ORIGINAL ARTICLE

Safe use of right lobe living donor livers with moderate steatosis in adult-to-adult living donor liver transplantation: a retrospective study

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ABSTRACT

Hepatic steatosis (HS) beyond a certain degree can jeopardize living donor (LD) safety, particularly in right lobe (RL) donors, making it a major obstacle for donor pool expansion in adult-to-adult living donor liver transplantation (ALDLT). From July 2004 to June 2016, 58 LDs donated their RLs despite having moderate HS (30%-50% steatosis) determined by intraoperative biopsy at a single center. We performed greedy matching to compare the outcomes of the donors and recipients of this group with those of LDs with no HS. The mean left lobe (LL) HS value in the 58 cases was 20.9 ± 12.4%, which was significantly lower than the mean RL HS value (38.8 ± 6.7%, $P < 0.001$). The mean ratio of the remnant LL to the total liver volume was 37.8 ± 2.2. No differences were observed in the postoperative liver function and donor and recipient morbidity and mortality rates. The liver regeneration rates in recipients and donors at 1 month, 6 months, and 1 year postoperatively did not differ significantly. The patient and graft survival rates of the recipients showed no differences. The use of well-selected RL grafts with moderate steatosis does not impair graft function, recipient outcomes, or donor safety.

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Key words
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Introduction

Living donor liver transplantation (LDLT) has become a feasible treatment modality for end-stage liver disease (ESLD) to alleviate the shortage of deceased donors and reduce waiting-list mortality. The obesity epidemic worldwide has made it increasingly common to encounter liver steatosis in living as well as deceased donor candidates. Previous studies on deceased donor liver transplantation (DDLT) have revealed the negative effects of graft steatosis on recipient outcomes because of a high incidence of ischemia-reperfusion injury (IRI), poor liver regeneration, primary nonfunction (PNF), and early graft dysfunction, all of which result in decreased graft and patient survival. [1-4] However, because of the critical shortage of deceased donor organs, the use of grafts with some degree of hepatic steatosis (HS) has become inevitable, and grafts with mild to moderate steatosis (<60% HS) have become acceptable in the DDLT setting. [5-7]

In contrast to the DDLT setting, a consensus on the upper limit of graft steatosis is lacking in the LDLT setting. [8] Since HS beyond a certain degree can jeopardize living donor (LD) safety, particularly in right lobe (RL) donors, many transplant centers are reluctant to perform LDLT using steatotic grafts where the degree of steatosis is more than moderate. [9,10] This has led to a lack of clinical data needed to establish an acceptable standard of graft steatosis. In addition, it is difficult to establish an absolute upper limit of graft steatosis as the acceptable range of graft steatosis in LDLT varies according to donor age, graft type and estimated remnant liver volume, preoperative condition of the recipient, and the estimated graft volume (GV) to recipient body weight ratio (GRWR). [11,12]

Several recent studies have demonstrated acceptable recipient outcomes following LDLT with a steatotic graft; however, the study populations were small, most grafts were left lobe (LL) grafts, and the degrees of HS were mild (<30%). [7,10,13-15] The primary aim of our study was to review our experiences with RL adult-to-adult LDLT (ALDLT) in donors with moderate HS (30%-50% steatosis) and evaluate its safety and feasibility by comparing the outcomes of such donors and recipients with those of RL ALDLT in LDs with no HS.

Materials and methods

Study population and design

We retrospectively reviewed the medical records of 2,796 RL ALDLTs performed between July 2004 and June 2016 at the Asan Medical Center (Seoul, South Korea). To eliminate confounding factors, recipients with major postoperative vascular complications such as right hepatic or portal vein obstruction and hepatic artery thrombosis were excluded. Dual-graft ALDLTs, ABO-incompatible ALDLTs, and pure laparoscopic donor hepatectomies were also excluded. Finally, 58 LDs with moderate HS (30%-50% steatosis) and 613 LDs with no HS, determined by intraoperative biopsy, were included in the present study.

In order to compare outcomes between the two groups, individual matching using the greedy algorithm was performed with 2:1 matching in 46 pairs and 1:1 matching in five pairs, resulting in the final enrollment of 153 LDs in this study (51: moderate HS group, 97: no-HS group). The matching was conducted according to donor and recipient ages, the estimated remnant liver volume determined by computed tomography (CT) volumetry and preoperative indocyanine green R15 values of the LD, model for end-stage liver disease (MELD) score, and GRWR of the recipient. The adequacy of individual matching was described based on standardized differences.

The primary endpoint was the comparison of LD safety including postoperative laboratory findings (peak aspartate transaminase [AST], alanine transaminase [ALT], total bilirubin [TB], prothrombin time [PT] values), operative morbidity, and the remnant liver regeneration rate. The secondary endpoints were the comparisons of graft function in recipients, including the in-hospital mortality; 1-, 5-, and 10-year graft survival rates; and incidence of functional small-for-size graft (SFSG) syndrome.

Preoperative evaluation and selection guidelines for RL donation

The preoperative donor evaluations began with the assessment of volunteers through interviews with social workers and psychiatrists. The medical evaluation process consisted of three phases. Phase I comprised of a physical examination, review of the past medical history, and basic laboratory tests, including viral serology. Phase II included triphasic liver CT and abdominal ultrasonography (US) to assess the hepatic volume, vascular anatomy, and steatosis. Phase III consisted of magnetic resonance (MR) cholangiography, and indocyanine green retention tests. Prior to 2010, percutaneous needle biopsy (PCNB) of the liver was routinely performed and selectively performed thereafter in donor candidates with a high body mass index (BMI) (≥30 kg/m^2), elevated AST,

ALT, or total bilirubin levels, abnormal findings on CT or US suggesting HS, or a family history of hereditary liver disease. [16] Fifty-eight LDs with moderate HS (30%-50% steatosis) in this study had CT or US findings that suggested HS, and all 58 LDs underwent PCNB preoperatively.

For preoperative assessment of HS, US-guided percutaneous biopsy of the RL was performed in selected cases via an intercostal approach with 18-gauge needles (Stericut with a coaxial guide, TSK Laboratory, Tochigi, Japan). For intraoperative evaluations in all patients, wedge biopsy samples of both hepatic lobes were performed just after laparotomy and sent for frozen section examination. The remaining tissue was formalin-fixed and paraffin-embedded for hematoxylin and eosin staining. The extent of macrovesicular (Mac) and microvesicular (mic) HS was quantified using a percentage scale (i.e., the amount of liver parenchyma that was replaced by Mac or Mic lipid droplets). Other histopathological features indicating clinically significant damage to the liver parenchyma such as inflammation, fibrosis, ballooning, or cirrhosis were examined by an expert pathologist.

The details of our guidelines for LD and graft type selection are described elsewhere. [17] In general, our team prefers donors with $< 15\%$ of Mac HS and $< 30\%$ of the sum of Mac and Mic HS on PCNB for RL donation; however, donation of RL grafts without the middle hepatic veins by LDs with moderate HS (30%-50% steatosis) was allowed if the LD met all of the following conditions: (1) donor age of ≤ 35 years, (2) an estimated ratio of the remnant LL to total liver volume (TLV) of $\geq 35\%$, (3) the degree of HS of the LL on MR was less than that of the RL, (4) a sufficient GRWR in the recipient, and (5) if recipients, because of medical conditions requiring urgent liver transplant (LT), were unable to wait for a weight reduction in the LD candidates. LD candidates not fulfilling all of the above conditions were reevaluated after weight reduction by diet control and exercise; alternatively, dual-graft ALDLT using grafts from two independent donors was considered.

Surgical technique and postoperative management

We used various surgical techniques to ensure LD safety and graft reconstruction. To prevent outflow obstruction at the anterior section, sizable ($\geq$5 mm diameter) tributaries of the middle hepatic vein were reconstructed with various kinds of interposition grafts in back-table surgeries. The standard techniques for procurement and implantation were employed. The detailed surgical techniques of donor hepatectomy and recipient surgeries are described elsewhere. [18]

All LDs were closely monitored during the first 1 or 2 days after donation, especially for the timely detection of bleeding. Oxygenation, nutritional support with early feeding, and early ambulation were emphasized. Intravenous patient-controlled analgesia was routinely used for 2 to 3 days after the operation. CT was performed at 1 week, 1 month, 6 months, and 1 year postoperatively using low-dose radiation CT protocols to minimize radiation exposure in the LDs.

Analysis of liver regeneration rates in donors and recipients

The regeneration rates of the remnant liver in the LDs and of grafts in recipients were measured using CT volumetry with a picture archiving and communication system (PetaVision for Clinics, Seoul, Korea) at 1 week, 1 month, 6 months, and 1 year postoperatively. When measuring the remnant liver or GV on CT, we outlined the parenchyma of the liver (or graft) on each CT slice and excluded the main portal vein and its first branch and the main trunk of the hepatic vein. The volume of the liver (or graft) (in mL) was then computed using CT volumetry. The regeneration rate (%) of the remnant liver or graft was defined using the following formula: regeneration rate (%) = [liver (or graft) volume by CT volumetry (mL) – liver (or graft) volume by previous CT volumetry (mL)]/liver (or graft) volume by previous CT volumetry (mL) $\times$ 100.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY). Descriptive statistics for numerical variables are recorded as means $\pm$ standard deviation, and categorical variables are presented as relative frequencies (percentages). We used the chi-square or Fisher's exact test to compare categorical data and Student's t-test or the Mann–Whitney test for numerical data. The outcomes between the groups were compared using least-squares means, the linear mixed model after log transformation, and cumulative logistic regression with generalized estimating equations. Patient and graft survival were analyzed using Cox regression with robust standard errors that accounted for the clustering of matched pairs. P-values < 0.05 were considered to indicate significant differences.

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Dummy

The LD process for every case was assessed and approbated by the Korean Network for Organ Sharing (KONOS) which is affiliated with the Ministry of Health and Welfare of the Republic of Korea. The study was approved by the Institutional Review Board of Asan Medical Center, University of Ulsan, Seoul, Korea (approval number: 2018-0085), which waived the requirement for informed consent because of the retrospective nature of this study.

Results

Recipient and donor baseline characteristics

Table 1 shows the differences in the demographic and clinical features between the groups with moderate HS and no HS. The moderate HS group comprised a significantly higher proportion of men and revealed a higher BMI and preoperative AST and ALT levels than the no-HS group. The GRWR and LL-to-TLV ratios were also significantly higher in the moderate HS group than in the no-HS group.

The mean HS value of the RL in the moderate HS group was 38.8 ± 6.7% (Mac HS, 20.0 ± 7.1%; Mic HS, 18.8 ± 8.0%). The mean HS value of the LL in the moderate HS group was 20.9 ± 12.4% (Mac HS, 11.7 ± 7.4%; Mic HS, 9.2 ± 9.1%). The mean HS value of the LL was, thus, significantly lower than that of the RL ($P < 0.001$). Among the 58 LDs with moderate HS, 45 (77.6%) had a lower degree of HS of the LL than of the RL; the remaining 13 LDs showed the same degree of HS between both lobes.

Comparison of laboratory findings of donors and recipients

The peak serum AST, ALT, and PT values were significantly higher in the moderate HS group after donor

Table 1. Comparison of recipient and donor demographic and clinical characteristics between recipients with moderate (30%-50% steatosis) and no hepatic steatosis

	No HS (n = 613)	Moderate HS (n = 58)	P-value
Recipient			
Age (years)	51.1 ± 8.5	52.8 ± 9.4	0.164
Sex ratio (male/female), n (%)	447 (72.9%)/166	41 (70.7%)/17	0.715
Underlying disease, n (%)			0.484
HBV	412 (67.2%)	38 (65.5%)	
HCV	36 (5.8%)	4 (6.9%)	
NBNC	165 (27.0%)	16 (27.6%)	
HCC, n (%)	270 (44.1%)	25 (43.8%)	0.567
BMI	23.6 ± 3.3	24.3 ± 4.2	0.202
MELD	16.6 ± 9.4	20.5 ± 10.2	0.018
GRWR (%)	1.1 ± 0.2	1.2 ± 0.2	0.002
CIT (minutes)	89.6 ± 94.6	80.6 ± 30.5	0.105
WIT (minutes)	46.5 ± 79.0	45.9 ± 23.4	0.902
Donor			
Age (years)	26.0 ± 7.5	27.3 ± 7.6	0.193
<35, n (%)	555 (90.5%)	49 (84.5%)	
≥35, n (%)	58 (9.5%)	9 (15.5%)	
Sex ratio (male/female)	374 (61.0%)/239	46 (79.3%)/12	0.006
BMI (kg/m^2)	21.8 ± 6.4	24.5 ± 2.4	0.001
Preoperative AST (IU/L)	19.1 ± 8.4	24.2 ± 5.4	0.014
Preoperative ALT (IU/L)	15.0 ± 9.1	22.7 ± 10.3	0.001
Preoperative bilirubin (mg/dL)	0.8 ± 0.4	0.8 ± 0.3	0.878
HS on RL (%)	0	38.8 ± 6.7	<0.001
HS on LL (%)	0.2 ± 1.0	20.9 ± 12.4	<0.001
LL/TLV ratio (%)	33.1 ± 3.3	37.8 ± 2.2	0.005

ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; CIT, cold ischemic time; GRWR, graft-to-recipient body weight ratio; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HS, hepatic steatosis; LL, left lobe; MELD, Model for End-Stage Liver Disease; NBNC, non-hepatitis B and non-hepatitis C; RL, right lobe; TLV, total liver volume; WIT, warm ischemic time.

right hepatectomy than in the matched no-HS group ($P < 0.001$). No significant difference in the peak serum total bilirubin value was observed. Laboratory parameters, except for AST ($P = 0.032$), showed comparable results on posthepatectomy day 7. However, the moderate HS group required a significantly shorter time than the no-HS group to achieve PT normalization. Detailed data are presented in Table 2.

Among recipients, no significant differences in the post-ALDLT laboratory profiles were observed except in the peak serum AST values (Table 3).

Comparison of postoperative morbidity of donors

The incidence of postoperative complications was comparable between the two groups for LDs ($P = 0.811$). One hundred forty-eight patients experienced a total of six complications, the two most common being bile leakage ($n = 3$) and postoperative bleeding ($n = 2$). In one patient, when removing the surgical drain, a cut of the drain occurred, which was left in the abdominal cavity and the drain fragment had to surgically removed. No significant differences in the postoperative length of hospital stay were observed in LDs ($P = 0.259$).

Comparison of postoperative morbidity and survival outcomes of recipients

No significant differences in the incidence of postoperative complications were observed in recipients ($P = 0.935$). A detailed description of the postoperative complications is provided in Table 4. The postoperative length of hospital stay was comparable between the two groups of recipients ($P = 0.384$). No cases of PNF or SFSG syndrome were observed in either group. The incidence of SFSG syndrome and in-hospital mortality did not differ significantly between the two groups.

Regarding survival outcomes, the 1-, 5-, and 10-year graft survival rates were comparable between the two groups (94.8%, 90.7%, and 90.7% in the no-HS group *vs.* 90.2%, 88.2%, and 84.8% in the moderate HS group; hazard ratio [HR], 1.535; 95% confidence interval [CI], 0.671–3.513; $P = 0.310$) (Figure 1).

Comparison of liver regeneration rates in LDs and recipients

A comparison of the graft regeneration rates in recipients at 1 month, 6 months, and 1 year postoperatively using CT-volumetric analysis and remnant liver

Table 2. Comparison of postoperative laboratory findings after donor hepatectomy between donors with moderate (30%-50% steatosis) and no hepatic steatosis

	No HS ($n = 97$) LS means (95% CI)	Moderate HS ($n = 51$) LS means (95% CI)	*P*-value
Posthepatectomy peak value			
AST (IU/L)*	148.0 (136.2–160.8)	183.4 (164.5–204.5)	0.002
ALT (IU/L)*	138.2 (127.6–149.5)	185.2 (167.6–204.7)	<0.001
Total bilirubin (mg/dL)*	2.61 (2.44–2.78)	2.67 (2.44–2.92)	0.622
PT (INR)	1.56 (1.53–1.60)	1.45 (1.40–1.50)	0.001
PT (%)*	47.5 (46.0–48.9)	54.0 (51.9–56.1)	<0.001
On posthepatectomy day 7			
AST (IU/L)*	54.7 (50.7–59.0)	46.7 (41.9–52.1)	0.032
ALT (IU/L)*	69.4 (63.1–76.4)	60.8 (53.7–68.8)	0.070
Total bilirubin (mg/dL)	0.95 (0.88–1.01)	0.97 (0.88–1.06)	0.680
PT (INR)	1.11 (1.10–1.13)	1.09 (1.07–1.12)	0.260
PT (%)	82.4 (80.1–84.8)	85.9 (82.5–89.2)	0.148
Duration for normalization after hepatectomy (days)			
AST	7.3 (6.7–7.9)	6.7 (6.0–7.5)	0.258
ALT	8.9 (7.8–10.0)	8.2 (6.8–9.6)	0.349
Bilirubin	4.8 (4.3–5.2)	5.0 (4.4–5.7)	0.581
PT (INR)	4.2 (3.9–4.6)	3.0 (2.5–3.6)	0.001
PT (%)	5.5 (5.1–5.9)	4.4 (3.9–5.0)	0.002

ALT, alanine transaminase; AST, aspartate transaminase; HS, hepatic steatosis; INR, international normalized ratio; LS, Least Squares; PT, prothrombin time.

*Linear mixed model after log-transformation.

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Table 3. Comparison of postoperative laboratory findings after living donor liver transplantation between recipients with moderate (30%–50% steatosis) and no HS

	No HS (n = 97) Lsmeans[†] (95% CI)	Moderate HS (n = 51) Lsmeans (95% CI)	P-value
Post-LDLT peak value			
AST (IU/L)*	305.4 (258.1–361.4)	426.5 (336.7–540.4)	0.018
ALT (IU/L)*	329.1 (283.3–382.3)	374.0 (305.6–457.6)	0.228
Total bilirubin (mg/dL)*	6.87 (5.97–7.90)	7.66 (6.59–8.91)	0.142
PT (INR)*	2.20 (1.99–2.44)	2.30 (2.02–2.61)	0.512
PT (%)	33.8 (1.8–35.8)	35.2 (32.7–37.7)	0.450
On post-LDLT day 7			
AST (IU/L)*	48.0 (42.4–54.3)	51.6 (43.7–61.0)	0.212
ALT (IU/L)*	95.0 (83.7–107.9)	102.2 (86.1–121.3)	0.242
Total bilirubin (mg/dL)*	3.43 (2.83–4.15)	4.55 (3.66–5.67)	0.012
PT (INR)	1.16 (1.13–1.18)	1.20 (1.17–1.24)	0.066
PT (%)	84.2 (80.9–87.4)	79.4 (74.9–83.9)	0.089
Duration for normalization after LDLT (days)			
AST (IU/L)*	5.8 (4.9–6.8)	5.3 (4.3–6.4)	0.516
ALT (IU/L)*	12.8 (10.3–15.9)	12.6 (9.6–16.7)	0.955
Total bilirubin (mg/dL)*	9.33 (7.26–12.00)	8.12 (5.55–11.87)	0.591
PT (INR)	3.40 (3.03–3.76)	3.93 (3.36–4.49)	0.131
PT (%)	4.9 (4.3–5.4)	5.5 (4.8–6.3)	0.159

ALT, alanine transaminase; AST, aspartate transaminase; HS, hepatic steatosis; PT, prothrombin time; INR, international normalized ratio.

*Linear mixed model after log-transformation.

[†]Least Squares Means.

regeneration rates between the moderate HS and no-HS groups showed no statistically significant differences in the graft and remnant LL regeneration rates (Figure 2).

Discussion

The results of the present study showed that the outcomes of ALDLT in LDs with moderate HS (30%-50% steatosis) were comparable to those in LDs without HS, with an acceptable biochemical profile and rate of liver volume regeneration after the operation in both LDs and recipients. The operative risk for LDs is associated with multiple factors such as LD age, the type of hepatectomy, remnant liver volume, degree of HS, the surgeon's skill, and experience of the center. Among these factors, the remnant liver volume, LD age, and HS are considered major determinants. HS is the most common medical cause of donor rejection, not only due to concerns regarding donor safety but also due to poor outcomes in recipients. Nugroho et al. reported an initial exclusion rate of 50.6% among 726 donor candidates, including 29.9% from donor-related issues, of which half were related to HS. [19] In terms of recipient outcomes, the estimated GV was corrected by assuming that each percentage of either Mac or Mic fatty change decreased the functional GV by 1%. [20]

As per our center's protocol for LD evaluation, LD candidates with HS > 30% in total or with Mac HS > 15% on PCNB are not approved for RL donation in principle. In such cases, LDs are re-evaluated after dietary modifications and weight reduction, a follow-up via noncontrast CT or US, or a repeat PCNB as needed. We previously reported that intentional weight reduction in donors led to a significant decrease in HS and enabled these livers to be utilized for transplantation. [21] As an alternative plan for recipients with several voluntary but suboptimal LD candidates, changing the graft type to dual-graft ALDLT using LL, left lateral segment (LLS), or posterior section grafts can be considered.

Although transplant surgeons should select more ideal donor candidates such as those without HS and with sufficient remnant liver volume to maximize LD safety, occasionally, it is necessary to adjust the acceptability level of these factors, within an acceptable range, to reduce waiting-list mortality in ESLD patients. Indeed, most surgeons have encountered cases involving recipients requiring urgent LTs in which there is no time to wait for the LD to lose weight or find several

Table 4. Comparison of postoperative complications in donors and recipients between moderate (30%–50% steatosis) and no HS groups

	No HS (n = 97)	Moderate HS (n = 51)	P-value
Donor			
Postop. complication, n (%)	5 (5.1%)	4 (7.8%)	0.811
Postoperative bleeding	1	1	
Bile leak	1	2	
Pleural effusion	0	1	
Ileus	1	0	
Leaving drain fragments	1	0	
Wound problem	1	0	
Highest C–D grade, n (%)*			
1	1 (1.0%)	0	
2	1 (1.0%)	0	NS
3A	1 (1.0%)	3 (5.9%)	
3B	2 (2.1%)	1 (2.0%)	
Postop. hospital stay (days)	11.6 (11.1–12.1)	12.0 (11.4–12.7)	0.259
Recipient			
Postop. complication, n (%)	49 (50.5%)	26 (51.0%)	0.935
Highest C–D grade*, n (%)			
1	2 (2.1%)	0	
2	3 (3.1%)	1 (2.0%)	NS
3A	39 (40.2%)	21 (45.1%)	
3B	2 (2.1%)	1 (2.0%)	
5	3 (3.1%)	3 (5.9%)	
Postop. hospital stay (days)	28.1 (25.1–31.4)	25.7 (22.1–29.7)	0.384
SFSG syndrome, n (%)	3 (3.1%)	2 (3.4%)	0.456
PNF, n (%)	0	0	NS
Re-LT, n (%)	0	0	NS
IHM, n (%)	3 (3.1%)	3 (5.9%)	0.392
Sepsis	2 (2.1%)	3 (5.9%)	
Graft damage due to shock	1 (1.0%)	0	

C–D, Clavien–Dindo classification; IHM, in-hospital mortality; PNF, primary nonfunction; Postop, postoperative; Re-LT, re-liver transplantation; SFSG, small-for-size graft.

*Cumulative logistic regression with generalized estimating equations (GEE) accounting for the clustering of matched pairs.

LDs. In the present study, we reviewed ALDLTs in LDs with moderate HS (30%-50% steatosis) by intraoperative biopsy. We achieved comparable and acceptable outcomes in terms of both LD safety and recipient graft function with a relatively large sample size and long-term follow-up period. We may come across LD candidates with moderate HS on preoperative liver biopsy not amenable to weight reduction because of reasons such as urgency of LT in the recipient owing to high MELD scores along with deteriorating portal hypertension or advanced hepatocellular carcinoma (HCC) in progress. In such cases, we can consider immediate ALDLT utilizing the RL without LD weight reduction to modify HS if the LD is young and has a sufficient remnant liver volume. In the present study, the mean HS value of the RL was 38.8 ± 6.7% (Mac HS, 20.0 ± 7.1%; Mic HS, 18.8 ± 8.0%) in 51 LDs with moderate HS. Among them, 17 LDs had HS values of > 40% in total; however, all were younger than 30 years, the estimated ratios of remnant LL volume to TLV were > 35%, and all matched recipients required urgent ALDLT. None of the donors experienced posthepatectomy hepatic failure or severe postoperative complications. There were no cases of SFSG syndrome or PNF. Interestingly, the findings of this study showed that the moderate HS group required a considerable shorter time than the no-HS group to achieve PT normalization. It is possible to hypothesize that the results may be related to the unmatched conditions of donor selection, but rather this seems to be a simple statistical result within this study group, and further studies with more donors are required to confirm this result.

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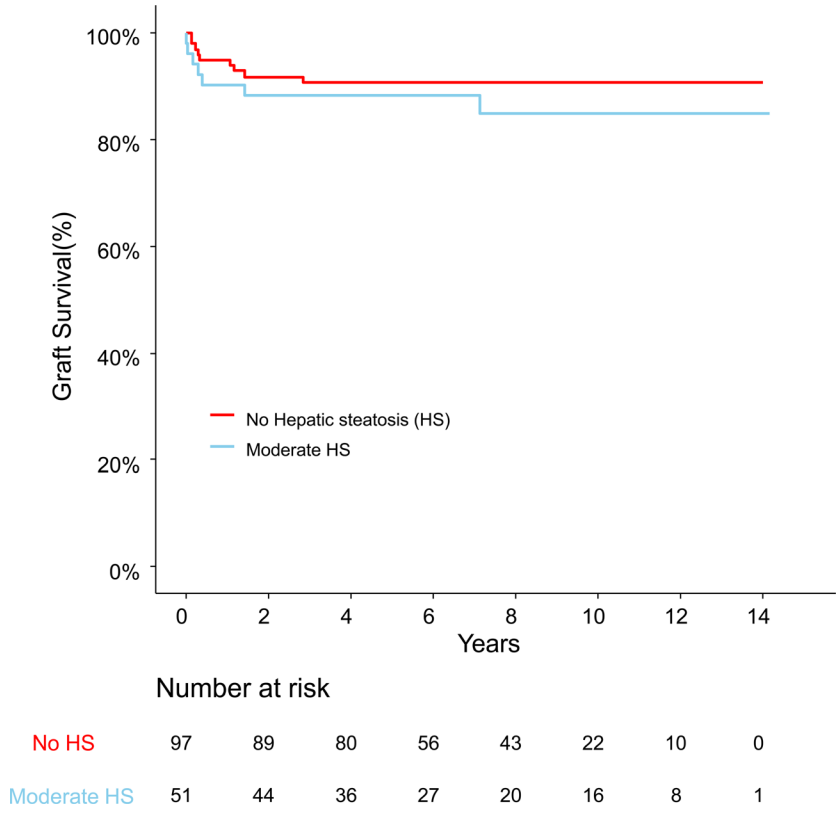

Figure 1 The 1-, 5-, and 10-year graft survival rates for adult-to-adult living donor liver transplantation (ALDLT) with moderate (30%-50% steatosis) and no hepatic steatosis (HS)

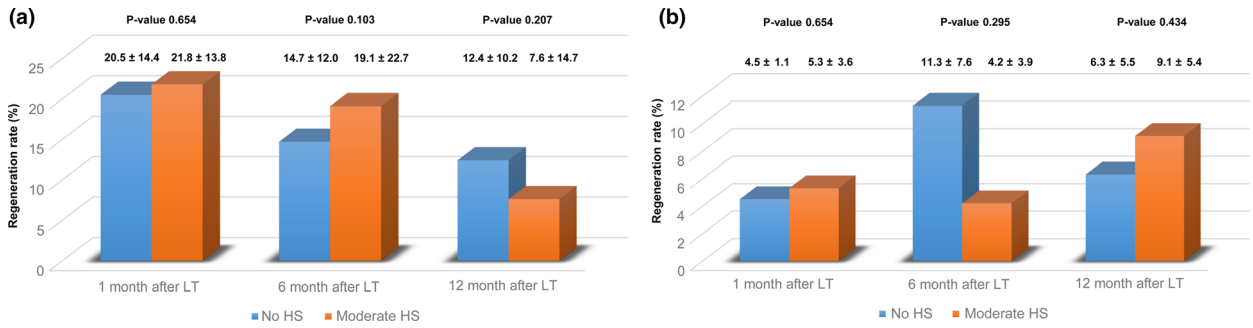

Figure 2 Comparison of (a) remnant liver and (b) graft regeneration rates between the moderate HS (30%–50% steatosis) and no-HS groups

Significant HS greatly affects the recovery of graft function after LT. In the DDLT setting, significant HS can potentiate preservation or IRI in association with prolonged cold ischemic time, or older LDs may increase the risk of PNF or delayed graft function. [3,4,18] While the exact mechanisms, by which HS negatively impacts IRI, remains unclear, the basic framework involves impaired hepatic microcirculation and mitochondrial dysfunction. [1,22] However, the influence of HS on IRI tends to be less evident in LDLT because the ischemic time is shorter than that of DDLT. Therefore, the primary concern related to HS in LDLT is not graft dysfunction but rather LD safety. The impact of HS on the operative risk after major hepatectomy remains controversial. Several studies, reporting the clinical outcomes of liver resection in hepatic neoplasms with HS > 30%, have shown increased perioperative morbidity that was associated with the extent of hepatic parenchyma resection, future liver remnant volume ratio to total liver volume, or the requirement for intraoperative red blood cell transfusion. [1,9,23-25] In contrast, HS < 30% neither increased postoperative complication and mortality rates nor impaired long-term regeneration in LDs. [8,10,15]

Liver regeneration is critical in LDLT, because it involves a partial liver graft intended to meet the metabolic demands of both the recipient and LD. In animal studies, severe steatosis with prominent inflammation negatively affected hepatocyte proliferation and resulted in impaired regeneration of the remnant liver after extensive (70%) hepatectomy. [1] In LDLT, liver regeneration was not impaired in grafts with mild steatosis (Mac HS < 30%). [9,15] However, there are no reports on liver regeneration after ALDLT in LDs with moderate or severe HS in human subjects, especially regarding LD safety. In the present study, while the regeneration of the remnant LL in LDs was not significant between the moderate HS and no-HS groups, the regeneration rate at 1 month and 6 months after donation was different, with the moderate HS group being higher than the no-HS group. It may therefore be possible that the moderate HS group may need addition volume regeneration because of the significant nonfunctioning cell volume in the remnant LL, which requires more hypertrophy. Although this study showed comparable regeneration of both the remnant LL in LDs and RL grafts in recipients between the moderate HS and no-HS groups, this could be the effect of small sample size, further studies on liver regeneration of LDs with significant HS in a large number of LDs and recipients, are required.

From another viewpoint, parenchymal abnormalities, including steatosis, are heterogeneously distributed between the RL and LL of the liver and even within the same lobe; thus, sampling errors are inevitable. Therefore, PCNB from two or three sites might not always reflect the state of the entire liver. [26-28] In the present study, 77.6% of LDs with moderate HS showed a lower degree of HS of the LL than of the RL. Furthermore, the mean HS value of the LL was significantly lower than that of the RL. In the context of LD safety, it would be to the LD's advantage to have a lower degree of HS in the LL t than in the RL and would support RL donation from LDs with moderate HS.

The present study was limited because of its retrospective observational study design, with inherent risks of confounding factors and bias. However, as LD safety in LDLT is unconditional, the results of this study are meaningful in that they suggest the safety of RL donation in carefully selected LDs with moderate HS. Furthermore, this study suggested the indications for RL donation in LDs with moderate HS, and this will enable the expansion of the donor pool for LDLT.

Conclusion

In conclusion, RL donation by LDs with moderate HS in ALDLT can be performed safely in strictly selected patients with sufficient remnant liver volume in younger LDs. Through the careful selection of cases, functional recovery and regeneration of the remnant liver in LDs and graft function, patient and graft survival, and graft regeneration in recipients were not impaired by moderate HS.

Authorship

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Conflict of interest

None declared.

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