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Liberal Use of Interposition Grafts for Arterial Reconstruction Is Safe and Effective in Adult Split Liver Transplantation

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Background. Split liver transplantation (SLT) addresses donor shortages by providing 2 partial grafts from a single donor liver. Arterial reconstruction using an interposition graft facilitates the use of split grafts with difficult recipient anatomy. Its use, however, remains controversial because of a reported increased risk of complications. **Methods.** A retrospective review of the prospectively maintained Australian National Liver Transplantation Unit database was performed. Donor, recipient, operative, and complications data for adults receiving an SLT between July 2002 and November 2019 were extracted. **Results.** Arterial reconstruction required an interposition graft in 46 of 155 patients. Overall graft and patient survival were not significantly different between the groups with 1-, 3-, and 5-y graft survivals of 82%, 77%, and 69% for those with interposition grafts and 86%, 79%, and 77% for those without interposition grafts, respectively ($P = 0.499$). There were more cut liver bile leaks in the interposition graft group (26% versus 9%, $P = 0.004$), but otherwise, no significant differences in the rate of biliary complications (39% versus 29% $P = 0.200$), hepatic artery thrombosis (7% versus 10%, $P = 0.545$), or hepatic artery stenosis (13% versus 10%, $P = 0.518$). **Conclusions.** Liberal use of interposition grafts for arterial reconstruction in SLT is safe and does not result in increased complications.

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INTRODUCTION

Split liver transplantation (SLT) involves division of a single donor liver into an extended right graft (ERG) for transplant into an adult recipient and a left lateral segment graft (LLSG) for a pediatric recipient with the goal of decreasing waiting lists and addressing donor shortages.[1] Using strict donor and recipient selection criteria, SLT has generally been found to have comparable graft and patient survival to whole liver transplants, albeit with an increase in postoperative complications, particularly relating to the biliary system.[2-4] Several groups have since broadened recipient selection criteria to include higher-risk patients with Model for End-Stage Liver Disease (MELD) score >35,[5,6] patients needing urgent transplant[7] or even patients requiring retransplantation,[8] with comparable outcomes to whole grafts.

The donor arterial trunk is usually kept with the LLSG for the pediatric recipient during the splitting procedure, and thus, the ERG intended for the adult recipient often has a short right hepatic artery for anastomosis.[9] This can necessitate arterial reconstruction using an interposition graft, which increases the number of anastomoses and reportedly increases the risk of complications including hepatic artery thrombosis (HAT).[10] Interposition grafts can also be required when there are no suitable recipient arteries because of anatomical variation, stenosis, thrombosis, intimal dissection, or atherosclerosis.[11] As such, this situation is more common in the setting of retransplantation. In this population, outcomes are mixed with some reporting excellent short- and long-term patency rates[12-15] and others finding an increased risk of HAT, as high as 10.4%.[16-18]

The use of interposition grafts in the setting of SLT has rarely been analyzed, although they are required in as many as 23% of patients.[10] Existing literature also suggests that the use of interposition grafts increases the risk of HAT in both

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SLT[19] and whole liver transplantation (WLT).[16-18] This does not seem to affect overall graft or patient survival but has led to hesitancy in the use of interposition grafts for arterial reconstruction.

Therefore, it is unclear whether the use of interposition grafts conveys a significantly increased risk of complication or has an effect on the overall patient and graft survival. Furthermore, the degree to which patients undergoing SLT can tolerate an increased risk of complication related to interposition graft reconstruction remains obscure, which has relevance to whether ERGs attained from SLT are suitable for use in retransplantation or other high-risk recipients. We analyzed our experience with SLT to determine whether the use of interposition grafts for arterial reconstruction can be performed with an equivalent risk and survival profile.

MATERIALS AND METHODS

SLT recipients were identified from a prospectively maintained database in the Australian National Liver Transplantation Unit at Royal Prince Alfred Hospital, Sydney, Australia. Adult patients who received an ERG between July 2002 and November 2019 were included. Retrospective review of medical records was performed and recipient, donor, operative, and complications data were extracted from the database. The coprimary endpoints were graft and overall patient survival and secondary endpoints were postoperative complications, including bile leak, biliary strictures, and HAT. This study was approved by the Sydney Local Health District Ethics Review Committee (Royal Prince Alfred Hospital Zone, Sydney, Australia; HREC/EXCOR/19-12).

Split Liver Transplantation Procedures

In Australia, SLT prioritizes the pediatric recipient such that when a donor becomes available, the decision is made to split the graft depending on the suitability for a pediatric recipient. Although all donors are considered, SLT is generally performed if the donor is young (age <50 y), nonobese, and hemodynamically stable. At our center, the remaining ERG is allocated by blood group, MELD score, and size compatibility to the most appropriate recipient on the waiting list that has been assessed as suitable for SLT. All adult recipients are assessed for suitability for split grafts at the time of listing, and decisions are made on a case-by-case basis without specific exclusion of recipients with urgent indications or a high MELD score. However, we generally do not use split grafts in cases of retransplantation.

Our routine is to use an in situ technique to divide the hepatic parenchyma along the line of the falciform ligament into an LLSG (segments 2 and 3) and an ERG (segments 1, 4A, 4B, 5–8). The recipient transplant procedure used a modified piggyback or bicaval technique, at the surgeon's discretion, and sequential reconstruction of the portal vein, hepatic artery, and bile duct.

Arterial reconstruction depended upon the available donor vessels with the main arterial trunk usually preserved with the LLSG for the pediatric recipient. As such, the donor right hepatic artery (RHA) was anastomosed to the recipient common hepatic artery or RHA directly using a fine polypropylene suture (Prolene, Ethicon, Somerville, NJ). If this was not possible because of lack of a suitable recipient vessel or a short donor artery, an interposition graft was used to lengthen the conduit on the back table (Figure 1A and C) and then anastomosed in vivo to the recipient hepatic artery (Figure 1B and D). Another indication to use an interposition graft was to make a challenging anastomosis easier and to compensate for inadequate donor vessel length or a significant size mismatch between recipient and donor vessels. Typically, donor iliac artery was the conduit of choice; however, donor inferior mesenteric artery was also used in our dataset. We have found that using interposition grafts liberally in this way makes technically challenging arterial anastomoses easier and we believe this improves the quality of the anastomoses and therefore reduces risk of complications for that patient.

A Doppler ultrasound was performed routinely on the first postoperative day in all patients. In recipients with an interposition graft, we routinely used long-term aspirin to improve arterial patency, but otherwise postoperative management was no different to those without an interposition graft. If a vascular complication was suspected, angiography or reexploration in theater was performed as appropriate. Hepatic artery stenosis was defined as a stenosis >70% detected on computed tomography angiography or digital subtraction angiography, as we have previously described.[20] Biliary complications included bile leaks, anastomotic leaks, anastomotic strictures, and nonanastomotic strictures. Strictures were only included if intervention was required, and those incidentally found on imaging were excluded. Routine postoperative biliary imaging was not performed. Highest grade morbidity per patient was classified using the Clavien-Dindo system.[21]

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics for Windows (Version 26; IBM Corp. Armonk, NY) and variables were analyzed using an independent samples *t* test, Mann-Whitney U test, or Pearson's chi-square test as appropriate. Kaplan-Meier survival curves were analyzed using the log-rank test. Results were considered significant if $P < 0.05$.

RESULTS

Patient Characteristics

During the study period, 1090 adult liver transplants were performed, of which 155 (14.2%) were SLT using an ERG. The median follow-up for the split grafts was 60 mo (interquartile range, 113). Arterial reconstruction was performed using an interposition graft in 46 of 155 (29.7%) patients and without an interposition graft in 105 of 155 (67.7%) patients (data for 4 patients not available). Recipient, donor, and operative factors for these patients are displayed in Table 1. The proportion of patients with a high MELD score (>15) was significantly lower in those who underwent an interposition graft reconstruction (55% versus 72%, $P = 0.036$). There were no other significant differences in donor or recipient characteristics between SLT recipients undergoing arterial reconstruction with versus without interposition graft. SLT with or without interposition graft overall was rarely used for urgent patients who were intensive care unit-bound (6.5% and 4.8%, respectively) but was used for retransplant on 3 occasions (twice with an interposition graft and once without). Cold ischemia time, warm ischemia time, and transfusion requirement were not significantly different between the 2 groups. However, the mean operative time required for reconstruction with an interposition graft was significantly

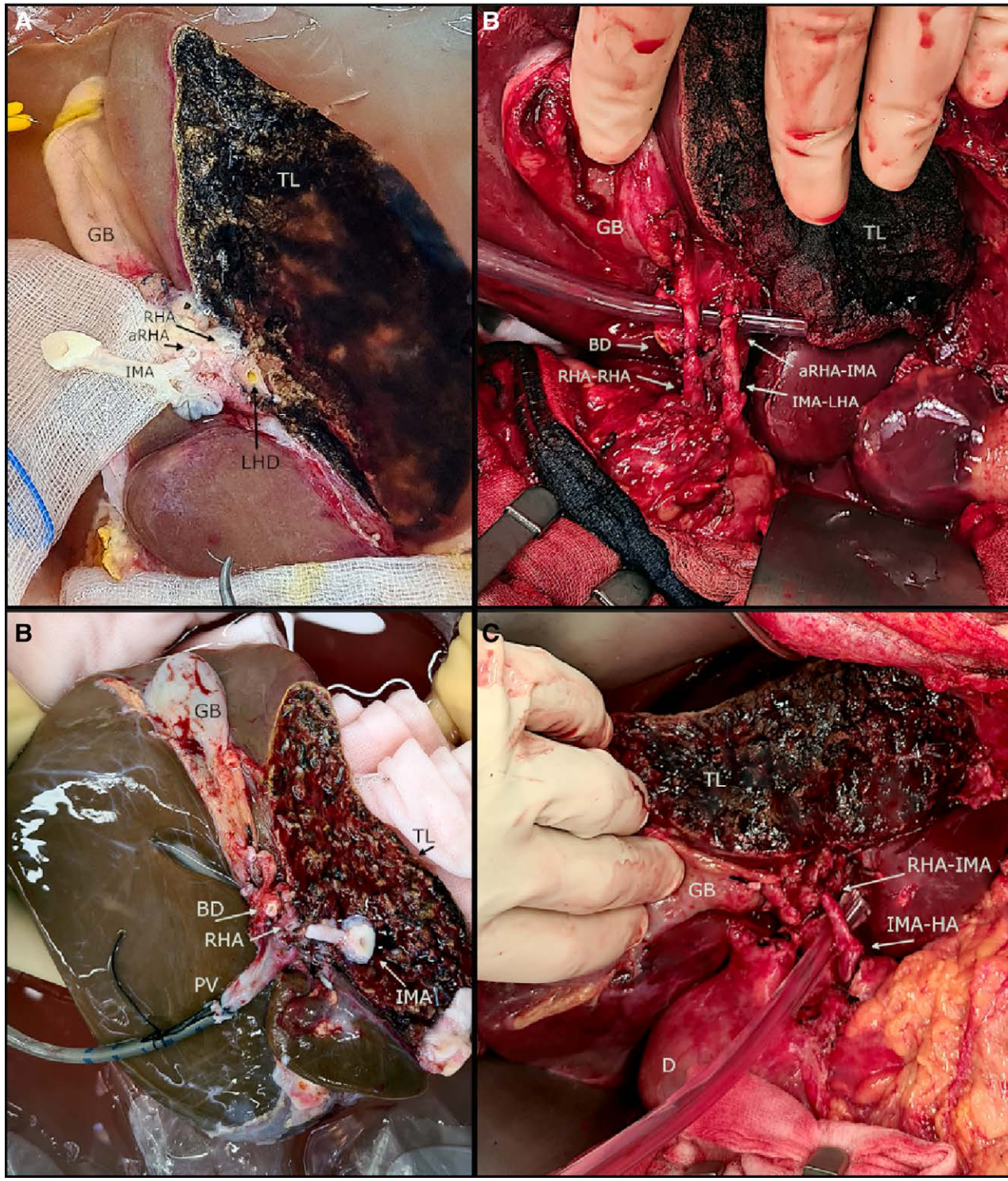

FIGURE 1. Donor IMA was used as an interposition graft to lengthen the donor hepatic artery during 2 split liver transplants, one in which the donor had a main RHA and an aRHA (A and B); and another in which the donor RHA was short (C and D). The IMA interposition graft was fashioned on the back table (A and C). In the donor with 2 RHAs, the main RHA was anastomosed directly to the recipient RHA and the aRHA was anastomosed to the recipient left hepatic artery using the IMA interposition graft (B). In the donor with the short RHA, the donor RHA was anastomosed to the recipient hepatic artery proper using the IMA interposition graft (D). Written consent was obtained for the use of these images. aRHA, accessory right hepatic artery; aRHA-IMA, donor accessory RHA to IMA interposition graft anastomosis; BD, donor main bile duct; D, duodenum; GB, gallbladder; HA, hepatic artery proper; IMA, donor inferior mesenteric artery; IMA-HA, IMA interposition graft to recipient HA anastomosis; IMA-LHA, IMA interposition graft to recipient LHA anastomosis; LHD, transected donor left hepatic duct; PV, portal vein; RHA, right hepatic artery; RHA-IMA, donor RHA to IMA interposition graft anastomosis; RHA-RHA, donor main RHA to recipient RHA anastomosis; TL, transected liver.

longer by 65 min (421 ± 217 versus 356 ± 107 min, $P = 0.015$), most likely related to the complexity of the recipient surgery necessitating an interposition graft.

Operative Details

In our series, the most common type of arterial reconstruction involved an anastomosis between the donor RHA to a recipient

TABLE 1.

Recipient, donor, and operative factors in patients undergoing split liver transplantation with and without interposition graft

		Arterial reconstruction with interposition graft (n = 46)	Arterial reconstruction without interposition graft (n = 105)	*P*
Recipient factors				
Age at transplant (mean ± S)		51.5 ± 11.2	51.4 ± 10.6	0.983
Sex, male (%)		27/46 (58.7%)	68/105 (64.8%)	0.478
BMI, median (IQR)		25.3 (5.2)	25.0 (5.1)	0.477
MELD score, mean ± SD		17 ± 8	19 ± 8	0.063
High MELD score (≥15)		24/44 (54.5%)	71/98 (72.4%)	0.036*
Indication for transplant	Alcohol	4/46 (8.7%)	13/105 (12.4%)	0.183
	Hepatitis B or C	15/46 (32.6%)	25/105 (23.8%)	
	HCC	14/46 (30.4%)	17/105 (16.2%)	
	PSC	2/46 (4.3%)	17/105 (16.2%)	
	NASH	1/46 (2.2%)	4/105 (3.8%)	
	PBC	0/46 (0%)	7/105 (6.7%)	
	Other	10/46 (21.7%)	22/105 (21.0%)	
Retransplant		2/46 (4.3%)	1/104 (1.0%)	0.220
Donor factors				
Age, mean ± SD		30.4 ± 10.2	33.0 ± 11.5	0.174
Sex (male, %)		24/46 (52.2%)	66/105 (62.9%)	0.218
BMI, median (IQR)		24.7 (4.9)	23.7 (5.0)	0.118
Cause of death	Trauma	18/46 (39.1%)	39/105 (37.1%)	0.913
	Cerebrovascular event	14/46 (30.4%)	41/105 (39.0%)	
	Cardiac arrest	1/35 (2.2%)	2/105 (1.9%)	
	Respiratory hypoxia	10/46 (21.7%)	17/105 (16.2%)	
	Other	3/46 (6.5%)	5/105 (4.8%)	
Donor risk index, median (IQR)		1.76 (0.43)	1.76 (0.38)	0.736
Donor recipient weight ratio, median (IQR)		0.97 (0.30)	1.07 (0.37)	0.099
Operative factors				
Urgency of transplant	1—ICU	3/46 (6.5%)	5/105 (4.8%)	0.875
	2—hospital bound	8/46 (17.4%)	14/105 (13.3%)	
	3—occasional inpatient	8/46 (17.4%)	19/105 (18.1%)	
	4—at home	27/46 (58.7%)	67/105 (63.8%)	
Cold ischemia time (min), median (IQR)		403 (201)	379 (206)	0.835
Warm ischemia time (min), median (IQR)		47.5 (15)	45 (19)	0.292
Packed cells, mean ± SD		6 ± 7	5 ± 6	0.364
Operative time (min), mean ± SD		421 ± 217	356 ± 107	0.015*

*$P < 0.05$.

BMI, body mass index; HCC, hepatocellular carcinoma; ICU, intensive care unit; IQR, interquartile range; MELD, model for end-stage liver disease; NASH, nonalcoholic steatohepatitis; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis.

common hepatic artery or RHA with 79 recipients (52.3%). Interposition grafts were used in 43 patients (28.5%) with single arteries. Eight patients had multiple arteries requiring anastomosis, either with an interposition graft (3 patients, 2.0%) or without an interposition graft (5 patients, 3.3%) (Table 2). The most common reason for needing an interposition graft was because of a short or small donor RHA (35 of 46, 76%), with the rest due to an inadequate recipient inflow artery (Table 2). The majority of interposition grafts were fashioned using donor iliac artery (42 patients, 91.3%); however, in 3 patients, the donor inferior mesenteric artery was used, and the donor splenic artery was used once. Biliary reconstruction was performed using a duct-to-duct anastomosis (interposition graft: 82.6%, no interposition graft: 84.8%) or a Roux-en-Y choledochojejunostomy (interposition graft: 17.4%, no interposition graft: 15.2%).

Outcomes

Graft survival and overall patient survival were similar in patients who underwent an interposition graft reconstruction and those who did not (log rank $P = 0.499$ and $P = 0.591$, respectively; Figure 2). Graft survival at 1, 3, and 5 y was 82%, 77%, and 69% for recipients in the interposition graft group versus 86%, 79%, and 77% for recipients who did not require an interposition graft, respectively. Overall patient survival at 1, 3, and 5 y was 85%, 80%, and 77% in recipients with an interposition graft versus 94%, 83%, and 81% for those in the noninterposition graft group, respectively. In total, there were 5 patient deaths <90 d post-SLT. Two of these occurred in patients who required an interposition graft for arterial reconstruction. One of these died from rupture of a splenic artery aneurysm and the other from neurological complications after delayed recognition of donor-derived ornithine transcarbamylase deficiency. Three other deaths occurred in patients who did not require an interposition graft from pneumonia, graft failure, and a cerebrovascular event.

Complications occurred in 67% of patients undergoing SLT with an interposition graft reconstruction versus 60% of patients undergoing SLT without an interposition graft

TABLE 2.

Technical details of arterial reconstruction

Reconstruction type	
Donor RHA to recipient CHA, RHA, or aorta	79 (52.3%)
Donor CHA to recipient CHA, RHA, or aorta	21 (13.9%)
Interposition graft, single artery	43 (28.5%)
Multiple hepatic arteries	5 (3.3%)
Multiple hepatic arteries with interposition graft	3 (2.0%)
Type of interposition graft	
Donor iliac artery	42 (91.3%)
Donor inferior mesenteric artery	3 (6.5%)
Donor splenic artery	1 (2.2%)
Indication for interposition graft	
Short or small donor hepatic artery	35 (76.1%)
Inadequate recipient inflow artery	11 (23.9%)

CHA, common hepatic artery; RHA, right hepatic artery.

reconstruction ($P = 0.388$; Table 3). Despite an era effect with an increase in the number of SLT between 2002–2010 and 2011–2019 due to increasing confidence with the technique (66 versus 89), there was no difference in the use of interposition grafts (19 of 62, 31% versus 27 of 89, 30%, $P = 0.968$) or the rate of surgical complications occurring <90 d between the time periods (35 of 66, 53%, versus 46 of 89, 51.7%, $P = 0.868$). Biliary complications were common but not significantly different overall between SLT recipients with or without an interposition graft reconstruction (18 of 46, 39% versus 30 of 105, 29%, $P = 0.200$). Further analysis of individual biliary complications showed that bile leaks from the cut liver edge were significantly more common in the interposition group compared with the noninterposition group (26 of 46, 26.1% versus 9 of 105, 9.6%, $P = 0.004$). There were no significant differences between the 2 groups with regard to other biliary complications (Table 3).

HAT was rare, occurring in 3 patients with an interposition graft (6.5%) and in 10 patients without an interposition graft (9.5%, $P = 0.545$). In the interposition group, one of the HATs occurred in a retransplant patient who died because of complications relating to the arterial thrombosis, whereas the other 2 required retransplantation for graft failure (at 15 d and 10 mo). In the group without interposition grafts, HAT was identified early in 6 patients and managed with thrombectomy and revision of the anastomosis. In 2 other patients, retransplant was required and the final 2 patients died because of unrelated complications (respiratory sepsis and hemorrhagic stroke). The rate of hepatic artery stenosis was also not significantly different between those with and without an interposition graft (6 of 46, 13% versus 10 of 105, 9.5%, $P = 0.518$).

DISCUSSION

In this study of 155 SLT recipients, interposition grafts were used in 29.7% of patients, which, as expected, is higher than the reported rates in WLT (range, 2%–16%).[12-18] This reflects the inherent challenges of SLT due to short and small donor arteries. This, however, is similar to rates in SLT reported in the literature (23%–36%).[10,19] The high rates of using interposition grafts in our study are likely due to our liberal policy of using interposition grafts to make challenging arterial anastomosis easier. By demonstrating an equivalent complications profile in this context, our results suggest that interposition grafts used in this way may not be as risky as previously described.[10,19]

This is one of only a few studies to assess in detail the effect of interposition graft arterial reconstruction on survival and outcomes in SLT. Based on studies in the WLT population, it has long been held that interposition grafts convey a significantly increased risk of HAT and therefore should be avoided whenever possible. Maggi et al attempted to address this question in a study of 28 in situ SLT. The authors found that there was an increased rate of HAT in the interposition graft group when compared with the WLT population (40% versus 18%).[19] In our study, the rate of HAT was 3 of 46 (6.5%) in the interposition graft group, which was similar to the standard reconstruction group at 10 of 105 (9.5%). This

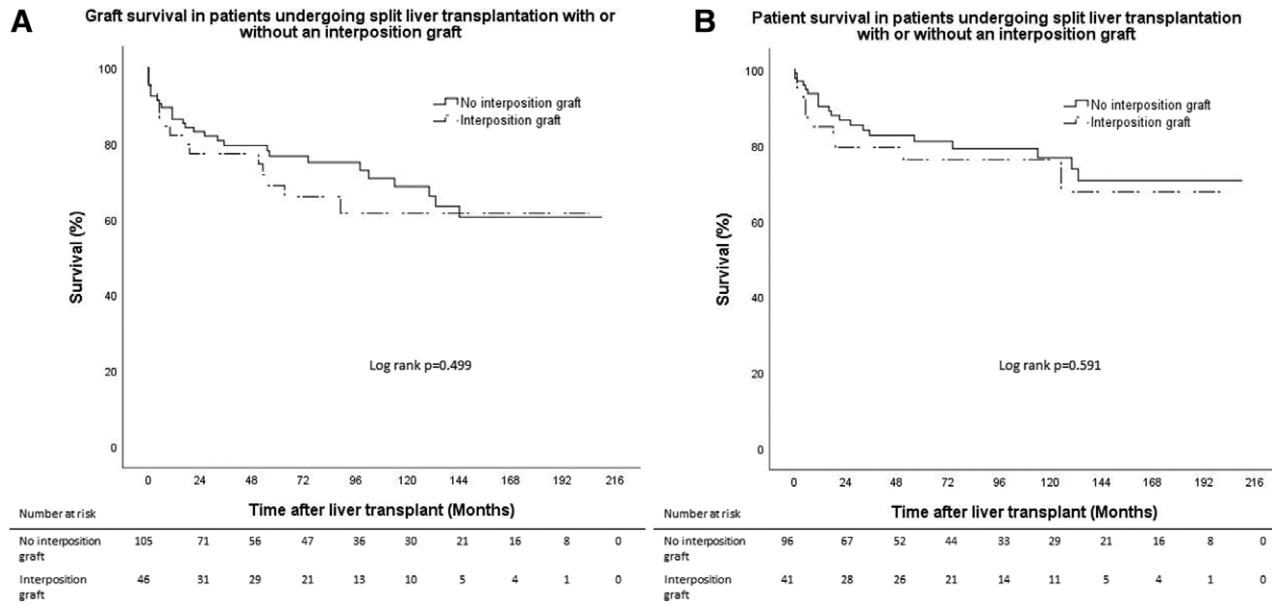

FIGURE 2. Graft survival (A) and patient (B) survival are not significantly different between those patients requiring an interposition graft and those not requiring an interposition graft during split liver transplantation (log rank $P = 0.499$ and $P = 0.591$, respectively).

TABLE 3.

Postoperative complications in patients undergoing split liver transplantation with and without interposition graft

		Arterial reconstruction with interposition graft (n = 46)	Arterial reconstruction without interposition graft (n = 105)	*P*
Any surgical complication		31/46 (67.4%)	63/105 (60.0%)	0.388
Biliary complication		18/46 (39.1%)	30/105 (28.6%)	0.200
Bile leak from cut edge		12/46 (26.1%)	9/105 (8.6%)	0.004*
Biliary anastomotic leak		5/46 (10.9%)	11/105 (10.5%)	0.942
Biliary anastomotic stricture		5/46 (13.0%)	17/105 (16.2%)	0.394
Biliary nonanastomotic stricture		0/46 (0%)	6/105 (5.7%)	0.098
Hepatic artery thrombosis		3/46 (6.5%)	10/105 (9.5%)	0.545
Hepatic artery stenosis		6/46 (13.0%)	10/105 (9.5%)	0.518
Portal vein thrombosis		2/46 (4.3%)	1/105 (1.0%)	0.220
Hepatic vein outflow obstruction		1/46 (2.2%)	2/105 (1.9%)	0.667
Primary nonfunction		1/46 (2.2%)	4/105 (3.8%)	0.517
Bleeding		3/46 (6.5%)	10/105 (9.5%)	0.399
Segmental ischemia		6/46 (13.0%)	14/105 (13.3%)	0.961
Infected collection		8/46 (17.4%)	14/105 (13.3%)	0.515
Wound complication		4/46 (8.7%)	11/105 (10.5%)	0.496
Most severe Clavien-Dindo grade <90 d	I	9/46 (19.6%)	14/105 (13.3%)	0.205
	II	8/46 (17.4%)	26/105 (24.8%)	
	IIIA	5/46 (10.9%)	3/105 (2.9%)	
	IIIB	9/46 (19.6%)	30/105 (28.6%)	
	IVA	2/46 (4.3%)	10/105 (9.5%)	
	IVB	2/46 (4.3%)	1/105 (1.0%)	
	V	2/46 (4.3%)	3/105 (2.9%)	
Pulmonary complication		9/46 (19.6%)	20/105 (19.0%)	0.941
Renal complication		8/46 (17.4%)	25/105 (23.8%)	0.380
Cardiac complication		5/46 (10.9%)	7/105 (6.7%)	0.283
DVT/PE		2/46 (4.3%)	4/105 (3.8%)	0.594
Mortality <90 d		2/46 (4.3%)	3/105 (2.9%)	0.483

*$P < 0.05$.

DVT/PE, deep vein thrombosis/pulmonary embolism.

could reflect our practice to use interposition grafts liberally to make technically challenging arterial anastomoses easier, which we believe improves the quality of the anastomoses and therefore reduces the complication rate. In our study, we have also been able to achieve equivalent long-term graft and patient survival in these groups, again supporting the use of interposition grafts in this way.

Biliary complications were again common in this study, which for the most part was accounted for by bile leakage from the cut liver edge. This is typically a minor complication but was significantly more common in the interposition graft group. The reason for this finding is not entirely clear, but we believe this relationship is a reflection of the recipient and donor factors specific to the patients that require an interposition graft rather than a complication of the graft itself. Specifically, recipients needing an interposition graft may have had small recipient or donor arteries, which may have resulted (despite an interposition graft) in sluggish arterial flow and therefore an increased risk of cut liver edge bile leak. Importantly, however, the rate of biliary stricture was not significantly greater in the interposition graft group, which is an indicator of long-term hepatic artery patency.

Another factor to consider is the choice of conduit. The most common conduit in our study and in the literature is donor iliac artery. This can result in difficulties with size mismatch with the donor RHA, making a "watertight" anastomosis without stenosis difficult to assure. Recently, we have also used donor inferior mesenteric artery for this purpose as we find the distal end has an excellent size match for the RHA and can be retrieved with a small aortic patch, ideal for the inflow side. To our knowledge, this is the first report of using donor inferior mesenteric artery for this purpose.

Interposition grafts are often required in retransplantation cases in which recipient vessel options are limited. In our study, only 3 patients were retransplant cases because of our general policy not to use split grafts in these situations. Two of these were acute retransplants for early graft failure, and the other was for chronic biliary strictures. Although our patient numbers are small, this raises the possibility of using split grafts at retransplantation, but consideration also needs to be given to other factors such as size adequacy, patient clinical urgency, and the need for a low-risk graft for a high-risk patient. This is reflected in our data, which showed that patients with a high MELD score were significantly less likely to have an interposition graft in our series, possibly because of perceived risk and avoidance of an additional anastomosis when possible. Overall, we recognize that a number of donor and recipient factors need to be considered apart from the technical aspects. In particular, there should be some distinction between recipients requiring urgent retransplant because of early graft failure and recipients with retransplants due to chronic complications or recurrent disease. Based on our data, we cannot draw firm conclusions about the use of interposition grafts and SLT for retransplants, but this may represent an area for future research.

The main limitation of this study is the retrospective design, with the decision to use an interposition graft left entirely

to the operating surgeon. There may be some selection bias with patients in the interposition graft group being inherently higher-risk due to the necessity for an interposition graft in the first place. The fact that despite this limitation, our data suggest no difference in overall patient or graft survival further lends weight to our conclusion that interposition grafts, when required, can be used safely in SLT. We also have no way of distinguishing those patients who required an interposition graft because of poor quality recipient vessels and those in whom it was performed somewhat "electively" to facilitate an easier arterial anastomosis. However, we believe this heterogeneity allows us to demonstrate that interposition grafts are safe across a range of situations and indications. Finally, our relatively small numbers mean that our study may be underpowered to detect small differences in endpoints between the groups. More research, ideally in a prospective or randomized manner, could address this limitation and expand our knowledge of the topic.

CONCLUSION

In conclusion, we have found that interposition grafts are a useful and occasionally necessary technique during SLT, and we would advocate for surgeons to not hesitate in using them when required. This technique can potentially facilitate expanding the applicability of SLT to include high-risk recipients and retransplantation, but other donor and recipient factors also need to be considered. Use of interposition grafts during SLT can make a technically challenging situation easier without compromising outcomes or rates of complications and should be considered during SLT for this purpose.

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