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Comparison of short- and long-term outcomes after early *versus* late liver retransplantation: a single-center experience

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ABSTRACT

Background: As the survival of patients after liver transplantation (LT) improves, the requirement of liver retransplantation (reLT) for late graft failure has grown. Although some have reported that the short-term outcome of late reLT was comparable with that of early reLT, it remains unknown whether long-term survival of late reLT is inferior to that of early reLT patients.

Materials and methods: We reviewed early (<6 mo after primary LT) and late (≥6 mo after primary LT) reLT cases performed between January 2000 and December 2010.

Results: Sixteen early and 32 late reLT cases were analyzed. There was no significant difference regarding the number of units of red blood cells transfused during the transplantation between the groups, whereas operative time was significantly longer in the late reLT cases. Graft loss within 3 mo after early and late reLT was 18.6% and 15.6%, respectively. Patient and graft survival rates after 1, 3, 5, and 10 y in the late reLT group were 80.6%, 73.3%, 73.3%, and 67.7% and 80.7%, 69.1%, 63.3%, and 54.3%, respectively, whereas those in the early reLT group were 75.0%, 75.0%, 64.3%, and 64.3% and 81.3%, 75.0%, 64.3%, and 32.1%, respectively. There was no significant difference in patient or graft survival rates between the groups ($P = 0.91$ and 0.91, respectively).

Conclusions: Acceptable short- and long-term survival were provided in early and late reLT. The time between the primary LT and reLT does not seem to play significant role in the prognosis of reLT in the long term.

1. Introduction

With improvements in surgical techniques, donor selection, and medical care, the patient and graft survival rates of liver retransplantation (reLT) have been reported to be improving, and second-transplant recipients can survive long enough to develop graft failure [1–7]. Therefore, the long-term outcome of reLT has been the important issue recently. The distinction between early and late reLT based on the time elapsed between primary liver transplantation (LT) and reLT has yet to be agreed on. The most frequent causes of early graft failure after primary LT are primary nonfunction, vascular complications including hepatic arterial thrombosis (HAT), and uncontrollable acute cellular rejection [8–11], whereas the most common indications for late reLT are disease recurrence and biliary tract complications [8,10]. Because the number of late reLT procedures for recurrent disease and chronic biliary graft failure is likely to increase [7,8] and these complications can also recur after reLT, diseases related to long-term survival are also likely to be encountered after reLT in the

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long term. In addition, the patients who underwent a late reLT had a longer period of time in an immunosuppressed state and with liver disease compared with those who underwent an early reLT. Few studies, however, have examined long-term outcomes of early and late reLT, separately, and it remains unclear whether the difference in indications and medical condition between early and late reLT can affect the long-term outcomes. Although reLT is the only curative option for patients with graft failure after primary LT, it is imperative to estimate the risks and benefits from the aspect of long-term results, because performance of two transplantations in the same patient raises important medical and ethical issues in the context of the considerable disparity between the donor availability and the demand for LT.

In the present study, we analyzed the indications, surgical aspects, and short- and long-term outcomes of early and late reLT cases treated at a single center during the same period to assess the potential impact of time to reLT on clinical outcomes in the long term.

To avoid the influence of primary LT on the outcome, we classified patients who underwent reLT at least 6 mo after their first LT into late reLT group in accordance with other studies [2,12–14].

2. Materials and methods

2.1. Patients and methods

In total, 778 LT procedures were performed at London Health Science Centre including 48 second-, 15 third-, and two fourth-LT procedures between January 2000 and December 2010. Of those who underwent a second LT procedure, it was performed within 6 mo after primary LT in 16 (early reLT group) and 6 mo or more after primary LT in the remaining 32 (late reLT group). We retrospectively reviewed the second LT cases in this cohort in regard to patient demographic characteristics, indications for primary LT and reLT, interval from the primary to second LTs, model for end-stage liver disease (MELD) score calculated at the time of reLT, and creatinine level at the time of the second procedure as pre-LT renal insufficiency has been reported to be an important predictor of post-LT mortality [15–17]. Donor risk index (DRI) was calculated according to Feng *et al.* [18]. We also analyzed the number of units of packed red blood cells transfused during the operation and the duration of operations as for the surgical aspects. In addition, we reviewed donor characteristics for the reLT, including cold ischemia time. Finally, patient and graft survival rates after the early and late reLT were investigated. Patients were examined on an as-needed basis and at least yearly. Preoperative and surgical technical aspects and clinical outcomes of the late reLT were compared with those of the early reLT cases. The hepatic veins were reconstructed by inferior *vena cava* replacement in most cases. A venovenous bypass was used selectively in patients who were judged to be intolerant of vena caval occlusion, and a piggyback technique was occasionally used. The bile duct was basically reconstructed in a duct-to-duct fashion, although a choledochojejunostomy was chosen when dictated by other circumstances at the discretion of the attending surgeon.

All patients received similar immunosuppression, which consisted of tacrolimus (trough levels of 8–12 ng/mL), mycophenolate mofetil, and scheduled tapering prednisone.

Third and fourth reLT cases were excluded as reLT of more than two grafts was reported to be associated with inferior results compared with a second reLT in the previous studies [19,20].

The present review of patient medical records was approved by the Ethics Review Board of the University of Western Ontario.

2.2. Statistical comparisons

Continuous variables are presented as median (range) and compared using a Mann–Whitney *U* test. Survival curve estimates were calculated according to the Kaplan–Meier method and compared using a log-rank test. Fischer exact test was used to compare categorical data. A *P* value of <0.05 was considered to indicate statistical significance. Statistical analyses were performed using Statistical Package for Social Sciences Statistics 19 (SPSS Inc, Chicago, IL).

3. Results

The indications for primary LT in early and late reLT groups were listed in Table 1. As listed in Table 2, the main indication for early reLT procedures was HAT and primary nonfunction, whereas that for the late reLT procedures was chronic rejection, followed by biliary complications and recurrent disease. In patients who underwent a late reLT, the median interval time from primary LT to reLT was 1832 d (402–8443 d), whereas that in the early reLT group was 14 d (1–116 d).

Table 3 listed the recipient and donor demographic characteristics in early and late reLT cases. Recipient age and sex in the early reLT cases were similar to those in the late reLT group. All reLT cases were brain death–donor transplantations. There was no significant difference in donor demographic characteristics between the groups. The median DRIs

Table 1 – Indications for primary LT in early and late reLT groups.

Indication	Early reLT ($n = 16$)	Late reLT ($n = 32$)
Primary sclerosing cholangitis	2	7
Hepatitis C	3	5
Alcoholic liver disease	2	3
Fulminant hepatic failure	2	2
Nonalcoholic steatohepatitis	2	2
Cryptogenic	0	3
Hepatitis B	1	2
Primary biliary cirrhosis	1	2
Other		
Autoimmune hepatitis	0	2
Wilson disease	1	1
Biliary atresia	0	2
Budd–Chiari syndrome	1	1
Polycystic liver disease	1	0