ORIGINAL ARTICLE

A retrospective analysis of re-exploration after living donor right lobe liver transplantation: incidence, causes, outcomes, and risk factors

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SUMMARY

Despite technical difficulties, right lobe liver grafting is preferred in living donor liver transplantation because of the graft size. Re-exploration after living donor right lobe liver transplantation (LRLT) has never been separately analyzed. We aimed to analyze the incidence, causes, outcomes, and risk factors of re-exploration after LRLT. We reviewed medical records of 1016 LRLT recipients from October 2003 to July 2017 and identified recipients who underwent re-exploration within hospital stay. Separate analyses were also performed according to cause of re-exploration. The overall incidence of re-exploration was 17.0% (173/1016). The most common cause of re-exploration was bleeding (50%). Overall re-exploration was associated with clinical outcome, but different results were shown on analyses according to cause of re-exploration. Risk factors of re-exploration were underlying hepatocellular carcinoma and operative duration [Odds ratio (OR), 1.49; 95% confidence interval (CI), 1.05–2.12; $P = 0.03$, and OR, 1.002; 95% CI, 1.001–1.004; $P = 0.0023$, respectively]. Re-exploration after LRLT is relatively common, and is strongly associated with mortality and graft failure.

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Key words
incidence, living donor right lobe liver transplantation, outcome, re-exploration

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Introduction

Re-exploration after surgery is associated with clinical outcome, and therefore has been reported as a quality of care measure [1]. In highly invasive procedures such as liver transplantation, re-explorations are relatively common and are usually direct results of errors in the surgical process [2]. Therefore, studies on the incidence and risk factors of re-exploration may be helpful in monitoring and improving clinical quality.

Although living donor liver transplantation (LDLT) has gained acceptance with surgical advancements [3,4], previous studies have reported that the incidence of re-exploration after LDLT remains high (9.2–24.3%) [5,6]. However, these studies showed conflicting results on the association with clinical outcomes of LDLT and the risk factors of re-exploration. Explanations for this inconsistency may be (i) the relatively small number of cases, (ii) inclusion of different lobe grafts, and (iii) not considering different causes of re-exploration. Moreover, living donor right lobe liver transplantation (LRLT),

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which is preferred in adult-to-adult transplantation because of the graft size, has constituted only small portion of participants in previous studies. Re-exploration after LRLT deserves a separate analysis considering surgical difficulties. Therefore, we focused our analysis to recipients of LRLT, and we also considered different causes of re-exploration. To our knowledge, this is the first analysis on re-exploration after LRLT in the largest cohort to date.

The aims of this study were (i) to report the incidence and causes of re-exploration, (ii) to analyze the association with clinical outcomes according to cause of re-exploration, and (iii) to evaluate risk factors of re-exploration in LRLT recipients.

Methods

Study population and data collection

We retrospectively reviewed medical records and the liver transplantation database at our institution. Our LDLT program began in 1997, and our electronic medical record system was adopted in 2003. In order to collect accurate data and exclude recipients from less-experienced era, we investigated from recipient case number 297 in October 2003 to recipient case number 1835 in July 2017, and 1047 adult-to-adult LDLT recipients were initially enrolled. We excluded 18 recipients who received a left lobe graft. In recipients with multiple liver transplantations, only the first transplantation was enrolled for analysis, and six cases of re-transplantations were excluded. We also excluded seven recipients with multiple organ transplantation. Finally, 1016 patients were left for analysis.

All data were collected by a trained coordinator using a standard form. The Institutional Review Board of our hospital approved this study, and all subjects were anonymously analyzed. All LRLT and re-explorations were performed after obtaining informed consent.

Study endpoints and definitions

The primary end points of this study were the incidence and causes of re-exploration. The secondary end points were the association of re-exploration with clinical outcomes and the risk factors. We also analyzed whether the cause of re-exploration correlated with clinical outcomes.

Intraoperative blood loss was estimated based on red cell mass using the following equation [7].

$$\begin{aligned}&\text{Esimated blood loss (ml)}\\&= \text{patient's estimated blood volume (ml)}\\&\times (\text{preoperative hematocrit in}\,\% \\&- \text{postoperative hematocrit in}\,\%)\\&+ (\text{transfused leukocyte-depleted red blood cell in units}\\&\times 213 \times 70\%) + (\text{transfused Cell Saver blood in ml}\\&\times 55\%).\end{aligned}$$

$$\begin{aligned}&[\text{Patients' estimated blood volume}\\&= 75\,\text{ml/kg} \times \text{body weight (for men) or}\,65\,\text{ml/kg}\\&\times \text{body weight (for women)}].\end{aligned}$$

The presence of ascites was detected by suctioning immediately after surgical insicion. Diabetes mellitus was defined as prior diagnosis of type 1 or type 2 diabetes mellitus, hemoglobin A1c > 6.5%, or fasting blood glucose >126 mg/dl on two separate occasions. Hypertension was defined as either self-reported use of antihypertensive medications or systolic blood pressure >140 mmHg.

Donor selection and surgical procedures

Our donor selection criteria have been previously described [8]. In brief, criteria were adult younger than 65 years, a body mass index lower than 35, biochemistries within normal ranges, adequate size of graft and expected remnant liver more than 30%, any other conditions related to increased risk of donor were also excluded.

All grafts consisted of segments 5–8 according to the Couinaud's classification. The surgical margin of the graft was determined based on anatomical variations. The extended right lobe graft including the middle hepatic vein was selected when the expected remnant liver was sufficient, and the most anterior section of the graft was drained through the territory of the middle hepatic vein. However, the middle hepatic vein was excluded from the graft when inadequate venous drainage was expected. In cases where the venous drainage existed for segments 5 and 8, the modified right lobe graft was selected. In donor hepatectomy, dissection of the ligaments around the liver and cholecystectomy were performed after full mobilization of the liver. Bifurcations of the hepatic duct, portal vein, and hepatic artery were identified, and intraoperative ultrasound was used to identify the intraparenchymal hepatic vein. After complete parenchymal dissection with cavitronic ultrasound aspirator, the bile duct was transected. Heparin (5000 U) was given intravenously 5 min before removal of the graft liver. The graft liver was flushed with histidine-tryptophan ketoglurate solution on the bench table.

Transplant International 2019; 32: 141–152

Grafts were implanted using a piggyback technique. The right hepatic vein was initially anastomosed, followed by the inferior hepatic vein, if it existed. After portal vein anastomosis, the graft was reperfused by unclamping the hepatic vein and portal vein. After reperfusion, segments 5 and 8 veins were anastomosed to the inferior vena cava using a cryopreserved allovascular graft. The hepatic artery and biliary tract were then anastomosed. For biliary anastomosis, bilobiliary anastomosis was the standard method, but in recipients with history of radiation therapy or biliary surgery, hepaticojejunostomy was considered. A biliary stent tube was not routinely inserted unless hepaticojejunostomy was performed. After LRLT, all recipients were transferred to the intensive care unit (ICU).

Anesthetic and postoperative management

Standardized anesthesia was performed in all recipients according to institutional protocol. After applying standard monitoring devices (peripheral capillary oxygen saturation, 5-lead electrocardiography, noninvasive arterial blood pressure), anesthesia was induced with thiopental sodium and maintained with isoflurane. Remifentanil was also infused in response to hemodynamic changes. The respiratory rate was adjusted to maintain normocapnea. Fluids and pressor drugs were infused to maintain mean arterial pressure 70 mmHg. Intraoperative indication of packed red blood cell transfusion was blood hemoglobin <8.0 g/dl.

Recipients were closely monitored for early detection of postoperative bleeding or thrombosis at ICU for the first 48 h after LRLT. Ultrasonography was used to detect thrombus. In cases where abdominal drainage revealed biliary leakage, or biliary stricture was suspected with elevated bilirubin after postoperative day (POD) 4, ultrasonography was initially performed and then confirmed by retrograde cholangiography. Routine blood tests were done daily during the hospital stay. Oxygenation, nutritional support, and early feeding and ambulation were encouraged.

Immunosuppression and anticoagulation regimen

Immunosuppression was based on a quadruple regimen: induction with methylprednisolone plus basiliximab and maintenance with tacrolimus starting on POD 3 plus mycophenolate mofetil. The plasma concentration of tacrolimus was titered at 10–15 ng/ml.

Anticoagulation therapy, to prevent thrombosis, was started immediately after reperfusion. The institutional regimen was to administer prostaglandin E immediately after reperfusion which was continued until POD 3 at a dose of 35 IU/kg/day. Dalteparin (50 IU/kg/day) was started immediately after hepatic artery anastomosis, and continued until postoperative day 6. Antithrombin-III was started from arrival at ICU, and administered in 500 units every 6 h until POD 9.

Re-exploration

Among surgical interventions, re-exploration was limited to those directly related to LRLT and performed under general anesthesia within the hospital stay. Interventions under local anesthesia (such as wound revision at bedside) or planned interventions, not directly related to LRLT (such as formation of a fistula for hemodialysis), were not analyzed as re-exploration.

Causes of re-exploration were categorized as bleeding, thrombosis, biliary complications, wound, and graft failure. Indications of re-exploration for bleeding were hemodynamic instability, hemorrhage above Grade B according to ISGLS (International Study Group of Liver Surgery) [9], or suspected intra-abdominal hematoma infection. Hepatic arterial thrombosis, portal venous thrombosis, or decreased portal flow on ultrasonography was indication of re-exploration for thrombus. Biliary complications were initially treated with interventional strategies, but cases with massive biliary leakage with risk of peritonitis, biliary obstruction or intrahepatic biliary dilatation, were treated with re-exploration.

Statistical analysis

Statistical analyses were performed using SPSS 20.0 for Windows (SPSS Inc, Chicago, IL, USA). Continuous

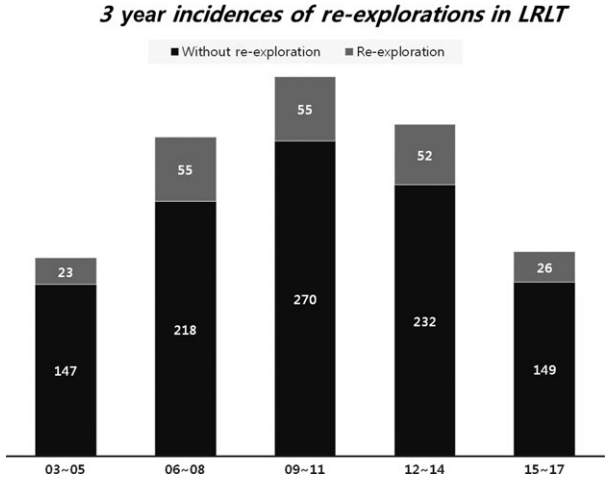

Figure 1 Three-year incidences of re-exploration.

data were presented as mean ± standard deviation (SD) or median ± interquartile range (IQR) as applicable. Differences were compared using the *t*-test or the Mann-Whitney test. We used Chi-square or Fisher's exact test to compare categorical variables. We used Cox regression analysis to evaluate the association with clinical outcomes, and logistic regression analysis for the risk factors. Covariates with clinical relevance or univariate effect with *P*-value <0.15 were retained in the multivariate analysis. The hazard ratio (HR) and odds

Table 1. Baseline characteristics of the entire population.

	No re-exploration (*N* = 843)	Overall re-exploration (*N* = 173)	*P*-value
Recipient variables			
Age	52.38 ± 8.6 (19–77)	52.18 ± 8.33 (21–71)	0.78
Male	672 (79.7)	134 (77.5)	0.54
BMI	24.53 ± 3.43 (15.5–39.5)	24.18 ± 8.33 (16–37)	0.49
Smoking	273 (32.4)	50 (28.9)	0.42
Alcoholics	294 (34.9)	65 (37.6)	0.54
Encephalopathy	190 (22.5)	28 (16.2)	0.07
Varix	168 (19.9)	25 (14.5)	0.11
Ascites	485 (54.3)	110 (63.6)	0.16
Hypertension	101 (12)	16 (9.2)	0.36
Diabetes	165 (19.6)	31 (17.9)	0.67
Tuberculosis	37 (4.4)	10 (5.8)	0.43
Hepatoreanl syndrome	42 (5)	10 (5.8)	0.7
Bacterial peritonitis	83 (9.8)	18 (10.4)	0.78
MELD score	17.7 ± 10.3 (5–48)	19.2 ± 11.4 (6–51)	0.1
Bilirubin, mg/dl	8.0 ± 12.6 (0.3–52)	10.8 ± 14.9 (0.4–51)	0.01
INR	1.84 ± 1.15 (0.9–11.2)	1.97 ± 1.31 (0.9–9.0)	0.2
Creatinine, mg/dl	1.01 ± 0.71 (0.2–7.9)	1.04 ± 0.74 (0.2–5.7)	0.66
Albumin, g/dl	3.16 ± 0.64 (1.7–5.8)	3.14 ± 0.60 (1.8–5)	0.65
CTP score	8.8 ± 2.7 (5–15)	9.0 ± 2.6 (5–15)	0.38
Preop ICU	65 (7.7)	15 (8.7)	0.64
Duration, days	0.4 ± 2.6 (0–64)	0.3 ± 1.7 (0–16)	0.89
Ventilator care	18 (2.1)	5 (2.9)	0.57
Pathology			
Alcohol related	77 (9.1)	19 (11)	0.48
Acute failure	86 (10.2)	16 (9.2)	0.78
Hepatocellular carcinoma	426 (50.8)	102 (59.0)	0.03
HBV-related	626 (74.3)	122 (70.5)	0.34
HCV-related	60 (7.1)	10 (5.8)	0.62
Operative variables			
Duration, min	567 ± 109 (298–980)	596 ± 125 (384–933)	0.002
Estimated blood loss, ml	1311 ± 2064 (304–24571)	1565 ± 2213 (300–18240)	0.15
Cold ischemia time, min	91.9 ± 39.2 (13–389)	94.1 ± 35.2 (22–298)	0.5
Warm ischemia time, min	37.6 ± 17.6 (13–234)	37.9 ± 24.9 (16–263)	0.88
RBC transfusion, unit	1.4 ± 3.8 (0–50)	1.5 ± 3.1 (0–18)	0.91
Donor variables			
Age	32.57 ± 11.51 (19–59)	31.69 ± 10.62 (18–60)	0.36
Male	558 (66.2)	108 (62.4)	0.38
BMI	23.20 ± 3.12 (13–40)	23.08 ± 2.96 (17–33)	0.63
Macrosteatosis	6.81 ± 5.76 (0–25)	7.34 ± 7.30 (0–30)	0.3
Microsteatosis	9.71 ± 9.24 (0–60)	10.18 ± 8.64 (0–50)	0.54
GRWR	1.11 ± 0.27 (0.6–2.0)	1.10 ± 0.25 (0.7–1.8)	0.36
Operative duration, min	354 ± 151 (150–489)	375 ± 109 (150–485)	0.08
Estimated blood loss, ml	258 ± 151 (10–782)	258 ± 141 (16–746)	0.97
Re-exploration	10 (11.9)	4 (2.3)	0.28

BMI, body mass index; CTP, Child-Turcotte-Pugh score; GRWR, graft to recipient-body weight ratio; ICU, intensive care unit; INR, international normalized ratio; MELD, model for end-stage liver disease; RBC, red blood cell.

Values are *n* (%) or mean ± SD (range).

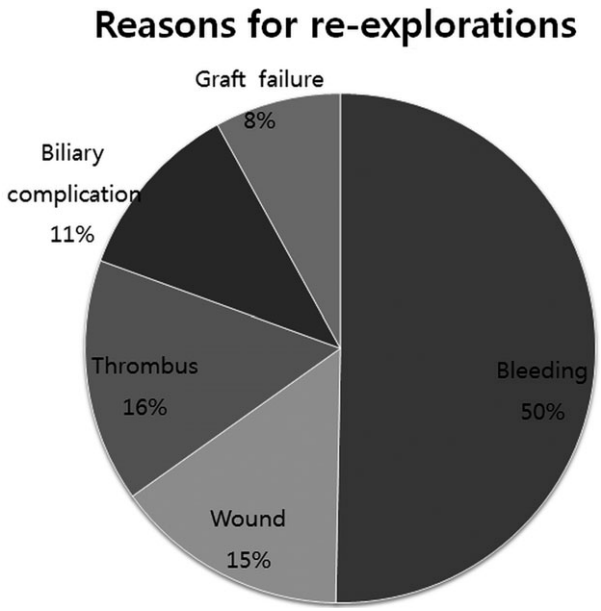

Figure 2 Causes of re-exploration.

ratios (OR) were reported with 95% confidence interval (CI), and *P*-value were presented. Survival curves for each cause of re-exploration were generated using Kaplan-Meier estimates. All tests were two-tailed, and $P < 0.05$ was considered statistically significant.

Results

Among the 1016 LRLT recipients, 173 underwent re-exploration (17.02%). Three-year incidences of re-exploration are presented in Fig. 1. The baseline characteristics of overall re-exploration group are presented in Table 1. The most common cause of re-exploration was bleeding in 50% of re-exploration, and the most common day of re-exploration was POD 1 (Figs 2 and 3). The bleeding sites detected during re-exploration were summarized in Table S1. Preoperative bilirubin, operative duration, and incidence of hepatocellular carcinoma (HCC) were higher in the re-exploration group (8.0 vs. 10.8, $P = 0.01$; 567 vs. 596, $P = 0.002$; 49.8% vs. 62.8% $P = 0.03$). The baseline characteristics according to cause of re-exploration are summarized in Table 2.

The association between overall re-exploration and clinical outcome is presented in Table 3. Re-exploration was highly associated with death or graft failure regardless of the length of follow-up period. (HR, 5.02; 95% CI, 2.97–8.47; $P < 0.001$ during inhospital stay, HR, 3.15; 95% CI, 2.03–4.87; $P < 0.001$ during 1 year follow-up, and HR, 2.32; 95% CI, 1.62–3.31; $P < 0.001$ during overall follow-up period). Re-exploration was also associated with longer duration of ICU and hospital stay (8.2 days vs. 12.1 days; $P < 0.001$, 35.8 days vs. 52.9 days; $P < 0.001$, respectively). The survival curve for overall re-exploration showed a significant association with death or graft failure ($P < 0.001$). However, survival curves showed different results according to cause of re-exploration. While re-explorations caused by bleeding and biliary complications showed a significant association with death or graft failure ($P < 0.001$), re-explorations caused by thrombus and wound were not significantly associated ($P = 0.491$, $P = 0.883$, respectively) (Fig. 4).

Risk factors of re-exploration were underlying HCC and operative duration (OR, 1.49; CI 95%, 1.05–2.12; $P = 0.03$, OR, 1.002; CI, 1.001–1.004; $P = 0.0023$, respectively). The incidence of re-exploration was lower in recipients with a history of encephalopathy (Table 4).

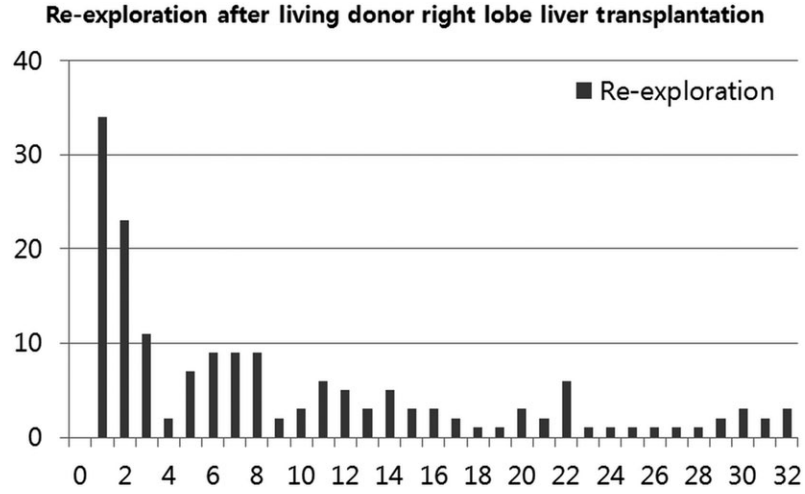

Figure 3 Postoperative day of re-exploration.

Table 2. Baseline Characteristics of the re-exploration group.

	Bleeding (*N* = 86)	Thrombus (*N* = 27)	Wound (*N* = 26)	Biliary complications (*N* = 20)	Retransplantation (*N* = 14)
Recipient variables					
Age	52.14 ± 7.80 (30–68)	53.82 ± 7.91 (34–69)	53.03 ± 7.76 (38–71)	53.00 ± 10.31 (21–71)	53.00 ± 10.31 (27–67)
Male	70 (79.5)	18 (66.7)	22 (84.6)	17 (85.0)	8 (57.1)
BMI	24.17 ± 2.91 (17–31)	29.14 ± 4.56 (17–35)	24.90 ± 4.03 (17–36)	21.73 ± 2.76 (17–26)	21.73 ± 2.76 (16–37)
Smoking	25 (28.4)	6 (22.2)	8 (30.8)	8 (40.0)	3 (21.4)
Alcoholics	35 (39.8)	7 (25.9)	10 (38.5)	8 (40.0)	5 (35.7)
Encephalopathy	16 (18.2)	2 (7.4)	3 (11.5)	3 (15.0)	4 (28.6)
Varix	12 (13.6)	4 (14.8)	3 (11.5)	3 (15.0)	3 (21.4)
Ascites	59 (67.0)	16 (59.3)	18 (69.2)	10 (50.0)	7 (50.0)
Hypertension	11 (12.5)	2 (7.4)	0	1 (5.0)	2 (14.3)
Diabetes	20 (22.7)	3 (11.1)	5 (19.2)	2 (10.0)	1 (7.1)
Tuberculosis	4 (4.5)	1 (3.7)	3 (11.5)	1 (5.0)	1 (7.1)
Hepatoreanl syndrome	7 (8.0)	2 (7.4)	1 (3.8)	0	0
Bacterial peritonitis	9 (10.2)	5 (18.5)	1 (3.8)	1 (5.0)	2 (14.3)
MELD score	20.3 ± 11.3 (7–51)	17.4 ± 11.0 (6–12)	19.2 ± 13.4 (6–51)	16.7 ± 7.6 (7–35)	16.7 ± 7.6 (6–41)
Bilirubin, mg/dl	12.1 ± 15.7 (0.4–49.8)	7.06 ± 11.5 (0.6–46.2)	12.13 ± 18.32 (0.5–51)	7.75 ± 10.87 (0.8–33)	7.75 ± 10.87 (0.4–37)
INR	1.86 ± 0.98 (0.9–5.3)	1.71 ± 0.61 (1.0–3.3)	2.25 ± 2.15 (1.1–9.0)	1.79 ± 1.14 (1–6)	1.79 ± 1.14 (1–7)
Creatinine, mg/dl	1.18 ± 0.84 (0.3–5.7)	0.89 ± 0.35 (0.6–2.1)	1.21 ± 1.02 (0.5–5.1)	0.93 ± 0.45 (0.6–2.7)	0.93 ± 0.45 (0.2–1.6)
Albumin, g/dl	3.09 ± 0.65 (1.8–4.4)	3.11 ± 0.68 (2.2–4.8)	3.22 ± 0.60 (2.5–5)	3.08 ± 0.54 (2.2–4.2)	3.08 ± 0.54 (2.4–4.2)
CTP score	9.02 ± 2.68 (5–15)	8.67 ± 2.43 (5–14)	8.62 ± 2.35 (5–13)	9.00 ± 2.49 (5–13)	9.00 ± 2.49 (5–13)
Preop ICU	8 (9.1)	2 (7.4)	1 (3.8)	2 (10.0)	2 (14.3)
Duration, days	0.5 ± 2.4 (0–16)	0.3 ± 0.94 (0–4)	0.4 ± 0.2 (0–1)	0.3 ± 0.79 (0–3)	0.3 ± 0.79 (0–1)
Ventilator care	4 (4.5)	0	0	1 (5.0)	0
Pathology					
Alcohol related	12 (15.9)	3 (11.1)	1 (3.8)	1 (5.0)	2 (14.3)
Acute failure	9 (10.2)	0	5 (19.2)	2 (10.0)	0
Hepatocellular carcinoma	48 (54.5)	20 (74.1)	12 (46.2)	11 (55.0)	11 (78.6)
HBV-related	61 (69.3)	19 (70.4)	16 (61.5)	15 (75.0)	11 (78.6)
HCV-related	6 (6.8)	0	2 (7.7)	2 (10.0)	0
Operative variables					
Duration, min	569 ± 110 (399–933)	594 ± 102 (411–685)	575 ± 97 (384–743)	587 ± 88 (412–775)	619 ± 174 (414–735)
Estimated blood loss, ml	1789 ± 2899 (502–18240)	1256 ± 656 (304–12579)	1383 ± 1180 (300–10248)	1173 ± 797 (345–9942)	1617 ± 1817 (327–15471)
Cold ischemia time, min	97.7 ± 38.5 (30–298)	86.7 ± 29.8 (53–155)	97.8 ± 36.5 (40–176)	87.6 ± 29.1 (22–136)	87.6 ± 29.1 (58–132)

Table 2. Continued.

	Bleeding (*N* = 86)	Thrombus (*N* = 27)	Wound (*N* = 26)	Biliary complications (*N* = 20)	Retransplantation (*N* = 14)
Warm ischemia time, min	36.8 ± 27.4 (18–263)	34.7 ± 10.1 (20–51)	40.4 ± 25.0 (19–151)	36.5 ± 30.6 (19–162)	36.5 ± 30.6 (16–176)
Intraoperative RBC transfusion, min	1.3 ± 2.9 (0–18)	2.2 ± 4.4 (0–16)	1.7 ± 2.8 (0–8)	0.7 ± 1.1 (0–4)	0.7 ± 1.1 (0–10)
Donor variables					
Age	31.24 ± 10.84 (18–60)	31.41 ± 9.61 (19–50)	32.35 ± 11.97 (18–51)	30.60 ± 8.39 (21–58)	30.60 ± 8.39 (25–60)
Male	47 (53.4)	19 (70.4)	19 (73.1)	13 (65.0)	11 (78.6)
BMI	22.89 ± 2.79 (17–30)	23.94 ± 3.31 (19–33)	23.01 ± 2.58 (18–28)	22.31 ± 3.04 (17–28)	22.31 ± 3.04 (19–31)
Macrosteatosis	7.02 ± 6.62 (0–30)	6.44 ± 3.85 (0–15)	7.42 ± 6.56 (0–25)	6.80 ± 4.81 (0–20)	6.80 ± 4.81 (0–30)
Microsteatosis	10.11 ± 9.14 (0–50)	7.67 ± 6.48 (0–30)	13.08 ± 9.17 (0–40)	9.55 ± 8.04 (0–30)	9.55 ± 8.04 (0–30)
GRWR	1.08 ± 0.27 (0.7–1.8)	1.02 ± 0.22 (0.7–1.5)	1.08 ± 0.25 (0.7–1.8)	1.23 ± 0.30 (0.8–1.7)	1.23 ± 0.30 (0.9–1.5)
Operative duration, min	369 ± 102 (150–485)	371 ± 88 (262–440)	390 ± 93 (255–415)	409 ± 158 (233–370)	364 ± 122 (325–445)
Estimated blood loss, ml	245 ± 138 (20–746)	292 ± 157 (16–540)	266 ± 168 (16–642)	253 ± 115 (19–448)	252 ± 121 (16–713)
Re-exploration	2 (2.3)	0	1 (3.8)	1 (5.0)	0

BMI, body mass index; CTP, Child-Turcotte-Pugh score; GRWR, graft to recipient-body weight ratio; ICU, intensive care unit; INR, international normalized ratio; MELD, model for end-stage liver disease; RBC, red blood cell.

Values are *n* (%) or mean ± SD (range).

Table 3. Clinical outcomes associated with re-exploration.

	No re-exploration (*N* = 843)	Re-exploration (*N* = 173)	Unadjusted HR (95% CI)	*P*-value	Adjusted HR (95% CI)	*P*-value
Inhospital follow-up						
Death or graft failure	40 (4.7)	37 (21.4)	5.46 (3.37–8.85)	<0.001	5.02 (2.97–8.47)	<0.001
Death	40 (4.7)	27 (15.6)	3.71 (2.21–6.24)	<0.001	3.28 (1.89–5.71)	<0.001
1 year follow-up						
Death or graft failure	80 (9.5)	47 (27.2)	3.56 (2.37–5.34)	<0.001	3.15 (2.03–4.87)	<0.001
Death	79 (9.4)	38 (22.0)	2.72 (1.77–4.18)	<0.001	2.38 (1.51–3.77)	<0.001
Retransplantation	1 (0.1)	14 (8.1)	74.14 (9.68–567.79)	<0.001	83.14 (10.34–668)	<0.001
Overall outcome						
Death or graft failure	199 (23.6)	77 (44.5)	2.60 (1.85–3.65)	<0.001	2.32 (1.62–3.31)	<0.001
Death	194 (23.0)	68 (39.3)	2.17 (1.54–3.06)	<0.001	1.92 (1.34–2.76)	<0.001
Retransplantation	5 (0.6)	14 (8.1)	14.76 (5.24–41.55)	<0.001	21.62 (6.53–71.61)	<0.001
ICU stay (days)	8.2 (±7.4)	12.1 (±16.9)		<0.001		<0.001
In-hospital stay (days)	35.8 (±26.1)	52.9 (±44.7)		<0.001		<0.001

ICU, intensive care unit.

Values are *n* (%) or mean (±SD).

Covariates include age, male, encephalopathy, MELD score, hepatocellular carcinoma, operative durations.

Discussion

The main findings of the present study are (i) the incidence of re-exploration after LRLT is 17.0%, (ii) the most common cause of re-exploration is bleeding, and the most commonly performed day is POD 1, (iii) re-exploration is associated with adverse outcomes, especially when caused by bleeding or biliary complications, and (iv) operative duration and underlying HCC are risk factors of re-exploration.

Living donor right lobe liver transplantation offers lower risk of small-for-size syndrome, but requires more sophisticated surgical procedures. In the light of immediate operative complications, LRLT is a different procedure than left lobe LDLT therefore, analysis on re-exploration focusing on LRLT is needed. This study showed that the incidence of re-exploration after LRLT was similar to those of other types of liver transplantations [5,6,10,11]. However, compared to hepatic resections other than transplantation, the incidence of re-exploration after any liver transplantation has consistently been reported to be high, ranging from 9 to 34% [12,13]. Reasons for the high incidence of re-exploration may be underlying conditions of recipients, postoperative medication, and sophisticated surgical techniques. Recipients with hepatic failure commonly present hemostatic imbalance, and postoperative care involves immunosuppression and anticoagulation. Hemostatic complications, such as bleeding or thrombosis, have been reported as the most common causes of re-exploration after liver transplantation [10,14]. Results of this study also showed that bleeding or thrombus posed 66% of the entire cause of re-exploration. However, the benefits of correcting coagulopathy before and during LRLT are unclear because laboratory tests such as prothrombin time, international normalized ratio, and platelet counts have a clear limitation in representing the complete coagulation profile [15]. Moreover, considering rebalanced hemostasis in patients with liver disease, preoperative correction might even promote hemostatic complications [16]. Another explanation for the high incidence of re-exploration is the sophistication of the surgical technique, which includes meticulous reconstructions of the hepatic vein, hepatic artery, portal vein, and bile duct because unplanned reoperation is more related to surgical errors (70%) rather to patient pathology (21%) [2].

Our surgical margins of the grafts were in accordance with Couinaud's classification, which divides the liver into eight functionally independent segments with their own vascular inflow, outflow, and biliary drainage. Anatomical structures such as the right hepatic vein, middle hepatic vein, Falciform ligament, and portal vein are used to divide the segments. The middle hepatic vein is used to define the right and left lobes of the liver. Compared to whole liver transplantation, the graft artery is smaller in LRLT. Therefore, early hepatic arterial thrombosis, which can be fatal after liver transplantation, has been one of our primary concerns [17]. In the absence of universal guidelines, we applied a strict anticoagulation regimen. Unlike early hepatic arterial thrombosis after whole liver transplantation which is frequently treated by nonsurgical intervention, re-exploration has been the primary choice of treatment for early hepatic arterial thrombosis after LRLT because the size of some graft arteries can be even smaller than 1 mm. In this study, re-explorations caused by thrombosis were not significantly associated with the clinical outcome.

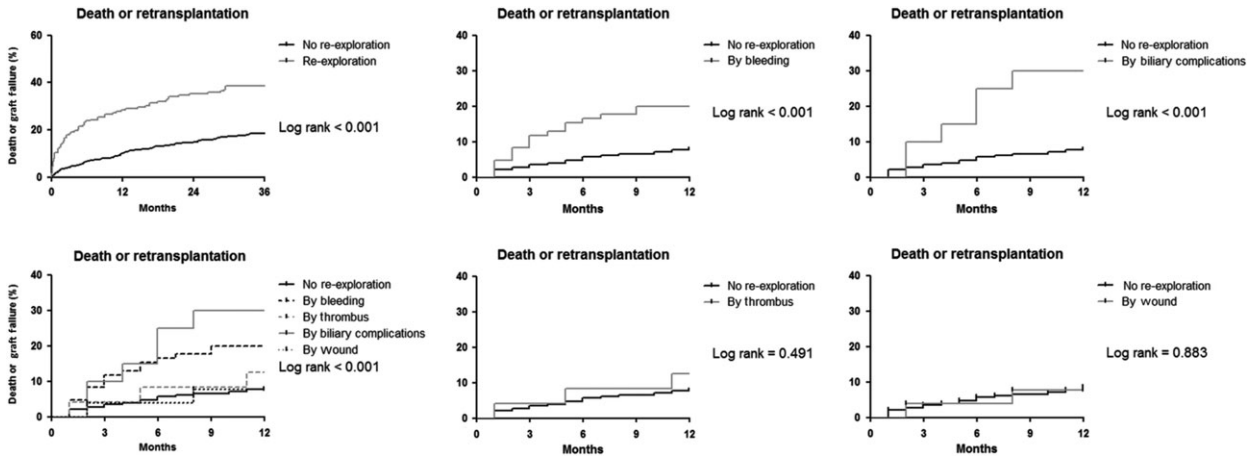

Figure 4 Survival curves for overall re-exploration and re-exploration according to cause.

Table 4. Risk factors of overall re-exploration.

	Unadjusted analysis		Adjusted analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Recipient variables				
Age	1.00 (0.98–1.02)	0.78		
Male	0.87 (0.59–1.30)	0.5		
BMI	0.98 (0.94–1.03)	0.49		
Smoking	0.85 (0.59–1.22)	0.37		
Alcoholics	1.12 (0.80–1.58)	0.5		
Encephalopathy	0.66 (0.43–1.03)	0.07	0.48 (0.29–0.80)	0.004
Varix	0.68 (0.43–1.07)	0.1	0.65 (0.40–1.05)	0.08
Ascites	1.36 (0.9–2.04)	0.15	1.37 (0.95–1.98)	0.1
Hypertension	0.75 (0.43–1.30)	0.31		
Diabetes	0.90 (0.59–1.37)	0.62		
Tuberculosis	1.34 (0.65–2.74)	0.43		
Hepatoreanl syndrome	1.17 (0.58–2.38)	0.67		
Bacterial peritonitis	1.06 (0.62–1.82)	0.82		
MELD score	1.01 (1.0–1.03)	0.1		
Bilirubin	1.02 (1.0–1.03)	0.01	1.02 (1.00–1.03)	0.11
INR	1.09 (0.96–1.23)	0.2	1.11 (0.92–1.34)	0.27
Creatinine	1.05 (0.85–1.30)	0.66		
Albumin	0.94 (0.73–1.22)	0.65		
CTP score	1.03 (0.97–1.09)	0.38		
Preop ICU	1.14 (0.63–2.04)	0.67		
ICU days	1.0 (0.93–1.07)	0.89		
Ventilator care	1.36 (0.5–3.73)	0.55		
Pathology				
Alcohol-related	1.23 (0.72–2.09)	0.45		
Acute failure	0.90 (0.51–1.57)	0.7		
Hepatocellular carcinoma	1.41 (1.01–1.96)	0.04	1.49 (1.05–2.12)	0.03
HBV-related	0.83 (0.58–1.19)	0.31		
HCV-related	0.80 (0.40–1.60)	0.53		
Operative variables				
Duration, min	1.00 (1.00–1.00)	0.002	1.002 (1.001–1.004)	0.002
Estimated blood loss, ml	1.00 (1.00–1.00)	0.18		
Cold ischemia time, min	1.0 (1.0–1.01)	0.5		
Warm ischemia time, min	1.0 (0.99–1.01)	0.88		
RBC transfusion, unit	1.0 (0.96–1.05)	0.91		
Donor variables				
Age	0.99 (0.98–1.01)	0.36		
Male	0.85 (0.61–1.19)	0.34		
BMI	0.99 (0.94–1.04)	0.63		
Macrosteatosis	1.01 (0.99–1.04)	0.3		
Microsteatosis	1.01 (0.99–1.02)	0.54		
GRWR	0.74 (0.39–1.41)	0.36		
Operative duration, min	1.00 (1.00–1.00)	0.14	1.00 (1.00–1.00)	0.14
Estimated blood loss, ml	1.00 (1.00–1.00)	0.97		
Re-exploration	1.97 (0.61–6.36)	0.26		

BMI, body mass index; CTP, Child-Turcotte-Pugh score; GRWR, graft to recipient-body weight ratio; ICU, intensive care unit; INR, international normalized ratio; MELD, model for end-stage liver disease; RBC, red blood cell.

Values are *n* (%) or mean (±SD).

This study showed that re-exploration may be more highly associated with the clinical outcome of LRLT when caused by bleeding or biliary complications. Adverse outcomes of re-exploration caused by bleeding may be related to hemodynamic instability, hemostatic imbalance, and massive transfusion. Postoperative

Transplant International 2019; 32: 141–152

bleeding is a complication that is not only common, but also immediate and severe. Therefore, as mentioned in the Method section, our ICU management focuses on detecting postoperative bleeding during the first 48 h after LRLT. As non-surgical intervention is the primary choice for biliary complications after liver transplantation, it is likely that individuals requiring re-exploration have poorly controlled biliary complications by nonsurgical interventions. Poorly controlled biliary complications may even progress to biliary sepsis. In addition, biliary complications may suggest poor perfusion on surgical sites because vulnerable blood supply to the bile duct causes biliary complications [18].

In previous studies, the association between re-exploration and clinical outcome of LDLT showed conflicting results [5,6]. One of the strengths of this study is the large cohort of re-exploration recipients, which allowed us to perform separate analyses for each cause. We showed different results according to cause, which explains that inconsistent results among previous studies might be related to different distributions of causes. Risk factors of re-exploration after liver transplantation also differ from one another among previous studies [5,6,10,11,19]. In this study, operative duration and HCC were risk factors of re-exploration. Operative duration is highly associated with surgical complexity and was reported to be an independent risk factor of postoperative complications and longer hospital stay [20]. Underlying HCC may be related to previous treatment modalities such as surgical resection, transcatheter arterial chemoembolization, radiofrequency ablation, and radiation therapy; it is widely known that adhesions from previous surgeries or radiofrequency ablation cause major surgical difficulties [21].

Some of our results should be interpreted with clinical relevance. History of encephalopathy, which is a severe complication of end-stage liver disease, showed a statistically significant protective effect against re-exploration. This may be explained by the development of collateral circulation. Portosystemic collateral circulation is a consequence of portal hypertension, which also occurs with a progression of liver disease [22]. Although it is a sign of progression, the presence of collateral circulation may be a benefit in the technical aspects of the liver transplantation procedure that involves clamping of the hepatic circulatory system. Another explanation might be high mortality rate of the recipients with encephalopathy. Although recipients with encephalopathy showed a protective effect against re-exploration, a survival benefit was not observed in these recipients. In this context, our result might also be interpreted as a lower chance for re-exploration to treat postoperative complications in these recipients. However, a clear limitation exists regarding the results of risk factor analysis, because separate evaluations, according to cause, were not performed. There is a clear etiologic difference according to cause of re-exploration. For example, re-explorations caused by bleeding and thrombus have opposite etiologies. A future study with a larger number of participants in each group, may be necessary.

The limitations of this study are the nature of a retrospective study. Although variables were adjusted, unmeasured intraoperative variables could not be analyzed. Despite the exclusion of initial cases, advancements in surgical techniques and postoperative management during the 13 years of the study period, could also have biased the results. Another limitation is the different etiologies between causes of re-exploration, as mentioned above. We analyzed the association between re-exploration and outcomes according to cause, but the risk factors of re-exploration were analyzed only as an overall re-exploration. The results of this study do not suggest any measure to decrease re-exploration after LRLT. Despite these limitations, to our knowledge, this is the first study, analyzing re-exploration limited to LRLT.

Conclusions

The incidence of re-exploration after LRLT is 17.0%, which is similar to other types of liver transplantation. Re-exploration after LRLT is highly associated with adverse outcomes, especially those caused by bleeding or biliary complications. Risk factors of re-exploration need further investigation.

Authorship

JP: designed the study, prepared the data, wrote the statistical analysis plan, performed the analysis, interpreted the results and drafted and revised the manuscript. GSC: designed the study, prepared the data, wrote the statistical analysis plan, performed the analysis, interpreted the results and drafted and revised the manuscript. MSG: interpreted the results and revised the manuscript. JSK: interpreted the results and revised the manuscript. BH: contributed the data. SH: contributed to the statistical analysis plan, interpreted the results and revised the manuscript. JWJ, SKL, and JK: contributed the data, interpreted the results and revised the manuscript. GSK: designed the study, cowrote the statistical analysis plan, interpreted the results and revised the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Bleeding sites of re-explorations.

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