Prognostic Factors and Outcomes of Patients After Liver Retransplantation

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ABSTRACT

Background. Despite great progress and improvement in results of orthotopic liver transplantation (OLTx), 10%–20% of patients still require retransplantation (re-OLTx). The aim of the study was to present long-term results of liver retransplantation and to determine the factors influencing outcomes.

Patients and Methods. From December 1994 to July 2014, a total of 1461 liver transplantations were performed in the Department of General, Transplant and Liver Surgery of Medical University of Warsaw. There were 92 retransplantations (6.3%), including 40 early re-OLTx (up to 30 days). The most common indication for re-OLTx were vascular complications (41/92, 44.6%). Influence of clinical variables on short- and long-term outcomes was analyzed.

Results. Postoperative mortality was 30.4% (28/92). One-year, 3-year and 5-year survival for all patients was 59.8%, 56.5% and 54.1%, respectively. The best results were achieved in patients undergoing retransplantation due to chronic rejection and biliary complications, whose 5-year survival rates were 75.0% and 72.9% respectively. There was no difference in long-term survival after early and late retransplantations (60.9% and 49.3%, respectively; $P = .158$). Multivariable analysis revealed factors associated with longer survival of patients, namely, higher preoperative hemoglobin concentration ($P = .001$), increased blood transfusions ($P = .048$), and decreased fresh frozen plasma transfusions ($P = .004$).

Conclusions. Liver retransplantation is a method providing satisfactory outcomes in selected patients. The perioperative period has a major impact on patient outcome.

ORTHOTOPIC liver transplantation (OLTx) is the only effective treatment for end-stage liver disease. Currently, in experienced centers, more than 70% of patients survive 5 years after surgery. However, better short-term outcomes translate into significant numbers of patients who experience late graft failure. Furthermore, despite improvements in surgical technique and perioperative care, complications such as hepatic artery thrombosis (HAT) and primary nonfunction (PNF) still occur. Accordingly, about 10%–20% of patients require retransplantation (re-OLTx) for various reasons [1–3]. These procedures are associated with significantly higher perioperative risk and worse long-term survival than primary OLTx [4,5]. In view of the ongoing shortage of organs and increasing number of transplantation candidates, retransplantation of the liver has generated some controversy, including ethical considerations [6]. The purpose of this study was to determine factors influencing long-term results of re-OLTx.

PATIENTS AND METHODS

A total of 1461 liver transplantations were performed in the Department of General, Transplant and Liver Surgery of the Medical University of Warsaw between December 1994 and July 2014. There were 92 retransplantations (6.3%), including 40 (43.5%) early (up to 30 days). The majority of cases (85/92, 92.4%) were first retransplantations; 6 patients (6.5%) underwent 2 re-OLTx, and 1 patient underwent 3 re-OLTx (1.1%). Detailed characteristics of the

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study group are presented in Table 1. The most common causes of retransplantation were vascular complications and disease recurrence, which accounted for 44.6% (41 patients) and 17.4% (16 patients), respectively. Among patients with vascular complications, 78% had hepatic artery thrombosis. Liver transplantation technique, immunosuppressive therapy, and follow-up scheme have been described in other publications [7,8]. Perioperative mortality (30-day) and 5-year survival were retrospectively calculated. The influence of certain variables on the results of the re-OLTx were analyzed. Clinical parameters were analyzed in univariate and multivariable analyses, using the Cox proportional regression model. Survival curves were calculated using the Kaplan-Meier method. Hazard ratios (HR) are given with 95% confidence intervals (95% CI). The level of statistical significance was set at $P < .050$. Statistica version 10 software (StatSoft Inc, Tulsa, OK, USA) was used for computing statistical analyses.

RESULTS

Perioperative mortality was 30.4% (28/92). Median follow-up was 35.8 months. One-year, 3-year, and 5-year survival for all patients was 59.8%, 56.5% and 54.1% respectively. The 5-year survival for the largest group of patients retransplanted due to vascular complications was 57.4%. Compared to that, 5-year survival of patients with biliary complications, disease recurrence, chronic rejection, primary nonfunction, and other/unknown reasons was 72.9% ($P = .562$), 62.5% ($P = .498$), 75.0% ($P = .493$), 50.9% ($P = .585$), and 25.0% ($P = .056$), respectively. There was no significant influence of timing of surgery (early vs late retransplantation) for long-term survival ($P = .171$). The number of retransplantations performed (ie, the transplantation center's experience) ($P = .770$), model for end-stage liver disease (MELD) score ($P = .689$), cold ischemia time ($P = .123$), and donor age ($P = .721$) had no significant impact on the outcome. Multivariable analysis showed that the only factors independently associated with survival of patients after re-OLTx were preoperative hemoglobin concentration (HR = 0.56 95% CI = 0.39–0.78 for the increase in hemoglobin by 1 g/dL; $P = .001$), blood transfusions (HR = 0.87 95% CI = 0.76–0.99 per unit transfusion; $P = .048$) and fresh frozen plasma transfusions (HR = 1.22 95% CI = 1.07–1.40 per unit; $P = .004$). The detailed results of the univariate and multivariable analyses are shown in Table 2.

Table 1. Characteristics of the Study Cohort

Characteristics	Values
Recipient age (y)	40.5 (19–67)
Recipient sex (male)	51 (55.4%)
Donor age (y)	44 (17–68)
Time between OLTx and re-OLTx (mo)	1.7 (0.0–146.3)
MELD	22.5 (7–47)
Blood transfusions (units)	8 (0–50)
FFP transfusions (units)	9 (0–41)
CIT (h)	8.5 (3.7–14.0)
Hb (g/dL)	10.1 (5.7–14.6)
PLT ($10^3/\mu L$)	86.5 (10.8–482.0)
WBC ($10^3/\mu L$)	8.4 (2.8–57.2)
AST (U/L)	123.0 (19.0–10220.0)
ALT (U/L)	129.0 (17.0–10394.0)
Bilirubin (mg/dL)	8.6 (0.3–48.0)
INR	1.3 (1.0–10.0)
Creatinine (mg/dL)	1.2 (0.5–17.8)
Indication for retransplantation	
Vascular complications	41 (44.6)
Biliary complications	8 (8.7)
Disease recurrence	16 (17.4)
Rejection	8 (8.7)
PNF	11 (12.0)
Other/unknown	8 (8.7)

Data are presented as median (range) or n (%).

Abbreviations: MELD, Model for End Stage Liver Disease; FFP, fresh frozen plasma; CIT, cold ischemia; AST, asparagine aminotransferase; ALT, alanine aminotransferase; Hb, Hemoglobin, WBC, white blood cells; INR, International Normalized Ratio; OLTx, orthotopic liver transplantation; re-OLTx, retransplantation; PNF, primary nonfunction.

DISCUSSION

Due to improving results of liver transplantations, late graft failure is becoming an increasingly apparent clinical problem. Liver retransplantation is the only effective form of therapy in these cases. Retransplantation rates range from 10% to over 20% [1–3]. In our study, this percentage was slightly lower and reached 6.3%. The most common indication for liver retransplantation in our center were vascular complications (41 patients) and disease recurrence in the transplanted organ (16 patients). The third most common cause was PNF (11 patients). In total, vascular complications and PNF accounted for more than half of the indications for retransplantation, which is consistent with data from the literature [9].

The results of retransplantation, depending on the indication, vary significantly in the literature. Most reports emphasize worse outcome in patients with recurrent hepatitis C virus (HCV) infection; however, some publications present very good results in this population [10]. The literature also draws attention to favorable prognosis in patients with PNF [4,11]. In our experience, the best results were achieved in patients with chronic rejection and biliary complications. On the contrary, in the study by Postma et al, patients with chronic rejection were the group with the worst prognosis [12]. We did not observe a statistically significant difference in results depending on the indication for retransplantation, which is consistent with the observations of other authors [13]. However, there was a trend toward worse results in patients with rare and not fully explained indications.

Many centers highlight the differences in outcomes depending on the time since the primary OLTx. We did not observe statistically significant differences in long-term prognosis between patients who underwent early and late retransplantation. These data are consistent with data from the literature [2,7,14]. Qualification for re-OLTx should be made before multi-organ failure is present. It seems that in patients with poor or deteriorating graft function, retransplantation should be done within 7 days or 1 month after the