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When to Re-explore Recipients in LRLT?

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Abstract

Re-exploration is one of the surgical complications of living donor liver transplantations. Re-explorations are of two types planned and unplanned. Unplanned re-exploration does always mean poor prognosis to the patient outcome? Was the aim of our study? We analysed retrospectively prospectively maintained data from Jan 2011 to August 2013. Total number of transplants done was 793. Total number of re-explorations was 80 in 66 patients. Re-exploration rate was 10.08%. Total mortality in our series was 10.5%. Mortality in Re-exploration group was 45.45%. Of the group of patients re-explored patients re-explored for early haemorrhage had better outcomes compared to patients explored for other reasons. Re-explored patients are at higher risk of fungal infections. Patients with multiple bile ducts are at higher risk of re-explorations. Patients re-explored in the immediate post-operative period had better outcomes compared to patients re-explored late. Overall it is a poor prognostic indicator of surgical outcome in living donor liver transplantation.

Keywords: Re-exploration; Living related liver transplantation; Mortality; Bile leaks; Hepatic artery thrombosis; Portal vein thrombosis

Introduction

Liver transplantation is the gold standard treatment for decompensated chronic liver disease. DDLT is the surgery of choice in patients with liver failure. Scarcity of organ had left to the evolution of LDLT. LDLT was primarily done with left lobe grafts in children. Advancements in imaging, surgical technique and better post-operative care led to more and more of Right lobe adult LT being performed with equivalent patient and graft survival rates as that of DDLT with negligible donor morbidities. This study was aimed at analysing the impact of re-exploratory laparotomy on the outcomes in patient and graft survival [1-10].

Materials and Methods

During the 32 months between 1 Jan 2011 and 31 August 2013, 791 patients underwent 793 OLTx for end-stage liver disease at the Indraprasta Apollo Hospital by the same team of surgeons. Of these 793 procedures, 791 were the initial transplantations the other 2 were retransplants, consisting of 2 second (100%). There were no intraoperative deaths. Total mortality was 83 (10.46%- 6 month mortality). Records and charts of the patients were reviewed retrospectively to study postoperative surgical complications of re-explored patients. Re-explorations were defined as any surgical exploration done other than retransplantation.

Hepatic allografts were harvested from healthy liver donors after protocol evaluation. The grafts were preserved in HTK solution during the first 16 months and University of Wisconsin solution for the last 16 months. Benching was done to drain all the hepatic veins in the middle hepatic vein territory with the use of portal vein /hepatic vein/Dacron grafts harvested from the recipient liver after explanation. All efforts were made to drain all the segments of the graft liver [10-15]. Temporary portocaval shunt was made in all cases without major shunts to avoid bowel oedema and prevent haemodynamic instability. OLTx was performed in a standard manner with IVC clamping in almost all patients. Very few patients who did not tolerate cava cross clamping, implantation was done with side clamping of cava. Hepatic veins were reconstructed with 4-0 Prolene. Portal vein was reconstructed with 5-0 prolene. Hepatic arteries were reconstructed with 8-0 prolene in interrupted fashion. With the knots in inside out fashion. Methods of reconstruction of the biliary tract consisted of choledochocholedochostomy (97%), choledochojejunostomy in (3%). No cell saver was used intraoperative as there was risk of infection. Few recipients were extubated on table but majority of them were electively ventilated and extubated once the metabolic acidosis has corrected and the patient was completely responsive to commands. All patients were placed on prophylactic antibiotics and antifungal medications. Postoperative immunosuppression consisted of tacrolimus, mycophenolate and corticosteroids. Steroids were started from a hepatic phase of transplantation. Other drugs were started after 36 hrs. If the patient had no sepsis and urine output was adequate. Patients non tolerant to tacrolimus were switched over to cyclosporine. Dose adjustments were done according to serum levels and LFTs. Drains were removed once the drain output was low and LFT has normalised along with HIDA (Done on POD 10) evidence of no leak. Before discharge all recipients had protocol CT liver angiogram and CMV DNA levels. SPSS 17 was used for statistical analyses in this study.

Results

Total re-explorations were 80 in 66 patients (10.08%) Rate of re explorations in our series was 10.21%. Intra-abdominal sepsis was the leading cause followed by haemorrhage, hepatic artery complications and portal vein and hepatic vein complications. Mortality rate in the re-explored group was 50% compared to 10% mortality in other patients. Patients re-explored for bleeding fared better compared to

other group of patients. Re-explored patients were at higher risk of fungal sepsis. After initial experience later on most of the patients received upgraded fungal prophylaxis. Early re-exploration was associated with better survival. Multiple re-explorations had increased cumulative mortality (Tables 1 and 2).

No	Indication	Total	%
1	ALF	1	1.5
2	ACLF	15	22.72
3	HBV Related CLD	8	12.12
4	HCV Related CLD	18	27.27
5	Ethanolic CLD	15	22.72
6	Cryptogenic CLD	12	18.18
7	EHBA	4	6.06
8	others	8	12.12
9	Paediatric	7	10.6

Table 1: Indications for transplantations.

No	Indications	Total	Mortality
1	Bleeding	13 (16.25%)	06 (50%)
2	Intra-abdominal collections	14 (17.50%)	04 (50%)
3	Bile leak	15 (18.75%)	06 (40%)
4	Biliary stricture	03 (3.75%)	01 (33.33%)
5	Portal vein obstruction	11 (13.75%)	06 (54.54%)
6	Hepatic artery thrombosis	04 (5%)	02 (50%)
7	Bowel related complications	07 (8.75%)	03 (42.85%)
8	Retransplantation	02 (2.5%)	02 (100%)
9	HVOT	04 (5%)	03 (75%)
10	Burst abdomen	03 (3.75%)	00 (0%)
11	Delayed graft function	03 (3.75%)	03 (100%)
12	Intraabdominal sepsis	29 (36.25%)	10 (34.48%)

Table 2: Indications and outcomes for re-explorations.

Haemorrhage

12 patients underwent 13 explorations with 6 mortalities for combined intraluminal and extra luminal abdominal haemorrhage. One patient was re-explored twice for haemorrhagic drains; in both the instances no source of bleeder could be identified. 2 patients had bleeders at the jejunojejunostomy site. They were re-explored JJ anastomosis was undone and haemostasis achieved. One patient recovered well the other suffered HIE (hypoxic ischemic encephalopathy) and was on prolonged ventilation and died of multiorgan sepis after 60 days. Two patients had hepatic artery pseudoaneurysm rupture. One was secondary to bile leak. He presented with bleed through the external wound. CT angiography revealed pseudoaneurysm [16-20]. He was taken up for angioplasty but he had massive haemorrhage and haemodynamic instability leading to emergency laparotomy and ligation of hepatic artery. He expired. The other patient presented with vague abdominal pain and shock. He was also re-explored and found to have pseudo aneurysm bleed leading to ligation of the bleeder. He also died. One patient had cut surface bleeder which was managed by suture haemostasis and patient recovered well. Two patients had bleeders from the diaphragmatic surface which was managed by suture haemostasis. They recovered well. One patient had bleeders from splenic collaterals which was suture ligated. He later on died from bile leak and sepsis. Four patients had haemorrhagic drains in whom the source was found to be retroperitoneum. Haemostasis was achieved. One patient had HJ site haemorrhage presenting with fall in HB and melena. He was managed by Re-exploration and redo HJ recovered well (Table 3).

S. No	Source of bleeding	No
1	JJ site	2
2	Diaphragmatic bleeder	2
3	Cut surface bleeder	1
4	Retroperitoneal bleeder	4
5	Hepatic artery pseudo aneurysm bleed	2
6	Source not identified	4
7	Collateral bleeder	1
8	HJ site bleeder	1

Table 3: Source of bleeding.

Infection

Nine patients underwent 14 laparotomies with four mortalities. One patient was re-explored 3 times and another was re-explored 4 times. No source of sepsis could be identified. One was HCV, 3 cryptogenic and 5 ethanolics. All had multi-cloculated intraabdominal collections. In all patients multiple PCDs were tried. They underwent extensive peritoneal lavage and drainage. Four of them died due to fulminant fungal sepsis with mucor grown in the intraoperative cultures.

Operations upon the gastrointestinal tract

There were 7 Re-explorations on 5 patients, mortality occurred in 3 patients. One patient had introperative accidental antrotomy. He was managed by primary repair which leaked on POD5. He was re-explored and managed by Graham's repair again along with FJ. That again leaked which was managed by re-exploration and lavage and gastrojejunostomy and FJ take down. He continues to have low output gastric fistula. One patient was explored for intra-abdominal sepsis. He had inadvertent bowel perforation. It was picked up in the immediate post-operative period by means of enteric contents in the drain. Immediate re-exploration and ileostomy was done and he recovered well. One patient had enteric contents in the drain [21-26]. She was managed conservatively in view of low output fistula. Since it did not settle she was re-explored and found to have leak at a point beyond jejunostomy. It was repaired primarily. It leaked on POD 10 and the

child succumbed to sepsis. One patient presented with vague upper abdominal pain and no flow in the hepatic arteries. He was re-explored and found to have D1 perforation and HAT (Table 4). Perforation was repaired by graham's patch technique along with hepatic artery revascularisation. He recovered well from the insult but he later developed non anastomotic biliary stricture, sepsis and died. One patient had PNF, he was retransplanted. He had an episode of hypotension in the immediate post-operative period. 3 days later he had an episode of melena. He was re-explored and found to have gangrene of whole of small intestine and part of large intestine. Abdomen was closed without any intervention and he expired.

No	Site	No	Mortality
1	Small bowel perforation	2	1
2	Anastotomy leak	3	0
3	Small bowel gangrene	1	1
4	Duodenal perforation	1	1

Table 4: Intestinal sources for re-exploration.

Portal vein thrombosis

PVT Low flow status leading to obstruction or no flow in portal veins secondary to occlusion of the hepatic veins was seen in more patients. Portal vein thrombectomy, portal vein flow augmentation techniques. There were 11 laparotomies with 5 mortalities. 3 patients had isolated portal vein thrombectomy alone. No major shunts could be identified in them. Nor the looping of left renal vein augmented the portal flow. However all four patients had good portal flow post thrombectomy on intraoperative Doppler. These patients had poor graft function in the post op period had prolonged hospitalisation, sepsis, multi-organ failure and death. One patient had poor portal flow on CT and USG. But intraoperative portal flow was good and things settled uneventfully. However she had high ascites for long time which settled with diuretics. Two patients had partial PVT into op had PVT post op. both were HCV positive. Both of them recovered well after Re-exploration and left renal vein ligation [26-30]. One patient had portal flow augmentation with LHA which was unsuccessful, 2 patients had cavoportal hemi-transposition of which one died the other is surviving more than 24 months. One had intraoperative portal vein stenting. The patient is doing well (Table 5).

No	Intervention	No	Mortality
1	Portal vein thrombectomy	4	3
2	PVT+Shunt ligation	1	0
3	PVT+Left renal vein ligation	2	0
4	PVT+Arterioportal anastamosis	1	1
5	PVT+ intraoperative stenting	1	1
6	PVT+Cavoportal hemitransposition	2	1

Table 5: Portal vein flow augmentations.

Hepatic vein outflow obstruction

Two patients had documented HVOT on Doppler and CT and failed angiographic revascularisation. They were re-explored and re-vascularised. One was re-vascularised immediately (24 Hrs) had good graft recovery though died later on because of gram negative septicaemia. The other was re-explored after one week though the thrombectomy was successful and flow was re-established patient succumbed to late graft dysfunction and sepsis

Hepatic arterial exploration

4 patients were re-explored after failed intervention for HAT. One patient had to be eventually retransplanted but died. Two patients survived although recovery was slow. The other one had HAT secondary to duodenal perforation. The graft was well vascularised after re-exploration and thrombectomy but had prolonged hospitalisation and NAS and cholangitis and death (Table 6).

1	Thrombectomy	3	One died
2	Retransplantation	1	Died

Table 6: Hepatic arterial exploration.

Biliary obstruction

Three patients were re-explored for biliary stricture in the immediate post-operative period. One patient was a case of PSC. He had RYHJ he was in sepsis in the immediate post op period. USG was suggestive of IHBRD. He was re-explored and HJ was revised. He recovered well although after 6 months he had recurrent stricture which is presently being managed by PTBD and stentings. The other two had D-D anastomotic strictures. Both were re-explored and anastomosis revised one patient recovered well, the other succumbed to sepsis (Table 7).

S. No	Type	No	Outcome
1	HJ site stricture	1	Repeated PTBDs
2	DD anastomotic stricture	2	one mortality

Table 7: Biliary obstruction.

Biliary leak

15 laparotomies were done for bile leaks with mortality of 6 patients. 2 HJ leaks, one caudate duct leak, 2 cut surface leaks, of the 2 HJ leaks one had minor leak which settled with taking extra stitches , the other one had complete disruption and severe peritoneal contamination, the anastomosis was redone but it leaked again. Both the cut surface leaks settled after re-exploration and biliostasis. One caudate duct leak was picked up in the POD 1 and was repaired and bile leak settled though patient expired later on because of portal flow related complications. Of the 10 duct to duct anastomotic leaks 5 deaths. One was converted to HJ which structured later on, with the patient presently on PTBD + dilatations (Table 8).

1	Cut surface leak	2	0
2	HJ leak	2	0
3	Choledochodochostomy leak	10	5
4	Caudate duct leak	1	1 (non-biliary cause)

Table 8: Source of bile leak.

Discussion

Despite its introduction for paediatric patients nearly 20 years ago, the use of living donors for liver transplantation in adults has emerged more slowly. Interest in adult-to-adult LDLT increased as experience with the procedure grew in Japan and Korea, where deceased donor organs were not readily available. The increased use of split livers in the United States and Europe also contributed to the surgical skills needed to successfully perform the LDLT procedure. Unlike living donor kidney transplantation, where advantages of living donor over deceased donor grafts have been demonstrated in both recipient and graft survival, and where the safety of the donor operation has been documented, LDLT is still under a high level of scrutiny [30-33].

Our study was on the demographic profile of the re-explored patients to assess the indications and outcomes. The most important differences in post-transplant morbidity between recipients of LDLT and DDLT were seen in surgical complications. Biliary complications (especially biliary leak), vascular complications and unplanned Re-explorations were observed at higher frequencies in LDLT recipients. Other authors have noted higher biliary and vascular complication rates among LDLT recipients compared to historic DDLT controls. Possible explanations include the greater technical demands of LDLT, inferior quality of the LDLT graft and the caliber of LDLT donor vessels available for anastomosis. Possible explanations for the higher rate of biliary complications after LDLT (and proposed solutions) have been described. One study characterized preoperative and intraoperative findings that were associated with a higher rate of biliary complications. The level of experience with a procedure, especially one as complicated as LDLT, should be considered in analyses of outcomes. The inability to accurately assess the viability of biliary tissue at the time of anastomosis may contribute to this problem.

Many advances in LDLT have occurred over the last decade, but its exact place in the treatment armamentarium for patients with end-stage liver disease and liver cancer is still being defined. This study not only provided details on complications of liver transplantation but also defined complications that are more frequent in LDLT. Despite a higher rate of complications among LDLT recipients, complications requiring re-transplantation or leading to death were not significantly higher in LDLT once centres were experienced with the procedure. This finding, in concert with our previous conclusion that choosing LDLT over continuing on the waitlist leads to a survival advantage in experienced centres, underscores the impact of the learning curve on this highly technical procedure. Potential LDLT recipients need to hear about the rates of complications, and this study will help to define those rates. The decision to proceed, however, must be balanced against the possibility of deteriorating or dying while on the waitlist. As the practice of LDLT matures, it will be important to continually re-evaluate the morbidity associated with the operation and identify opportunities to improve its outcomes.

Conclusion

Re-exploration rate in our series was 10%. Mortality rate in our series was 50%. Commonest indication was intra-abdominal sepsis. Mortality was high in sepsis group of patients. Overall the re-exploration group of patients had high mortality rate compared to the non-re-explored group of patients. Early Re-explorations had better outcomes compared to late explorations. Re-explored patients had high incidence of fungal sepsis hence need to be placed on upgraded antifungals.

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