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Reoperative Complications after Primary Orthotopic Liver Transplantation: A Contemporary Single-Center Experience in the Post–Model for End-Stage Liver Disease Era

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BACKGROUND: Data on complications requiring reoperation after orthotopic liver transplantation (OLT) are limited. We sought to describe the spectrum of reoperative complications after OLT, evaluate the associations with graft and patient survival, and identify predictors of need for reoperation.

STUDY DESIGN: We retrospectively studied adult patients who underwent primary OLT at our institution from February 2002 to July 2012. The primary outcomes included occurrence of a reoperative complication. Secondary outcomes were graft and patient survival. Multivariable logistic regression analysis was used to model the associations of recipient, donor, and operative variables with reoperation.

RESULTS: Of 1,620 patients, 470 (29%) had complications requiring reoperation. The most common reoperative complication was bleeding (17.3%). Compared with patients not requiring reoperation, patients with reoperative complications had greater Model for End-Stage Liver Disease scores and need for pretransplantation hospitalization, mechanical ventilation, vasopressors, and renal replacement therapy; considerably longer cold and warm ischemia times and greater intraoperative blood transfusion requirements; and substantially worse 1-, 3-, and 5-year graft and patient survival rates. In multivariable analysis, predictors of reoperative complications included intraoperative transfusion of packed RBCs (odds ratio [OR] = 2.21; 95% CI, 1.91–2.56), donor length of hospitalization >8 days (OR = 1.87; 95% CI, 1.28–2.73), recipient pretransplantation mechanical ventilation (OR = 1.65; 95% CI, 1.21–2.24), cold ischemia time >9 hours (OR = 1.63; 95% CI, 1.23–2.17), warm ischemia time >55 minutes (OR = 1.58; 95% CI, 1.02–2.44), earlier major abdominal surgery (OR = 1.41; 95% CI, 1.03–1.92), and elevated donor serum sodium (OR = 1.17; 95% CI, 1.03–1.31).

CONCLUSIONS: Patients who require reoperation for complications after OLT have high pretransplantation acuity and inferior post-transplantation survival. We identified factors associated with reoperative complications to guide perioperative donor–recipient matching and improve outcomes. (J Am Coll Surg 2014;219:993–1000. © 2014 by the American College of Surgeons)

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Postoperative complications after orthotopic liver transplantation (OLT) are common and can be attributed to the illness acuity of recipients, technical demands of the operation, and quality of donor organs. Since the implementation of the Model for End-Stage Liver Disease (MELD) scoring system in February 2002, organs are allocated to the sickest patients in a geographic area,[1,2] and OLT is increasingly performed on high-acuity patients, who are at greater risk of postoperative

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Abbreviations and Acronyms

CIT = cold ischemia time
LOS = length of stay
MELD = Model for End-Stage Liver Disease
OLT = orthotopic liver transplantation
uPRBC = units packed RBCs
WIT = warm ischemia time

complications because of the severity of their liver disease.[2,3] Complications such as bleeding, biliary or vascular compromise, and intra-abdominal infection can require urgent reoperation to prevent early graft loss, long-term graft dysfunction, or mortality.[4,5]

Although the general surgery literature indicates that relaparotomy increases mortality,[6-8] data about reoperative complications after OLT are limited. Few series in the literature report reoperative complication rates ranging from 34% to 44% in the pre-MELD era[9,10] and 17% to 26% in the post-MELD era.[11] The effect of reoperation on patient and graft survival is not reported, and the perioperative factors that contribute to complications requiring reoperation are unknown. Identification of modifiable perioperative factors that predict reoperation can lead to improved post-transplantation outcomes.

The specific aims of this study were to describe the scope of reoperative complications after OLT; examine the effects of reoperation on patient and graft survival; and identify recipient, donor, and operative factors that are associated with reoperative complications after OLT in the post-MELD era.

METHODS

We retrospectively reviewed a prospectively maintained transplant database and identified all adult patients (age 18 years and older) who underwent primary OLT between February 2002 and July 2012 at the University of California, Los Angeles. Recipients who underwent liver retransplantation were excluded. The University of California, Los Angeles Institutional Review Board approved the study.

Recipient variables analyzed included age, sex, cause of liver disease, BMI, MELD score, presence of ascites, medical and surgical comorbidities, pretransplantation hospitalization status and post-transplantation length of hospital stay (LOS), and pretransplantation need for mechanical ventilation, vasopressor support, and renal replacement therapy. Medical comorbidities included hypertension, diabetes, and coronary artery disease. Coronary artery disease was defined as history of MI, earlier percutaneous or open revascularization, or nonocclusive coronary atherosclerosis detected on angiography. Surgical comorbidities included earlier abdominal operations, categorized as minor (eg, pelvic or gynecologic surgery, laparoscopic cholecystectomy, appendectomy, and inguinal or ventral hernia repairs) and major (any exploratory laparotomy, gastric, small or large intestinal operation, open cholecystectomy, and liver resection). Recipient LOS was calculated from the day of transplantation to the day of discharge from the hospital.

Donor variables included age; sex; serum sodium; LOS; and graft type, such as whole or split cadaveric heart-beating, non–heart-beating donation after cardiac death, and living donor grafts. Donor LOS was calculated from the day of hospital admission to the day of organ procurement. Operative variables included cold ischemia time (CIT), warm ischemia time (WIT), use of venovenous bypass, transfusion of units packed RBCs (uPRBC), and biliary reconstruction.

A reoperative complication was defined as a return to the operating room for relaparotomy within 30 days of transplantation or within the same hospital admission. Minor operations, such as tracheostomy, gastrostomy, and central venous access procedures, were excluded, as were operations not specifically related to the transplantation, such as inguinal hernia repairs. Indications for reoperation included bleeding, coagulopathy at initial transplantation requiring intra-abdominal packing with need for later relaparotomy and biliary reconstruction, infection, retransplantation, biliary and vascular complications, and other miscellaneous reasons. Multiple complications apparent at a single reoperation were counted individually to summarize all reoperative complications.

Statistical analysis

The 2 groups for all comparisons were patients with and without a reoperative complication. Continuous variables were compared using the Mann-Whitney U test and summarized as medians and interquartile ranges. Categorical variables were compared using chi-square or Fisher's exact tests and summarized as percentages. Patient and graft survival curves were computed using Kaplan-Meier methods and compared using log-rank tests. Multivariable logistic regression model was used to evaluate the associations of recipient, donor, and operative variables with risk of reoperation.

For descriptive statistics and bivariate comparisons, the numbers of patients with a given characteristic are reported. The percentages were calculated excluding patients with missing data for any given variable. Most variables had no missing data (recipient age, sex, coronary artery disease, pre-OLT hospitalization, LOS, diagnosis, and earlier abdominal surgery) or <5% missing data: hypertension (n = 58 [3.7%]), diabetes (n = 60 [3.8%]), ascites

(n = 53 [3.4%]), MELD (n = 47 [3.0%]), mechanical ventilation (n = 51 [3.3%]), vasopressors (n = 82 [5.3%]), renal replacement therapy (n = 73 [4.7%]), donor age (n = 2 [0.1%]), donor sex (n = 41 [2.6%]), graft type (n = 1 [0.1%]), CIT (n = 13 [0.8%]), WIT (n = 20 [1.3%]), venovenous bypass (n = 7 [0.4%]), uPRBC (n = 51 [3.3%]), and biliary reconstruction (n = 18 [1.1%]). Three variables had >5% missing data, including BMI (n = 164 [11.3%]), donor LOS (n = 129 [8.7%]), and donor serum sodium (n = 123 [8.2%]).

For the multivariable analysis, missing values were singly imputed by the Markov chain Monte Carlo method, allowing for arbitrary missing data patterns. Final models were selected using backwards stepwise search with $p < 0.25$ as the retention criterion and summarized as odds ratios (OR) and 95% CI. Goodness of fit was evaluated using the Hosmer–Lemeshow test. A p value of ≤ 0.05 was considered statistically significant.

RESULTS

During the study period, 1,620 adult patients underwent primary OLT. Median age was 55 years, and 64.8% were male. Hepatitis C virus was the most common indication for OLT (45.7%), followed by alcoholic liver disease (13.1%) and nonalcoholic steatohepatitis (8.7%). Median follow-up time was 3.4 years.

Recipient characteristics and pretransplantation acuity

Baseline recipient characteristics and pretransplantation acuity are shown in Tables 1 and 2. Compared with recipients not requiring reoperation, patients with reoperative complications were significantly more likely to have ascites (53.5% vs 42.6%; $p < 0.01$), earlier major abdominal operations (19.8% vs 13.2%; $p < 0.01$), greater MELD scores (33 vs 27; $p < 0.01$), and to require pretransplantation hospitalization (53.6% vs 42.7%; $p < 0.01$), mechanical ventilation (26.7% vs 14.6%; $p < 0.01$), vasopressors (15.2% vs 7.9%; $p < 0.01$), and renal replacement therapy (37.4% vs 25.9%; $p < 0.01$). There were no significant differences in age, sex, BMI, medical comorbidities, cause of liver disease, or pre-OLT LOS among the groups.

Donor and operative characteristics

Donor and operative characteristics are shown in Table 3. Compared with patients without reoperative complications, recipients requiring reoperation had significantly

Table 1. Comparison of Pretransplantation Recipient Characteristics in Patients With and Without Reoperative Complications

Variable	All patients (n = 1,620)	Reoperation (n = 470)	No reoperation (n = 1,150)	p Value
Demographics				
Age, y, median (IQR)	55 (49–61)	55 (49–61)	55 (49–62)	0.18
Sex, male, n (%)	1,050 (64.8)	315 (67.0)	735 (63.9)	0.25
Comorbidities				
BMI, kg/m^2, median (IQR)	27.4 (24.5–31.4)	28.1 (25.0–31.5)	27.3 (24.3–31.4)	0.09
Hypertension, n (%)	445 (28.5)	135 (29.9)	310 (27.9)	0.42
Diabetes, n (%)	392 (25.1)	124 (27.6)	268 (24.1)	0.18
Coronary artery disease, n (%)	93 (5.7)	33 (7.0)	60 (5.2)	0.16
Ascites, n (%)	717 (45.8)	243 (53.5)	474 (42.6)	<0.01
Earlier abdominal operation, n (%)				
None	853 (52.7)	234 (49.8)	619 (53.8)	<0.01*
Minor	522 (32.2)	143 (30.4)	379 (33.0)	
Major	245 (15.1)	93 (19.8)	152 (13.2)	
Cause of liver disease, n (%)				
HCV	741 (45.7)	204 (43.4)	537 (46.7)	0.66*
ALD	212 (13.1)	65 (13.8)	147 (12.8)	
NASH	141 (8.7)	46 (9.8)	95 (8.3)	
HBV	138 (8.5)	35 (7.4)	102 (8.9)	
Acute liver failure	105 (6.5)	36 (7.7)	69 (6.0)	
PBC/PSC	91 (5.6)	23 (4.9)	68 (5.9)	
Other	193 (11.9)	61 (13.0)	132 (11.5)	

*Mutually exclusive groups, overall p value derived from chi-square test.
ALD, alcoholic liver disease; HBV, hepatitis B virus; HCV, hepatitis C virus; IQR, interquartile range; NASH, nonalcoholic steatohepatitis; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis.

Table 2. Comparison of Pretransplantation Acuity in Patients With and Without Reoperative Complications

Variable	All patients (n = 1,620)	Reoperation (n = 470)	No reoperation (n = 1,150)	p Value
MELD, median (IQR)	29 (15–38)	33 (19–40)	27 (14–37)	<0.01
Hospitalized, n (%)	743 (45.9)	252 (53.6)	491 (42.7)	<0.01
Pre-OLT LOS, days, median (IQR)	11 (5–21)	12 (5–12)	11 (5–21)	0.45
Mechanical ventilation, n (%)	284 (18.1)	121 (26.7)	163 (14.6)	<0.01
Vasopressors, n (%)	154 (10.0)	68 (15.2)	86 (7.9)	<0.01
RRT, n (%)	452 (29.2)	168 (37.4)	284 (25.9)	<0.01

IQR, interquartile range; LOS, length of hospital stay; MELD, model for end-stage liver disease; OLT, orthotopic liver transplantation; RRT, renal replacement therapy.

longer cold (418 minutes vs 387 minutes; $p = 0.01$) and warm (41 minutes vs 40 minutes; $p < 0.01$) ischemia times, greater blood transfusion requirements (16 uPRBC vs 10 uPRBC; $p < 0.01$), and more frequent use of venovenous bypass (47.8% vs 32.9%; $p < 0.01$) and biliary reconstruction with a T tube (51.2% vs 44.0%; $p < 0.01$). There were no significant differences in donor age, sex, serum sodium, LOS, or graft type.

Reoperative complications

Of the 1,620 patients, 470 (29.0%) had complications requiring reoperation, with a single reoperation in 321 (19.8%) and multiple reoperations in 149 (9.2%). Median time to reoperation was 2 days. Specific reoperative complications are shown in Table 4. The most common complication was bleeding (17.3%), followed by delayed biliary reconstruction in recipients who required intra-abdominal packing due to coagulopathy at the initial transplantation (6.2%), retransplantation for early graft failure (5.2%), biliary complications (4.1%), intra-abdominal infection (4.0%), and concern for vascular compromise (2.3%). Thirty-eight recipients were explored for vascular compromise; 13 had hepatic artery thrombosis, 7 had portal vein thrombosis, and 2 had vena cava thrombosis. No vascular complications were found in the remaining 16 patients. Other miscellaneous complications required reoperation in 33 patients (2%) for graft dysfunction or compression (n = 16), wound complications (n = 11), and bowel obstruction (n = 6).

Graft and patient survival

Kaplan-Meier graft and patient survival estimates are shown in Figure 1. Compared with recipients not requiring reoperation, patients with reoperative complications had significantly inferior 1-, 3-, and 5-year graft survival rates (63%, 55%, 52% vs 87%, 76%, 72%; $p < 0.001$) and patient survival rates (74%, 66%, 63% vs 88%, 75%, 73%; $p < 0.001$). Recipients requiring multiple reoperations had significantly inferior 1-, 3-, and 5-year graft survival rates (42%, 36%, 34% vs 74%,

Table 3. Comparison of Donor and Operative Characteristics in Patients With and Without Reoperative Complications

Variable	All patients (n = 1,620)	Reoperation (n = 470)	No reoperation (n = 1,150)	p Value
Donor characteristics				
Age, y, median (IQR)	41.8 (25.0–53.0)	41 (24–52)	42 (25–53)	0.14
Sex, male, n (%)	989 (62.6)	282 (61.3)	707 (63.2)	0.49
Sodium, mEq/L, median (IQR)	149 (142–155)	149 (143–156)	148 (142–155)	0.22
LOS, d, median (IQR)	3.0 (2.0–5.0)	4 (2–6)	3 (2–5)	0.09
Nonstandard donor,* n (%)	159 (9.8)	49 (10.4)	110 (9.6)	0.65
Operative characteristics				
CIT, min, median (IQR)	397 (293–508)	418 (302–530)	387 (289–500)	0.01
WIT, min, median (IQR)	40 (35–45)	41 (36–48)	40 (35–45)	<0.01
Venovenous bypass, n (%)	600 (37.2)	224 (47.8)	376 (32.9)	<0.01
Transfusion, U, median (IQR)	11 (7–18)	16 (10–27)	10 (6–15)	<0.01
Biliary reconstruction, n (%)				
Choledochocholedochostomy	1512 (94.1)	435 (93.5)	1077 (94.3)	0.56
Roux-en-Y choledochojejunostomy	95 (5.9)	30 (6.5)	65 (5.7)	0.56
T tube	740 (46.0)	238 (51.2)	502 (44.0)	<0.01

*Nonstandard donor includes non–heart-beating cadaveric donor, cadaveric split, or living donor.
CIT, cold ischemia time; IQR, interquartile range; LOS, length of stay; WIT, warm ischemia time.

Table 4. Reoperative Complications after Primary Liver Transplantation in 1,620 Patients from 2002 to 2012

Reoperative complications	
Total patients, n	1,620
Any reoperative complication, n (%)	470 (29.0)
Single reoperation	321 (19.8)
Multiple reoperations	149 (9.2)
Reoperations, median (IQR)	2 (2−3)
Time to first reoperation, d, median (IQR)	2 (1−7)
Specific complications, n (%)	
Bleeding	281 (17.3)
Coagulopathy requiring packing	100 (6.2)
Retransplantation	84 (5.2)
Biliary anastomotic complication	67 (4.1)
Revised with T tube	44 (2.7)
Revised with Roux-en-Y choledochojejunostomy	23 (1.4)
Intra-abdominal infection	65 (4.0)
Vascular compromise	38 (2.3)
Hepatic artery thrombosis	13 (0.8)
Portal vein thrombosis	7 (0.4)
Vena cava thrombosis	2 (0.1)
Negative exploration	16 (1.0)
Other	33 (2.0)

IQR, interquartile range.

64%, 61%; $p < 0.001$) and patient survival rates (60%, 53%, 52% vs 80%, 72%, 68%; $p < 0.001$) compared with recipients requiring a single reoperation (Fig. 2). Among patients with a single reoperative complication, patient survival was worse for recipients with biliary or infectious complications compared with bleeding complications. Recipients with a single reoperative bleeding complication had survival rates similar to patients not requiring reoperation (Fig. 3).

Multivariable logistic regression analysis of reoperative complications

Multivariable logistic regression analysis identified 7 significant factors associated with reoperative complications after OLT (Table 5). These included operative transfusion of uPRBC (OR = 2.21 per log SD increase; 95% CI, 1.91−2.56; $p < 0.01$), donor LOS >8 days (OR = 1.87; 95% CI, 1.28−2.73; $p < 0.01$), recipient pretransplantation mechanical ventilation (OR = 1.65; 95% CI, 1.21−2.24; $p < 0.01$), CIT >9 hours (OR = 1.63; 95% CI, 1.23−2.17; $p < 0.01$), WIT >55 minutes (OR = 1.58; 95% CI, 1.02−2.44; $p = 0.04$), earlier major abdominal surgery (OR = 1.41; 95% CI, 1.03−1.92; $p = 0.03$), and donor serum sodium (OR = 1.17 per SD increase; 95% CI, 1.03−1.31; $p = 0.01$). Our model

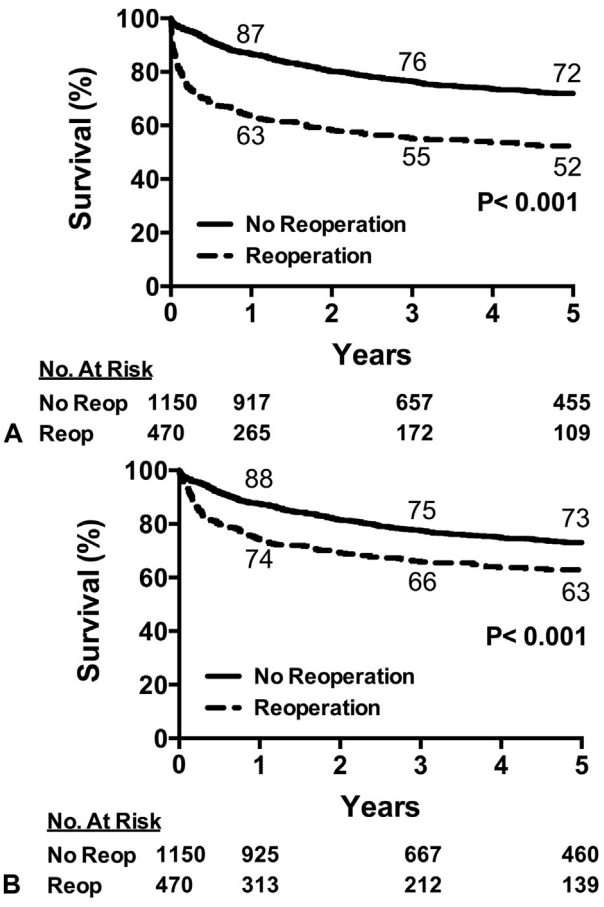

Figure 1. (A) Kaplan-Meier graft and (B) patient survival curves with 1-, 3-, and 5-year estimates comparing recipients with and without reoperative complications.

fit well with the data (Hosmer−Lemeshow goodness of fit p value = 0.42).

DISCUSSION

Data on post−liver transplantation complications specifically requiring reoperation are scarce, with few studies reporting on pre-MELD era cohorts[4,9,10] or limited by sample size.[11-13] Although many large series have reported the overall rates of postoperative graft nonfunction; vascular thromboses; and biliary, infectious, and hemorrhagic complications,[5,11,12,14-19] neither the specific management nor the effects of these complications on graft and patient survival are described.

This study represents the largest contemporary single-center experience to report the scope of reoperative complications after primary liver transplantation and their associations with graft and patient outcomes. We have identified potentially modifiable factors associated with risk of reoperative complications. The nearly 30%

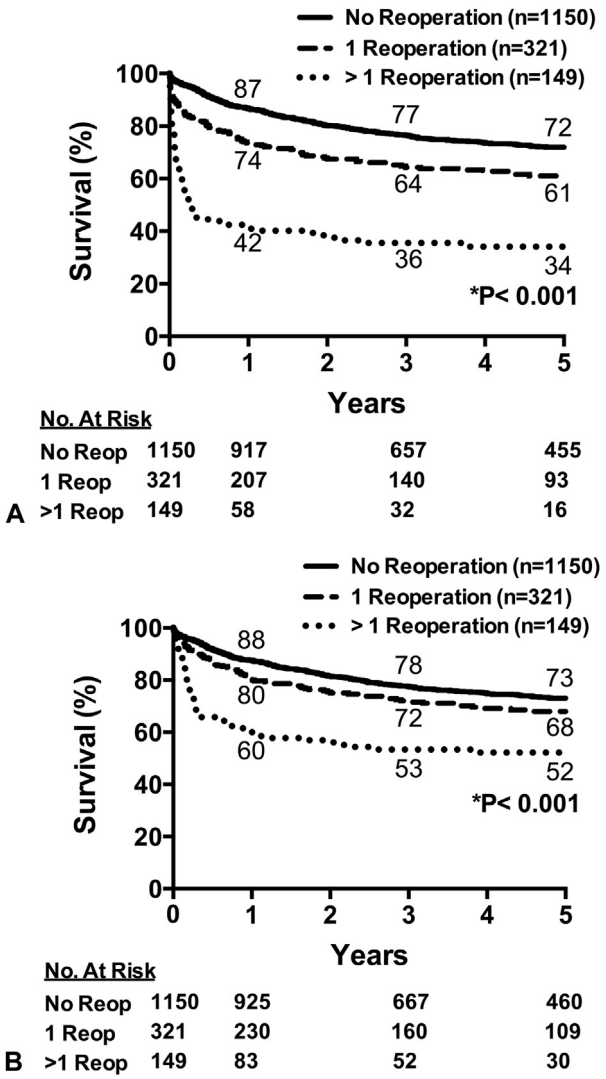

Figure 2. (A) Kaplan-Meier graft and (B) patient survival curves with 1-, 3-, and 5-year estimates comparing recipients based on number of reoperative complications. *Overall log-rank test.

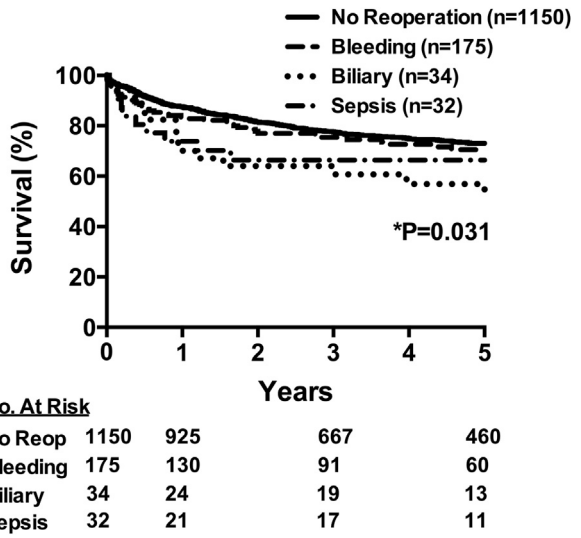

Figure 3. Kaplan-Meier patient survival curves with 1-, 3-, and 5-year estimates comparing indications for reoperation among recipients requiring a single reoperation. *Overall log-rank test.

reoperative complication rate in our series is comparable with other pre-MELD (34% to 44%)[9,10] and post-MELD (17% to 26%) era series.[11] Intra-abdominal bleeding was the most common indication for reoperation (17.3%), followed by delayed biliary reconstruction in recipients who required intra-abdominal packing due to coagulopathy at the initial transplantation (6.2%), retransplantation for early graft failure (5.2%), biliary complications (4.1%), intra-abdominal infection (4.0%), and concern for vascular compromise (2.3%).

Recipients requiring reoperation had significantly greater illness acuity compared with patients not requiring reoperation, with greater MELD scores and need for hospitalization, mechanical ventilation, vasopressors, and renal replacement therapy before transplantation. Compounding their critical illness, >50% of recipients requiring reoperation had ascites at the time of transplantation, and nearly 20% had a history of earlier major abdominal surgery. Peritonitis from ascites and adhesions from earlier surgery increase the difficulty of dissection and bleeding during the initial transplantation, which explains, in part, the more frequent use of venovenous bypass, longer CIT and WIT, and larger transfusion requirements in the recipients who ultimately had reoperative complications. The literature has shown that a large intraoperative transfusion requirement is an important determinant of reoperative intervention and mortality.[10,20,21]

A major objective of this study was to evaluate the association of reoperative complications with post-transplantation outcomes. The number of reoperations affected graft and patient survival considerably, with inferior 1-, 3-, and 5-year graft and patient survival rates in recipients with multiple reoperative complications compared with recipients with a single or no reoperative complication. Among recipients with a single reoperative complication, the indication for reoperation was significantly associated with outcomes; survival rate was inferior for recipients with a biliary or infectious reoperative complication compared with those not requiring reoperation or re-explored for hemorrhagic complications.

In contrast to earlier reports,[10,12] a single reoperation for bleeding did not impair graft or patient survival in our study. We believe that our approach to the management of post-transplantation bleeding has mitigated the

Table 5. Results of Multivariable Logistic Regression Analysis for Predictors of Reoperative Complications in 1,620 Patients Undergoing Primary Orthotopic Liver Transplantation

Variable	OR	95% CI	p Value
Transfusion uPRBC (per log SD)	2.21	1.91−2.56	<0.01
Donor LOS >8 days	1.87	1.28−2.73	<0.01
Pretransplantation mechanical ventilation	1.65	1.21−2.24	<0.01
CIT >9 hours	1.63	1.23−2.17	<0.01
WIT >55 minutes	1.58	1.02−2.44	0.04
Earlier major abdominal operation*	1.41	1.03−1.92	0.03
Donor serum sodium (per SD)	1.17	1.03−1.31	0.01
Recipient CAD	1.39	0.86−2.23	0.18
Donor sex, female	1.22	0.96−1.56	0.10

*Reference group includes no earlier and minor earlier abdominal operations.
CAD, coronary artery disease; CIT, cold ischemia time; LOS, length of stay; MELD, Model for End-Stage Liver Disease; OR, odds ratio; uPRBC, units packed RBCs; WIT, warm ischemia time.

negative impact of reoperation for this indication. All post-transplantation patients are closely monitored in an ICU, with liberal transfusion of platelets, cryoprecipitate, and fresh frozen plasma to correct the coagulopathy often found in critically ill recipients in the early post-transplantation period. Patients are returned to the operating room immediately for signs of substantial bleeding. Even in hemodynamically stable patients, the requirement of 6 uPRBCs in the first 24 to 48 hours prompts early reoperation, limiting the accumulation of substantial intra-abdominal blood that can lead to detrimental graft compression, liver infarcts, vascular thrombosis, and infected hematomas.

Finally, we analyzed perioperative factors that might predict reoperative complications as a step toward improving outcomes. Similar to earlier reports,[10,20] intraoperative transfusion requirement was the most important predictor of reoperative complications after OLT, with other important predictors, including recipient factors (pretransplantation mechanical ventilation, earlier major abdominal operation), donor quality (donor LOS, serum sodium), and operative factors (CIT, WIT). Although it might be impossible to modify each factor individually, recipient−donor matching might allow collective modification of the overall risk of reoperative complications. For example, a high-acuity recipient on mechanical ventilation in the ICU with earlier major abdominal surgery ideally should receive a low-risk donor organ (eg, lower donor serum sodium and donor LOS <8 days) with minimization of CIT and WIT. Conversely, a high-risk donor organ, such as a steatotic liver with extended donor hospitalization and longer anticipated ischemia times, might be best suited for a low-risk recipient.[22]

The main limitation of this study is its retrospective, single-center design. Although variation in patient management over time is a potential bias in any retrospective study, we minimized this effect by limiting the analysis to post-MELD era recipients. Our high-acuity patient population with a median physiologic MELD score of 29 also represents a study group that is different from recipients with a lesser severity of illness in many modern centers. This initial examination of reoperative complications might inform a multicenter, prospective study to investigate strategies to reduce complications after OLT and mitigate futile outcomes.

CONCLUSIONS

We have reported the scope of reoperative complications after OLT in a contemporary post-MELD era cohort. The number of reoperations and indications for reoperation affect graft and patient survival rates substantially. We identify important, potentially modifiable factors associated with reoperative complications that can be used to optimize recipient−donor matching and improve post-transplantation outcomes.

Author Contributions

Study conception and design: DiNorcia, Lee, Hiatt, Busuttil, Agopian
Acquisition of data: DiNorcia, Lee, Harlander-Locke, Zarrinpar, Kaldas, Yersiz, Farmer, Busuttil, Agopian
Analysis and interpretation of data: DiNorcia, Lee, Hiatt, Agopian
Drafting of manuscript: DiNorcia, Lee, Hiatt, Busuttil, Agopian
Critical revision: DiNorcia, Lee, Harlander-Locke, Zarrinpar, Kaldas, Yersiz, Farmer, Hiatt, Busuttil, Agopian

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