer; HCC, hepatocellular carcinoma; LT, liver transplantation; MC, Milan criteria.

at: <http://links.lww.com/JS9/G691>). Univariate analysis showed that the Milan criteria, history of HCC treatments, lymph node metastasis, portal vein tumor thrombosis, maximum tumor size, and tumor number were predisposing factors for HCC recurrence (Table 4). Multivariable analysis demonstrated that only the Milan criteria were closely associated with HCC recurrence. Blood type did not affect HCC recurrence. Multivariable

analysis showed that the Milan criteria and ABO incompatibility were associated with OS in patients after LDLT (Table 5).

The combination of the Milan criteria and ABO compatibility

We combined ABO compatibility and the Milan criteria to establish four groups, including type I: compatible & within

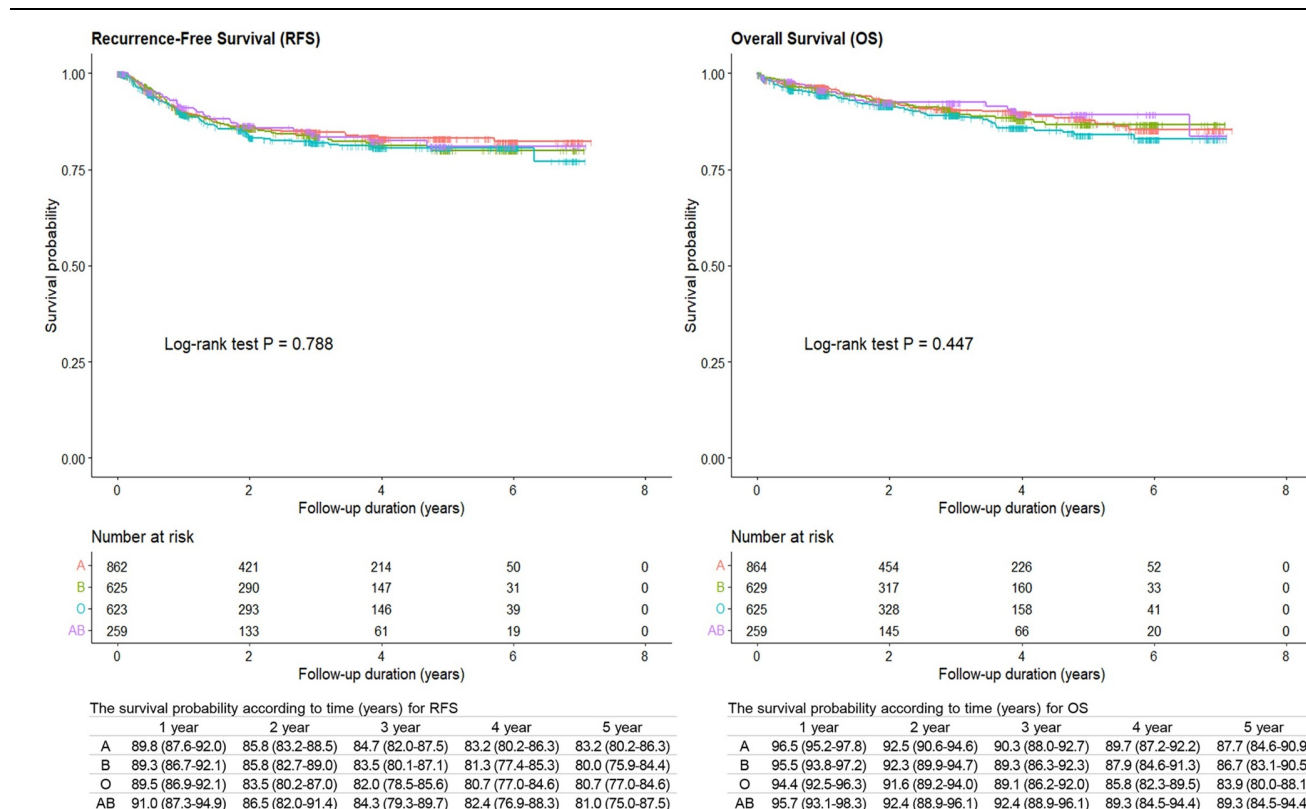


Figure 2. Survival according to ABO blood type. (A) Recurrence-free survival and (B) overall survival.

Table 4**Predisposing factors for HCC recurrence**

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
ABO type				
A	Reference		Reference	
B	1.081 (0.812–1.440)	0.592	1.014 (0.736–1.399)	0.930
O	1.150 (0.869–1.522)	0.329	1.150 (1.036–1.828)	0.393
AB	1.013 (0.689–1.490)	0.946	0.988 (0.626–1.559)	0.957
HCC				
Within MC	Reference		Reference	
Beyond MC	3.048 (2.374–3.913)	<0.001	3.121 (2.428–4.013)	<0.001
History of HCC treatments before LT	1.906 (1.335–2.721)	<0.001		
Lymph node metastasis	5.490 (2.719–11.087)	<0.001		
Portal vein tumor thrombosis	5.924 (3.982–8.815)	<0.001		
Maximum tumor diameter (cm)	1.298 (1.258–1.340)	<0.001		
Numbers of tumors	1.083 (1.068–1.099)	<0.001		

CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; LT, liver transplantation; MC, Milan criteria.

the Milan criteria, type II: compatible & beyond the Milan criteria, type III: incompatible & within the Milan criteria, and type IV: incompatible & beyond the Milan criteria. We then conducted a Cox regression analysis on recurrence and OS (Table 6). Patients meeting the Milan criteria and exhibiting ABO compatibility (type I) demonstrated superior RFS and OS relative to other groups. Type II and type IV, which fall beyond the Milan criteria, showed a significantly lower RFS compared with type I and type III, which fall within the Milan criteria. Within the Milan criteria group and beyond the Milan criteria group, the ABO-incompatible group showed a significantly

lower RFS and OS compared with the ABO-compatible group (Fig. 3). Therefore, ABO incompatibility in conjunction with exceeding Milan requirements (type IV) was linked to the worst outcome.

Discussion

The present study is the first to evaluate the influence of ABO blood type in a large cohort of Korean patients with HCC following LDLT. We assessed the predictive significance of ABO blood

Table 5**Predisposing factors for overall survival**

	Univariable analysis		Multivariable analysis	
	HR	P-value	HR	P-value
Recipient				
ABO type				
A	Reference		Reference	
B	1.048	0.797	0.967	0.856
O	1.270	0.167	1.239	0.223
AB	0.921	0.747	0.876	0.610
Sex (female)	0.820	0.308		
Hypertension	1.382	0.035		
Diabetes	1.216	0.191		
Previous laparotomy	0.843	0.336		
HBsAg positive	0.884	0.424		
HCC				
Within MC	Reference			
Beyond MC	2.455	<0.001	2.547	<0.001
ABO incompatibility	1.786	<0.001	1.932	<0.001
History of HCC treatments before LT	1.356	0.124		
Lymph node metastasis	3.366	0.016		
Portal vein tumor thrombosis	4.070	<0.001		
Donor				
Sex (female)	1.326	0.045		
Hypertension	1.771	0.078		
Diabetes	3.525	0.015		
Cardiovascular disease	1.868	0.691		

CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; MC, Milan criteria.

Table 6
Univariable Cox proportional hazard model for recurrence-free survival and overall survival in subgroup analysis

	Recurrence-free survival		Overall survival	
	HR	P-value	HR	P-value
Total subgroup set				
Type I	Reference		Reference	
Type II	3.541	<0.001	2.741	<0.001
Type III	1.731	0.002	2.207	<0.001
Type IV	3.748	<0.001	4.687	<0.001
ABO compatible subgroup				
Group A	0.803	0.213	0.789	0.307
Group B	0.810	0.272	0.878	0.600
Group O	Reference		Reference	
Group AB	0.867	0.514	0.884	0.667
ABO-incompatible subgroup				
Group A	1.135	0.627	1.109	0.704
Group B	1.373	0.213	0.923	0.788
Group O	Reference		Reference	
Group AB				
Within the Milan criteria subgroup				
Group A	0.676	0.067	0.645	0.069
Group B	0.876	0.545	0.699	0.167
Group O	Reference		Reference	
Group AB	0.821	0.498	0.579	0.141
Beyond the Milan criteria subgroup				
Group A	0.990	0.969	0.587	0.092
Group B	0.815	0.454	0.823	0.544
Group O	Reference		Reference	
Group AB	0.764	0.468	0.623	0.310

HR, hazard ratio.

Type I: Compatible & within the Milan criteria, Type II: Compatible & beyond the Milan criteria, Type III: Incompatible & within the Milan criteria, Type IV: Incompatible & beyond the Milan criteria.

type in HCC recurrence and patient survival after LDLT using data from the KOTRY. Our data revealed no substantial correlation between ABO blood type and HCC recurrence or OS in HCC patients after LDLT. These findings offer significant insights into the influence of ABO blood type on post-transplant outcomes for HCC patients. Meticulous selection of patients for LT remains a crucial strategy for minimizing the risk of post-transplant HCC recurrence^[29]. Thus far, the recipient's ABO blood type has not been considered a selection criterion for LT.

Tumor necrosis factor- α (TNF- α) and epidermal growth factor genes have been revealed to be related to HCC risk^[13,30]. ABO blood group antigen may be a source of systemic inflammation. TNF- α and soluble intercellular adhesion molecule 1 (sICAM-1) are inflammation markers that are associated with polymorphisms at the ABO locus^[12,31,32]. Elevated TNF- α plays a role in the pathogenesis of liver inflammation and cancer pathogenesis, and increased plasma levels of sICAM-1 have been suggested to be a predictor of HCC development. These markers may also be predictive markers of HCC development and survival^[30,33]. These factors may be involved in possible molecular mechanisms that explain the relationship between the ABO blood group and HCC risk. Several studies have found a relationship between ABO blood groups and Rh with various types of cancers and their tumor characteristics^[20,23,33,34]. However, the direct relationship between tumor characteristics and ABO and Rh blood groups is still unclear.

Several studies reported that ABO blood group type is associated with HCC survival after hepatectomy^[21–23,34]. Kaibori *et al*

reported that blood type A is an independent unfavorable prognostic factor for recurrence-free and OS after hepatectomy^[22]. Okada *et al* found neoexpression of the ABH blood group antigens in HCC tissues^[35]. Another study suggested that patients with blood group A may have diminished tumor immune response due to the reduced ability of the immune system to recognize and attack tumor cells expressing antigens that are structurally similar to the ABO antigen^[36]. However, the opposite outcome was observed in other reports. A large study in China demonstrated that patients with non-O blood type (i.e., types A, B, and AB) had reduced OS compared with type O patients with HCC, which is in contrast to results from the study in Japan^[23]. Moreover, no correlation was observed between the tumor size of HCC, ABO blood groups, and Rh factor. A limitation of their study is that they did not evaluate the vascular invasion and multicentric localization of tumors. A recent study also did not report a significant relationship between blood group type and the survival rate of HCC patients after hepatectomy^[20].

The prognostic role of the ABO system has also been assessed in HCC patients, but the findings of those studies were contradictory. Some studies reported an absence of prognostic impact^[20,24], while others found a certain degree of correlation between patient survival and various blood groups, with several discrepancies among the reports^[21–23,25,33].

A previous study in France was the first to assess the prognostic value of the ABO blood group system in patients undergoing LT for HCC^[25]. The authors demonstrated that the ABO blood group type was strongly associated with the risk of HCC

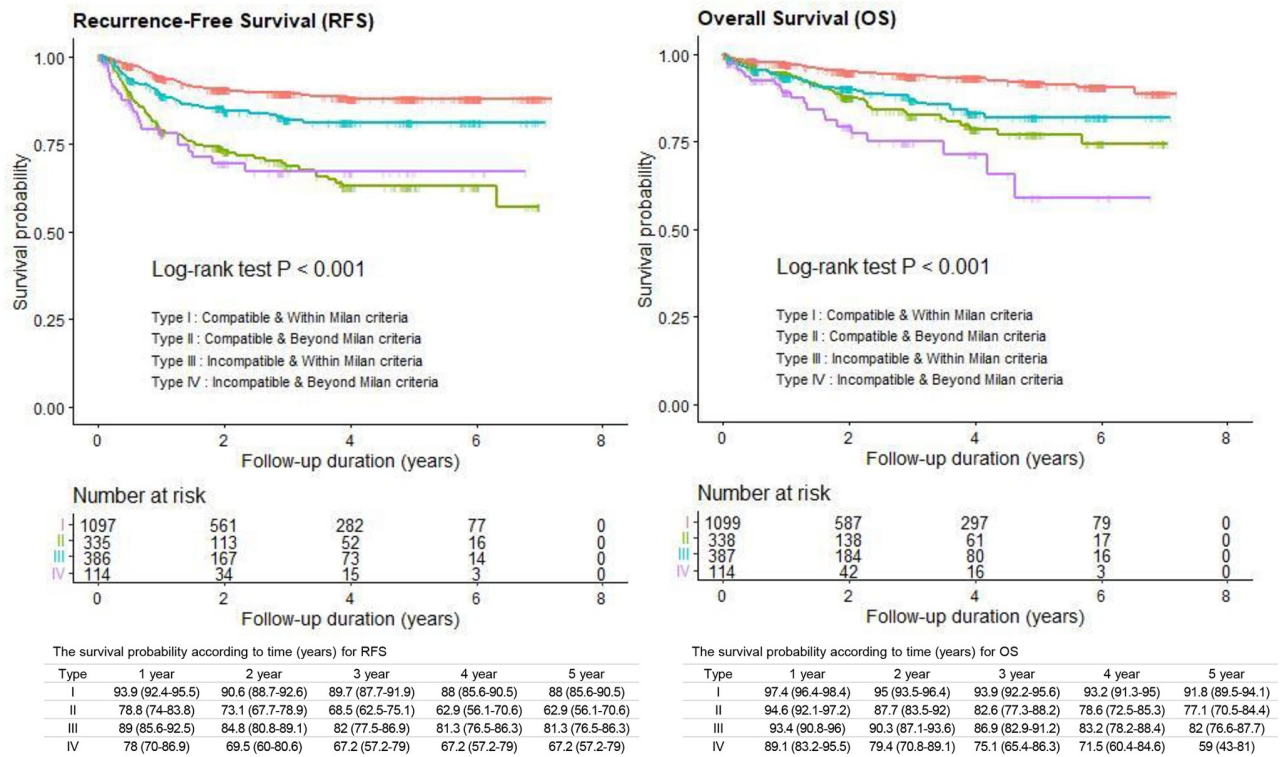


Figure 3. Survival according to the combination of the Milan criteria and ABO-incompatibility. (A) Recurrence-free survival and (B) overall survival.

recurrence following LT. Compared with recipients of other blood group types, LT recipients in blood group A had a significantly increased risk of tumor recurrence, which translated to decreased RFS. However, their study raises questions regarding the selection of living donors. Recently, one Korean high-volume center reported that ABO blood group type had no prognostic impact on the oncological outcomes of patients undergoing LT for HCC^[24]. However, their results were controversial regarding the impact of ABO blood type on HCC recurrence after LT. Thus, we analyzed large cohort data using the KOTRY dataset in patients stratified by ABO blood type. In the study in France, the number of cases was small; the blood type O group was smaller than the other blood type groups. Our study had a sufficient number of cases in all blood type groups to analyze and compare the characteristics of each blood type.

The divergence between these studies and our results may be ascribed to variations in patient demographics, research methodology, or the incorporation of LDLT in our cohort, which introduces supplementary variables such as donor-recipient compatibility and graft quality. In our study, the primary predictors of OS were HCC status beyond the Milan criteria and ABO incompatibility. These considerations underscore the significance of tumor biology and immunological compatibility in influencing post-transplant outcomes, rather than solely ABO blood type. The absence of a correlation between ABO blood type and HCC recurrence indicates that alternative clinical criteria, such as tumor load and treatment history, may be more significant in forecasting recurrence risk after LT.

Our study has several limitations. First, the retrospective design inevitably restricts the capacity to identify causal linkages.

Additionally, the selection bias of included studies should not be ignored. A comprehensive analysis is not feasible due to the lack of detailed data in the KOTRY database, such as trough levels of immunosuppressants, information on pre-transplant locoregional therapies, and preoperative radiologic findings. Second, blood type A is composed of the AA genotype and AO genotype. Blood type B is composed of the BB genotype and the BO genotype. Because of the absence of relevant data regarding genotype, our study did not clarify whether there is a protective association of AO and BO genotypes with HCC. In addition, the association between Rh blood type and risk of HCC was not explored. Third, the impact of ABO blood type may vary by geographic region. Our study population was confined to Korean patients, which may limit the generalizability of the study findings to other ethnic groups. Fourth, the study did not investigate the possible molecular pathways connecting ABO blood type to HCC outcomes, including changes in glycosylation patterns or cytokine modulation^[23]. Notwithstanding these limitations, this study possesses significant strengths. The analysis was performed using an extensive, multi-center database, yielding a substantial sample size. Moreover, this is one of the few studies that have explicitly investigated the influence of ABO blood type on LDLT results for HCC patients, providing significant insights into this neglected domain.

In conclusion, our analysis of the KOTRY database reveals that ABO blood type does not substantially influence HCC recurrence or overall patient survival after LDLT. The combination of ABO-incompatibility and beyond the Milan criteria is linked to an increased risk of mortality after LDLT, indicating that ABO blood type independently affects patient survival except for tumor status and ABO-incompatibility. Additional

research is required to confirm these findings and investigate the molecular mechanisms that underlie the observed relationships.

Ethical approval

The authors are 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. This study was approved by the KOTRY, which is the only authorized national LT registry in South Korea. The study was initiated after obtaining approval from the ethics committee for each participating center, following the Regulations on Human Organ Transplant and national legal requirements. The procedures were in accordance with the Helsinki Declaration. The Samsung Medical Center Ethics Committee approved this study (SMC-2023-11-038), which complied with the Declaration of Helsinki. The institutional review board waived the need for patient consent because this observational study was retrospective, and all data were collected from patient medical records.

Consent

All patients provided informed consent before their registration in the KOTRY database.

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Conflicts of interest disclosure

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

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data availability statement

The data that support the study findings are available upon reasonable request from the corresponding author (Jongman Kim). The full data are not publicly available due to limitations imposed by the legal regulations at some of the participating centers.

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