Original Article

A rising necessity: Liver retransplantation: A single center experience

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Abstract

Aim: Compared to primary liver transplantation, poor outcomes still remain an issue for liver retransplantation.

Materials and Methods: We used registry data from our liver transplantation unit to perform a retrospective cohort study on liver retransplantations performed between January 2012 and October 2019. We considered patients who underwent retransplantation at least one month after primary transplantation as the late group. Patients who had retransplantation within the first month after the first transplantation were considered the early group. We analyzed features of patients, indications, donor types, characteristics of operations, and outcomes.

Results: Among 782 patients who underwent liver transplantation, 29 patients underwent retransplantation in our center. Of these 29 patients, 19 patients were in the early group, while 10 patients were in the late group. The 3-year patient survival rates were 47.3% and 80% for the early and late groups, respectively. The overall 1-year survival rate for all retransplanted patients was 58.6%.

Conclusion: Despite better results reported for liver retransplantation, there are poor outcomes compared with primary transplantation, especially in the early group. However, the necessity of retransplantation increases every passing year in spite of a shortage of donors. Thus, the justification for liver retransplantation remains controversial.

Keywords: Deceased donor; liver graft failure; living donor

INTRODUCTION

In the last two decades, an increasing number of liver transplantations have led to the necessity of retransplantation (reLT), as expected. Various incidence rates for reLT have been reported and range between 5 and 22% (1). As in initial end-stage liver disease, reLT is the only treatment option for patients with failed grafts who are otherwise in a life-threatening situation. Since the first studies have been reported (2,3), the results of reLT have improved due to technical and medical advances, but the outcomes are still worse than in primary transplantation. The survival rates of retransplanted patients at 5 years vary from 47 to 67% in different studies (4).

The reason for reLT differs based on the time following the initial transplantation. Studies on reLT have had different definitions of early reLT, such as 30 days or 6 months after the first transplantation (1,5). The reasons detected most often for early reLT are primary non-function (PNF) and vascular complications like hepatic artery thrombosis (HAT). The recurrence of the primary disease, chronic rejection, and biliary complications are most often seen as causes of late reLT (6, 7). The decision to perform reLT depends on the surgical challenge of the operation and the shortage of donors, which leads to ethical problems (8). In this single-center study, we evaluated the causes, surgical features, and outcomes of patients who underwent early and late reLT.

MATERIALS and METHODS

This study was designed as a retrospective study and was approved by the local ethics committee (protocol number: 2019-20/12). The data of patients who underwent reLT between January 2012 and October 2019 were evaluated. Demographic and clinical features, surgical characteristics like operation time and blood loss, the reason for reLT, and outcomes were assessed and compared with the initial operation. The grafts for reLT were procured from both living and deceased donors.

The types of reLT were determined in regard to the time between primary transplantation and reLT. We considered patients who underwent reLT at least one month after the primary transplantation as the late group.

Patients who had reLT within the first month after the first transplantation were considered the early reLT group. The national criteria for early reLT indicate PNF if two of the following are present: AST>5000, INR>2.5, arterial lactate>twice the normal value, and/or HAT within the first seven days following transplantation.

Statistical Analysis

Descriptive statistics were stated as percentages for categorical variables, and mean ± standard deviation or median and range were used for continuous variables.

RESULTS

During the study period, 782 patients had liver transplantations, of which 29 patients underwent reLT in our center. The primary transplantations of six patients were in different centers, so the reLT ratio of our series was 2.9%. Of the 29 patients, 19 patients underwent early reLT, while 10 patients had late reLT. In the early reLT group, the mean interval was 6 days (2-11 days). Cirrhosis related to hepatitis B was the most common etiological factor for primary transplantation in this group (10/19 patients, 52.7%). In spite of this, PNF was the most frequent reason for early reLT (10 patients, 52.6%). The ratio of deceased/living donors for the first transplantation was 7/12 (36.8%/63.2%), but grafts were mostly procured from deceased donors in the early reLT group (84.2%). The clinical characteristics of the early reLT are shown in Table 1.

Table 1. Clinical characteristics of patients		
	Early group (n=19)	Late group (n=10)
Age (mean, years)	52.5 (24-70)	38.6 (1-56)
Gender (Female/Male)	9/10	3/7
MELD score	28±3	30±2
The interval (mean: min.-max.)	6 days (2-11)	2755 days (368-9808)
The etiology of first LT (3 patients had also HCC)	HBV:10 (52.7%)	PSC:4 (40%)
	Criptogenic:4 (21%)	HBV:2 (20%)
	AH:4 (21%)	HCV:2 (20%)
	Alcocholic:1 (5.3%)	AH:1 (10%)
		Biliary atresia:1 (10%)
The indication of reLT	PNF:10 (52.7%)	Recurrence of PSC:4 (40%)
	HAT:5 (26.3%)	Chronic rejection:3 (30%)
	PVT:3 (15.7%)	SBC:2 (20%)
	SFSS:1 (5.3%)	HCV recurrence: 1(10%)

HBV: Hepatitis B virus, HCC: Hepatocellular carcinoma, HCV: Hepatitis C virus, AH: Auto-immune hepatitis, PSC: primary sclerosing cholangitis, PNF: primary non function, HAT: hepatic artery thrombosis, PVT: portal vein thrombosis, SBC: secondary biliary cirrhosis, SFSS: small for size syndrome

During early reLT operations, standardized hepatic artery reconstruction was performed on 16 patients. Apart from this, the gastroepiploic artery was used to ensure arterial inflow in two patients, and the arterial patch of the coeliac trunk was anastomosed directly to the abdominal aorta. Portal vein inflow was provided by standard anastomosis between the portal vein of the graft and recipient except for one patient, who already had reno-portal anastomosis from the first transplantation.

Biliary anastomosis was applied between the graft's biliary tract and the recipient's choledoch in all patients. The mean operating times (OTs) were 500 minutes (420-660 minutes) and 274 minutes (180-420 minutes) for the initial transplantation and reLT in the early group, respectively. The mean perioperative blood loss (BL) was 1913 mL (110-3800 mL) and 836 mL (380-1900 mL) for the initial transplant and reLT in this group, respectively. The operative features of patients who underwent early reLT are shown in Table 2.

Table 2. Surgical features and outcomes		
	Early group (n=19)	Late group (n=10)
Type of graft in fir (Living/deceased)	12/7 (63.2% /36.8%)	5/5 (50% /50%)
Type of graft in reLT (Living/deceased)	3/16 (15.8%/ 84.2%)	4/6 (40%/60%)
reLT type		
Living donor-to-deceased donor	12 (63.2%)	3 (30%)
Deceased donor-to-deceased donor	4 (21%)	3 (30%)
Living donor-to-living donor	3 (15.8%)	2 (20%)
Deceased donor-to-living donor	-	2 (20%)
Operation time (mean: min.-max.)	274 min. (180-420)	531 min. (400-660)
Blood loss (mean: min.-max.)	836 mL (380-1900)	1850 mL (350-4600)
Portal vein anastomosis in reLT (anatomic/extra-anatomic)	18/1 (94.7% /5.3%)	Anatomic 100%
Hepatic artery anastomosis in reLT (anatomic/extra-anatomic)	16/3 (84.2% /36.8%)	8/2 (80% /20%)
Biliary anastomosis in reLT (standard/hepaticojejunostomy)	Standard 100%	3/7 (30% /70%)

In the late reLT group, the mean interval was 2755 days (368-9808 days). Auto-immune liver diseases like primary sclerosing cholangitis (PSC) and auto-immune hepatitis (AH) were the most frequent indications for the first transplantation in this group (5/10, 50%). Most patients in this group underwent reLT due to recurrence of the primary disease (5/10, 50%).

The type of donor was living donors for half of the patients (5, 50%) in the first transplantation. Also, 4 patients had living-donor reLTs (40%) in this group. The clinical characteristics of patients who underwent late reLT are shown in Table 1. Standardized hepatic artery anastomosis was established in 8 patients in this group, but hepatic artery inflow was provided by extra-anatomic anastomosis in two patients using gastroepiploic and splenic arteries. Portal vein anastomosis was routinely performed in all patients. Biliary reconstruction was applied through hepaticojejunostomy (HJ) in 7 patients, and the other three patients had biliary anastomosis between the choledochs of the graft and recipient.

The mean OTs was 589 minutes (490-720 minutes) and 531 minutes (400-660 minutes) for the first transplantation and reLT in this group, respectively. The mean BLs was 2060 mL (700-4200 mL) and 1850 mL (350-4600 mL) for the first transplant and reLT in this group, respectively. The operative features of patients who underwent late reLT are shown in Table 2.

In the early reLT group, 9 patients reached 3 years of survival (47.3 %). Among these patients, no patient experienced biliary or vascular complications, but 8 patients were lost within the first days following reLT. Seven of them died shortly after reLT due to sepsis. One other patient experienced serious vascular complications. This patient had complete portal vein thrombosis before the first liver transplantation, and renoportal anastomosis using the interpositional iliac vein graft was performed to provide portal inflow. However, the portal vein was thrombosed even with intrahepatic branches in the early postoperative period, and the graft was lost. Despite early reLT from a deceased donor, ensuring a sufficient portal inflow was not possible, and the patient was lost.

Another two patients were lost due to pneumonia and rupture of a cerebral aneurysm in the first six months following reLT. In brief, 10 patients died in the first year following reLT. Also, two patients experienced recurrence of hepatocellular carcinoma within 3 and 4 years after reLT and have lost their lives due to malignancy.

In the late reLT group, three patients experienced biliary complication following reLT. Biliary stent replacement via endoscopic retrograde cholangiopancreatography (ERCP) was successful in two patients for stenosis of biliary anastomosis. In a third patient, ERCP failed due to hepaticojejunostomy, and a biliary stent was placed via percutaneous transhepatic cholangiography (PTC) to overcome the problem of biliary leakage. In only one patient, we detected hepatic artery thrombosis following surgery. Following thrombectomy, it was necessary to use an interpositional saphenous vein graft between the graft's hepatic artery and the recipient's common hepatic artery due to intimal depredation.

Of the 10 patients who underwent late reLT, 2 patients were lost, and the mortality rate was 20%. One of them underwent living-donor reLT because of end-stage liver disease due to the recurrence of hepatitis C. Unfortunately; he experienced thrombosis involving the portal vein and hepatic artery following reLT. Postoperatively, the other patient was maintained in the intensive care unit for two months, but the patient was lost due to sepsis.

The outcomes of the early and late reLT patients are summarized in Table 3. The 3-year patient survival rates were 47.3% and 80% for the early and late reLT groups, respectively. The overall 1-year survival rate for all retransplanted patients was 58.6%. Unfortunately, the small sample size of reLT patients has prevented us from performing a statistical analysis between the early and late groups and between patients who underwent reLT and those who underwent standard liver transplantation.

Table 3. Outcomes of patients following reLT

	Early group (n=19)	Late group (n=10)
Vascular complications	2 (12.5%)	5 (50%)
Biliary stenosis, leakage	none	3 (30%)
Portal vein thrombosis	1	1
Hepatic artery thrombosis	1	2[#]
Mortality, total	12 (63.1%)	2 (20%)
Mortality in first month	8	2
Mortality in first year	2	None
Mortality after first year	2	None
Causes of mortality		
Sepsis	7	1
PVT/HAT	1	1
Pneumonia	1	
Cerebral aneurysm rupture	1	
HCC recurrence	2	

[#]: A patient who had portal vein thrombosis also had hepatic artery thrombosis
PVT: Portal vein thrombosis, HAT: Hepatic artery thrombosis, HCC: Hepatocellular carcinoma

DISCUSSION

Transplantation centers that mostly perform deceased-donor liver transplantation report the rates of reLT between 7 and 23% (9). In contrast, the rate of reLT was 2.9% in this study, which is similar to results reported from centers performing living-donor liver transplantation (LDLT). The number of the patients waiting for reLT is also limited (only 2 patients) in our series. Unfortunately, we lost four patients on the reLT waiting list. The scarcity of deceased donors is well known and still main problem in Eastern countries. We performed primary liver transplantation mostly from living donors, who were evaluated in detail and selected carefully. This might be a reason for the low indication of reLT like in other studies from Eastern countries (9,10).

The indications for reLT for the early and late groups in this study show similarity to the literature (11). Most of the centers that perform LDLT report low rates of PNF following LDLT (1,9). We also mostly perform LDLT (71.2%) in our institute. Although the rate of PNF was 52.7% for reLT in the early group, the proportion of PNF in all LDLTs was 1.6% (9/557) in this study.

The rate of HAT after LDLT was reported to be 2-5%. Published data demonstrated that HAT is responsible for 11.5–36.0% of all reLTs. In our series, 23 patients (4.1%) experienced HAT after LDLT, and in five patients, the problem was not overcome without reLT. Published data demonstrated that HAT is responsible for 11.5–36.0% of all reLTs. The most common reason for late reLT was recurrence of the disease and chronic rejection, as reported in the literature (8,10-13).

The timing of reLT has a significant effect on patient survival. The literature demonstrates a high mortality rate in early reLT groups compared with late groups. Marudanayagam et al. (13) reported that early reLT has poor outcomes within 7 days of the primary operation. Similarly, Chen et al.6 discussed the importance of the interval between the initial operation and reLT and reported that an interval of 8–30 days leads to a lower survival rate. But a nationwide analysis from Australia and New Zealand demonstrated no significant difference in graft or patient survival when comparing intervals of <7 days, 8–30 days, and >30 days (14).

In our early group, the patients who had the opportunity to have reLT >7 days of the first transplantation had significantly poor survival that was similar to previous reports (15). As mentioned before, there are strict criteria for PNF in Turkey, and it takes time to call for an urgent deceased donor. We also have a problem of scarcity of deceased donors. As a result, the clinical status of patients deteriorates.

Transplant surgeons have to face great challenges in reLT surgery. In early reLT, cases associated with HAT cause difficulty in providing arterial inflow. A long deceased donor artery is needed when hepatic artery of the recipient is inconvenient. We had to use the right gastroepiploic artery for arterial reconstruction in two patients who underwent living-donor reLT. Dissection of the conglomerated hilar structures and adhesions due to synthetic grafts are mostly used for venous reconstruction during LDLT and require great effort during surgery.

Hwang et al. (9) reported that living-donor late reLT is almost not practical. We successfully performed this type of late reLT with acceptable OTs and BL in two patients. Living-donor reLT still remains controversial in high-risk recipients. In this study, we performed living-donor reLT for seven patients (7/29, 24.1%). Beyond any doubt, it is truly problematic to justify living-donor reLT for deteriorated patients. In spite of considering limited healthcare resources, the decision must be individualized.

We have to use extended deceased-donor criteria to expand the donor pool. For this reason, procurement of unstandardized grafts from deceased donors is not rare in Turkey, especially for early reLT cases. Using extended criteria donor grafts for clinically unstable patients might be one important reason for the high mortality rate in our early reLT group, in which an emergency retransplantation was required.

LIMITATIONS

The main limitation of this study is its retrospective, single-centre design. The small sample size of the study group has not allowed performing a statistical compare. However, the outcomes of the study provide meaningful results for reLT.

CONCLUSION

Even today, the necessity of reLT is a debated issue. In addition to graft and patient survival, other ethical and financial factors must be considered. Without a doubt, the decision to perform reLT has to be made very carefully to limit the occurrence of ineffective transplantation.

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