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Outcomes of living donor liver transplantation using graft with multiple hepatic arteries on the graft: Propensity score-matched analysis

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Background: This study aims to analyze the outcomes of living donor liver transplantation (LDLT) using grafts with multiple hepatic arteries (HAs), compared to those with a single HA.
Methods: A retrospective analysis was conducted on 1,059 LDLT patients from July 2005 to December 2022 at Severance Hospital, South Korea. Patients were categorized into multiple-HA and single-HA groups. Propensity score matching was employed to balance baseline characteristics, with primary outcomes being graft survival and secondary outcomes including HA, biliary, and total vascular complications.
Results: The study included 27 patients in the multiple-HA group and 925 in the single-HA group before matching. After propensity score matching, no significant difference in 5-year graft survival rates was observed between the groups (60.4% for multiple-HA vs. 72.8% for single-HA, p=0.172). However, the multiple-HA group exhibited a higher incidence of bile duct complications (80.0% vs. 48.3%, p=0.038). Multivariable Cox regression analysis did not find multiple HAs to be a significant predictor of graft loss but confirmed their association with increased bile duct complications.
Conclusion: LDLT using grafts with multiple HAs does not adversely affect overall graft survival compared to single-HA grafts. Nevertheless, the increased risk of bile duct complications associated with multiple HAs necessitates careful surgical planning and postoperative management to mitigate this risk.

Keywords: Living donors; Liver transplantation; Hepatic artery

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INTRODUCTION

Living donor liver transplantation (LDLT) has emerged as a crucial solution to the organ shortage crisis, offering a lifeline to patients with end-stage liver disease [1]. The use of liver grafts from living donors, despite their potential to

expand the donor pool, introduces complexities due to anatomical variations [2]. These variations necessitate refined surgical techniques to ensure the successful viability of the graft and the patient's outcome [3].

The presence of multiple hepatic arteries (HAs) in living liver grafts represents a significant anatomical challenge, requiring meticulous surgical planning [4]. Arterial reconstruction techniques have evolved to optimize graft perfusion while minimizing the risk of complications related to the HA and biliary system, which are crucial for graft survival [5]. Research has investigated various strategies for managing this complexity, underscoring the necessity of a customized approach based on the specific vascular anatomy of the donor and recipient [6,7].

Recent studies suggest that LDLT with grafts containing multiple HAs can yield comparable outcomes to those with standard anatomical configurations, provided there is careful preoperative assessment and the application of advanced microsurgical techniques [8-11]. This study aims to compare the outcomes of liver transplants between propensity score (PS)-matched LDLT recipients who received grafts with multiple HAs versus those with a single HA.

MATERIALS AND METHODS

Study Population and Outcomes

We retrospectively analyzed data from 1,059 patients who underwent LDLT between July 2005 and December 2022 at Severance Hospital, South Korea. Exclusions were made for patients under 18 years of age (n=92), dual living donor cases (n=4), grafts other than right or left lobe (n=9), combined organ transplants (n=7), retransplantations (n=3), and cases with incomplete data (n=1) (Fig. 1). Of the eligible 952 LDLTs, patients were divided into two groups according to the number of HAs on the graft; the multiple-HA group (n=27) and the single-HA group (n=925). The primary outcome was graft survival (time to death or retransplantation), and secondary outcomes included HA, biliary, and total vascular complications.

Reconstruction of HAs

Graft HAs were primarily anastomosed to branches of the recipient's HA. Alternative arterial sources, such as the gastroduodenal artery or the right gastroepiploic artery, were utilized when a healthy recipient HA was not viable due to pretransplant interventions like transarterial chemoembolization. HA anastomosis was meticulously performed under microscopic guidance or with 5× magnification loupes, using 8-0 or 9-0 monofilament interrupted sutures. In grafts with multiple HAs, the larger branch was first anastomosed to a similarly sized recipient HA branch. The decision to perform additional anastomoses or ligate smaller HAs was based on assessing backflow and intrahepatic communication through intraoperative Doppler ultrasound. Post-transplant prevention of HA thrombosis was initiated immediately after anastomosis and continued until postoperative day 7 with the administration of prostaglandin E1 at a dose of 0.3–0.5 μg/kg/hr. Patients without a bleeding risk were then prescribed aspirin at a dose of 100 mg/day for thromboprophylaxis, extending to one year post-transplant or longer.

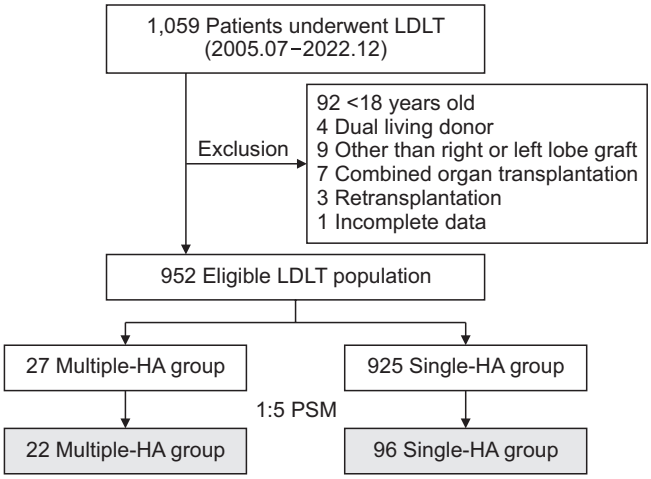

Fig. 1. Study flow. HA, hepatic artery; LDLT, living donor liver transplantation; PSM, propensity score matching.

Statistical Methods

The multiple-HA and single-HA groups were matched using a PS at a ratio of 1:5. The PS matching utilized the nearest neighbor technique with a caliper width of 0.1 to ensure precise matching. The PS were derived from a comprehensive analysis of all initial patient characteristics. The matching process was considered successful when the standardized mean differences for all baseline variables did not exceed 0.1, ensuring a balanced comparison between the two groups [12]. Cases without a suitable match were excluded from both categories to maintain the integrity of the analysis.

Data presentation favored median values with interquartile ranges (IQRs) for continuous variables and counts with percentages for categorical variables. Continuous and categorical variables were evaluated using Student's t-test, the

Wilcoxon rank-sum test, or the chi-square test, as appropriate. Kaplan-Meier survival curves and the log-rank test were employed for graft survival rate analysis in the matched groups. Significant covariates from univariate Cox regression models with p-values less than 0.1 were included in multivariate Cox regression models to assess their impact on graft survival across the entire study population. All statistical analyses were performed using the R software package, version 4.3.0, tailored for macOS environments, available at the Comprehensive R Archive Network (CRAN). A p-value of less than 0.05 was established as the criterion for statistical significance throughout our study.

Ethic Approval

This study was performed in accordance with the Declaration of Helsinki and Declaration of Istanbul and was approved by the Institutional Review Board at Severance Hospital, Yonsei University Health System (IRB No. 4-2023-1567). Informed consent was not required because of the study's retrospective design.

Table 1. Baseline characteristics of propensity score-matched population

Variable	Before matching			After matching		
	Multiple-HA (n=27)	Single-HA (n=916)	p-value	Multiple-HA (n=22)	Single-HA (n=96)	p-value
Age (yr)	56 (49–66)	55 (50–60)	0.271	56.0±9.5	54.9±9.0	0.594
Sex (female)	11 (40.7)	253 (27.6)	0.201	8 (36.4)	17 (17.7)	0.101
BMI (kg/m^2)	22.9 (20.2–26.3)	23.8 (22.0–25.9)	0.403	23.7 (21.2–26.4)	24.6 (22.5–26.5)	0.566
Year of LT			0.012			0.712
2012–2015	3 (11.1)	278 (30.3)		3 (13.6)	18 (18.8)	
2016–2018	6 (22.2)	279 (30.5)		5 (22.7)	26 (27.1)	
2019–2022	18 (66.7)	359 (39.2)		14 (63.6)	52 (54.2)	
Hypertension	7 (25.9)	211 (23.0)	0.905	6 (27.3)	29 (30.2)	0.990
Diabetes mellitus	10 (37.0)	291 (31.8)	0.712	8 (36.4)	37 (38.5)	0.894
Cardiovascular disease	2 (7.4)	58 (6.3)	0.972	0 (0.0)	6 (6.2)	0.506
Underlying liver disease			0.302			0.773
Viral	13 (48.1)	575 (62.8)		11 (50.0)	56 (58.3)	
Alcoholic	8 (29.6)	198 (21.6)		7 (31.8)	26 (27.1)	
Others	6 (22.2)	143 (15.6)		4 (18.2)	14 (14.6)	
HCC	14 (51.9)	517 (56.4)	0.782	12 (54.5)	56 (58.3)	0.932
Pretransplant MELD	15 (9–23)	12 (9–17)	0.333	12 (9–21)	13 (9–19)	0.934
Operation time (min)	600 (546–711)	642 (543–720)	0.650	591 (552–684)	600 (477–675)	0.337
Cold ischemic time (min)	108 (96–150)	130 (102–157)	0.057	111 (96–150)	120 (96–150)	0.500
RBC transfusion (pack)	5 (2–12)	3 (1–8)	0.067	4 (1–11)	4 (2–7)	0.524
Portal flow modulation	4 (14.8)	67 (7.3)	0.278	2 (9.1)	5 (5.2)	0.845
Donor age (yr)	46 (39–49)	31 (24–41)	<0.001	45 (36–49)	42 (32–50)	0.939
Donor sex (female)	9 (33.3)	355 (38.8)	0.712	9 (40.9)	41 (42.7)	0.946
Donor BMI (kg/m^2)	23.3 (22.0–25.4)	22.9 (21.0–24.7)	0.148	23.5±2.7	23.3±2.6	0.727
ABO incompatibility	7 (25.9)	190 (20.7)	0.680	6 (27.3)	24 (25.0)	0.971
GRWR<0.8	3 (11.1)	46 (5.0)	0.334	3 (13.6)	6 (6.2)	0.464
Graft type			<0.001			0.515
Right lobe	18 (66.7)	892 (97.4)		18 (81.8)	86 (89.6)	
Left lobe	9 (33.3)	24 (2.6)		4 (18.2)	10 (10.4)	
Macrovesicular steatosis>10%	6 (25.0)	121 (14.1)	0.225	4 (21.1)	13 (14.9)	0.755
Donor minimally invasive surgery	4 (14.8)	203 (22.2)	0.501	3 (13.6)	15 (15.6)	0.978

Values are presented as median (interquartile range), number (%), or mean±standard deviation.

HA, hepatic artery; BMI, body mass index; LT, liver transplantation; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease; RBC, red blood cell; GRWR, graft-recipient weight ratio.

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RESULTS

Baseline Characteristics

As depicted in Table 1, both the multiple-HA and single-HA groups exhibited comparable demographics, including age, sex distribution, body mass index, and underlying comorbidities such as hypertension, diabetes mellitus, and cardiovascular disease. The multiple-HA group was more frequently observed in the latter part of the study period (66.7% for the multiple-HA group vs. 39.2% for the single-HA group during 2019–2022, p=0.012). The prevalence of hepatocellular carcinoma was similar between the groups (51.9% for the multiple-HA group vs. 56.4% for the single-HA group, p=0.782), as were operation and cold ischemic times. Notably, the multiple-HA group had older donors (46 years IQR [39–49 years] vs. 31 years [24–41 years]; p<0.001) and a higher proportion of left lobe grafts (33.3% vs. 2.6%, p<0.001). Donor sex, degree of macrovesicular steatosis, and the rate of minimally invasive donor hepatectomy were comparable. Post-propensity score matching (PSM), the variables were well-balanced across both groups (Supplementary Fig. 1).

Other Anatomical Variations of Graft

In the matched cohort, the multiple-HA group exhibited a marginally higher proportion of dual portal veins compared to the single-HA group (18.2% vs. 4.2%, p=0.059; Supplementary Table 1). The occurrence of inferior hepatic veins and multiple bile duct openings was similar, albeit with a slightly higher incidence of multiple bile ducts in the multiple-HA group (68.2%, 22.7%, and 9.1% vs. 61.5%, 37.5%, 1.0% for 1, 2, and 3 bile duct openings; p=0.055).

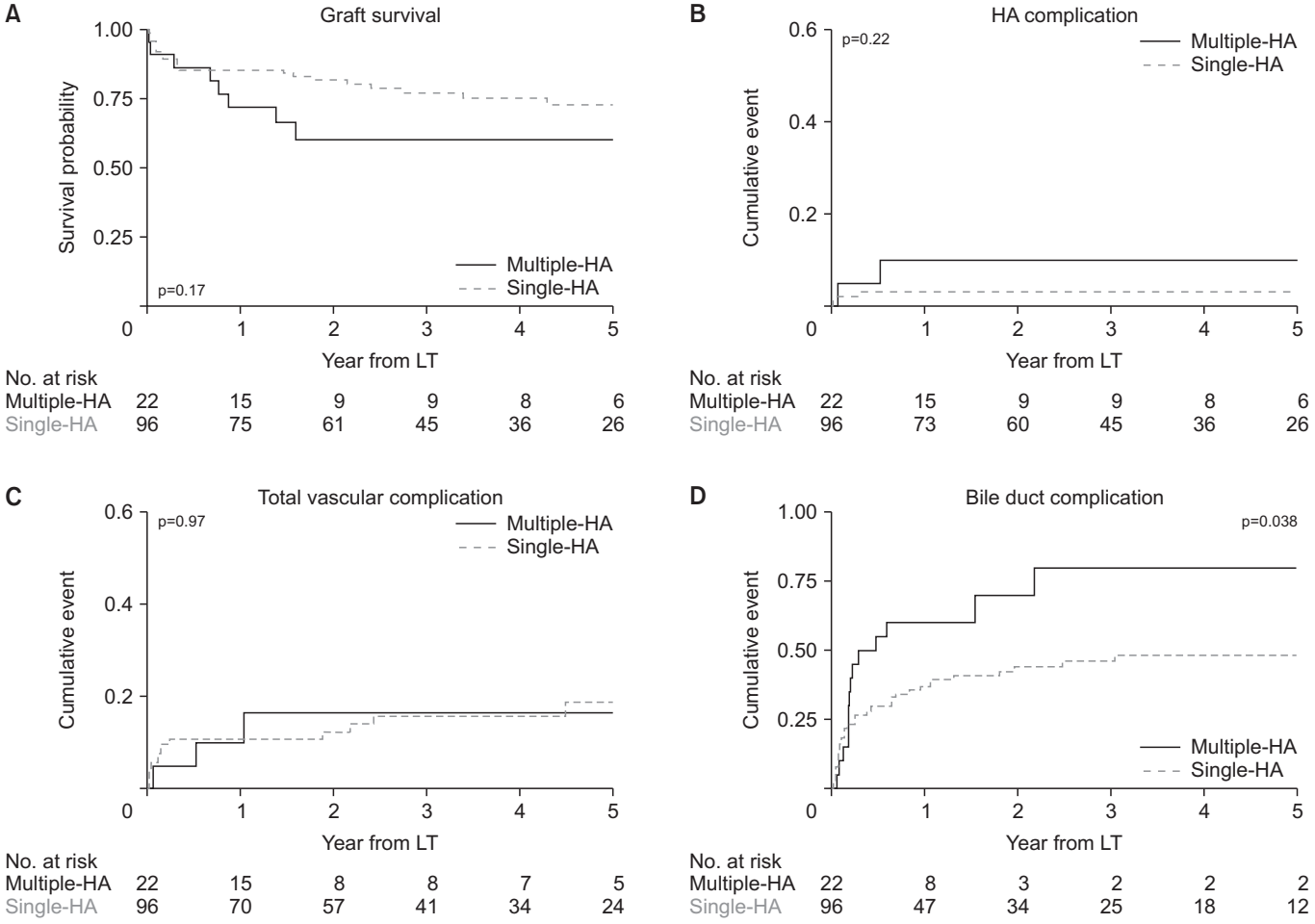

Fig. 2. Kaplan-Meier curve analyses comparing outcomes in matched population. (A) Graft survival, (B) hepatic artery (HA) complication, (C) total vascular complication, (D) bile duct complication. LT, liver transplantation.

Table 2. Recipient anastomosis site for multiple graft hepatic artery (HA)

Recipient anastomosis site	Total (n=22)
One anastomosis to HA branch (one ligated)	8 (36.4)
Two HA branches	11 (50.0)
HA branch and gastroduodenal artery	2 (9.1)
Mid colic artery and right gastroepiploic artery	1 (4.5)

Values are presented as number (%).

Outcomes

As shown in Fig. 2, Within the matched population, there was no significant difference in 5-year graft survival rates between the groups (60.4% for multiple-HA vs. 72.8% for single-HA, p=0.172). Rates of HA complications (10.0% vs. 3.2%, p=0.224) and total vascular complications (16.4% vs. 18.8%, p=0.971) were also comparable. However, the incidence of bile duct complications was significantly higher in the multiple-HA group (80.0% vs. 48.3%, p=0.038). Multivariable Cox analysis revealed that multiple HAs were not associated with graft loss (adjusted hazard ratio [aHR], 1.44; 95% confidence interval [CI], 0.67–3.11; p=0.348; Supplementary Table 2) but were significantly correlated with an increased risk of bile duct complications (aHR, 1.79; 95% CI, 1.09–2.94; p=0.021; Supplementary Table 3).

Comparison According to Anastomosis for Multiple HAs

In the multiple-HA group, the larger HA was anastomosed to a recipient HA branch, with smaller HAs ligated in 36.4% of cases (Table 2). Two graft HAs were anastomosed separately to recipient HAs in 50.0% of patients. In a few instances, recipient HA and gastroduodenal artery were utilized for multiple HA anastomoses. Graft survival did not differ significantly based on the number of HA anastomoses (56.2% for one-HA anastomosis vs. 60.9% for two-HA anastomosis, p=0.790; Supplementary Fig. 2).

DISCUSSION

LDLT presents anatomical challenges that necessitate precise surgical interventions to ensure outcomes comparable to those achieved with standard anatomical configurations. Our study demonstrates that grafts with multiple HAs do not compromise graft survival in LDLT, irrespective of whether smaller HAs were ligated. However, a significant correlation was found between multiple HAs and an increased incidence of biliary complications.

Previous research has indicated that multiple HAs might lead to higher rates of HA complications and graft loss [4,13]. Our findings, however, show low rates of HA complications, which were not influenced by the number of HAs in right lobe grafts. Advances in arterial anastomosis techniques have facilitated the reconstruction of all HAs, thereby reducing the risk of early graft loss due to HA thrombosis [14]. Although the presence of multiple HAs could extend anastomosis and operation times which could result in poor outcome [15], our data suggest that these factors do not adversely affect graft or patient survival.

In our study, graft survival in the multiple-HA group was significantly lower than in the single-HA group prior to PSM. However, after PSM, the statistical difference in graft survival between the two groups disappeared. It's noteworthy that the overall 5-year graft survival rate in the matched population was approximately 50% to 60%, which is 20% to 30% lower than the outcomes typically reported for LDLT [16]. The application of PSM also resulted in poorer outcomes for the matched single-HA group compared to the overall LDLT results. This suggests that the inferior outcomes observed in the multiple-HA group within our cohort may not be solely attributable to the presence of multiple HAs. Instead, clinical characteristics such as older donor age, intensive care unit stays, and the use of the left lobe—factors known to adversely affect graft outcomes—were more prevalent in the multiple-HA group. Previous literature also indicates that, even after matched analysis, graft survival rates around 60% are somewhat lower than the expected outcomes for LDLT. Therefore, our findings emphasize the necessity of careful evaluation and management of other risk factors when conducting LDLT with multiple HA grafts.

Selective HA anastomosis, combined with the ligation of smaller branches, has been shown not to impact graft outcomes adversely [9]. This strategy, which relies on adequate back-bleeding from smaller arteries, may optimize LDLT outcomes by avoiding unnecessary anastomoses and shortening operation times. Despite the limited size of our cohort and the relatively short follow-up period, our findings support the viability of this approach, indicating comparable survival rates.

Biliary complications pose significant postoperative challenges, affecting patient morbidity and graft survival [17]. The technical intricacies associated with multiple HAs can compromise the arterial flow to the bile ducts, thereby heightening the risk of biliary strictures and leaks. Optimal arterial reconstruction is pivotal, not only for ensuring graft perfusion but also for minimizing the risk of biliary complications. Our analysis indicates a higher risk of bile duct

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complications associated with multiple HAs, which could be still controversy among literatures [8-10], suggesting the need for further research to refine surgical techniques and improve outcomes.

One of the limitations of this study is its single-center, retrospective nature, which necessitates caution in the generalized interpretation of our findings. Additionally, the technical diversity in the anastomosis of the HA across institutions poses a significant challenge to the generalizability of our study. To address the risk associated with multiple HA in LDLT, further investigation involving multicentric data is warranted.

In conclusion, our findings underscore the feasibility of using grafts with multiple HAs in LDLT. The increased incidence of biliary complications remains a challenge, highlighting the importance of selecting the most suitable arterial reconstruction technique based on comprehensive preoperative planning and an in-depth understanding of the patient's vascular anatomy.

SUPPLEMENTARY MATERIAL

Supplementary data related to this article can be found online at https://doi.org/10.52604/alt.24.0002.

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CONFLICT OF INTEREST

All authors have no conflicts of interest to declare.

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AUTHORS' CONTRIBUTIONS

Conceptualization: DGK. Data curation: DGK, MK. Formal analysis: DGK, MK. Investigation: HHK, SHY, MCC, EKM, JGL, DJJ, MSK. Methodology: MK, HHK, SHY. Project administration: DGK. Resources: MCC, EKM, JGL. Software: DGK. Supervision: DGK. Validation: DJJ, MSK. Visualization: MK. Writing – original draft: MK.

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