ELSEVIER

Negative Prognostic Impact of Renal Replacement Therapy in Adult Living-donor Liver Transplant Recipients: Preoperative Recipient Condition and Donor Factors

H. Iwata, S. Mizuno, E. Ishikawa, A. Tanemura, Y. Murata, N. Kuriyama, Y. Azumi, M. Kishiwada, M. Usui, H. Sakurai, M. Tabata, N. Yamamoto, K. Sugimoto, K. Shiraki, Y. Takei, M. Ito, and S. Isaji

ABSTRACT

Background. In deceased-donor liver transplantation settings, post-transplantation acute renal failure with the induction of renal replacement therapy (RRT) is known to have negative effects on graft and patient survivals. However, the impact of RRT in living-donor liver transplantation (LDLT) has not been well investigated. The aim of this study was to elucidate risk factors requiring RRT and prognostic factors after its induction.

Methods. Clinical data on the consecutive 113 adult patients who underwent LDLT from March 2002 to May 2013 were retrospectively reviewed. They were divided into 2 groups: RRT ($n = 33$) and Non-RRT ($n = 80$). The primary reasons for receiving RRT were hepatorenal syndrome ($n = 17$), sepsis ($n = 12$), and renal hypoperfusion ($n = 4$).

Results. Although there were no significant differences in age or sex, the Model for End-Stage Liver Disease (MELD) score was significantly higher in the RRT group than in the Non-RRT group (23 ± 13 vs 16 ± 7; $P = .002$). The graft-recipient weight ratio (GRWR) was significantly lower in the RRT group (0.86 ± 0.3 vs 0.99 ± 0.2; $P = .025$). The 1- and 5-year patient survival rates were significantly higher in the Non-RRT group than in the RRT group (respectively, 91.3% and 84.3% vs 42.9% and 25.5%; $P < .001$). In multivariate analysis, independent risk factors for receiving RRT were MELD score >20 ($P = .044$) and GRWR <0.7 ($P = .039$). In the RRT group, donor age >50 years ($P = .042$) and preoperative serum creatinine level >1.5 mg/dL ($P = .049$) were significant prognostic risk factors.

Conclusions. In adult LDLT patients, the induction of RRT after LDLT was a negative predictor of survival. In addition to the preoperative recipient's condition, donor factors including graft size and donor age influenced prognosis after the induction of RRT.

ACUTE renal failure (ARF) is common in the perioperative period of deceased-donor liver transplantation (DDLT) [1,2] and is associated with prolonged hospitalization, significant financial costs, and increased mortality rates, especially in the intensive care unit setting [3–5]. Although some of the patients who suffered from ARF needed renal replacement therapy (RRT), ARF with the induction of RRT had negative effects on graft and patient survivals after DDLT [6,7]. Most of the analyses regarding RRT after LT have been performed in the DDLT but not the living-donor liver transplantation (LDLT) setting.

The reasons for induction of RRT after DDLT are multifactorial: hepatorenal syndrome (HRS) due to liver failure, drug-induced toxicity, septic episodes, and intraoperative hemodynamic instability [8–10]. In contrast, only

From the Department of Hepatobiliary Pancreatic and Transplant Surgery (H.I., S.M., A.T., Y.M., N.K., Y.A., M.K., M.U., H.S., M.T., S.I.), Department of Cardiology and Nephrology (E.I., M.I.), and Department of Gastroenterology and Hepatology (N.Y., K. Sugimoto, K. Shiraki, Y.T.), Mie University School of Medicine, Tsu, Mie, Japan.

Address reprint requests to Shugo Mizuno, MD, Department of Hepatobiliary Pancreatic and Transplant Surgery, Mie University School of Medicine, 2-174 Edobashi, Tsu, Mie, 514-0001, Japan. E-mail: mizunos@clin.medic.mie-u.ac.jp

0041-1345/14/$–see front matter
http://dx.doi.org/10.1016/j.transproceed.2013.11.113

a few studies on RRT after LDLT have been reported [11,12], and the usefulness and appropriate indication of RRT in LDLT remain unclear.

LDLT differs greatly from DDLT in terms of graft liver size, graft ischemia time, surgical process, and complexity [13]. Particularly in adult LDLT, graft size mismatching with partial liver transplantation can cause various problems, including ARF, when the graft can not sustain excessive portal blood perfusion [14].

The aim of the present study was to clarify the usefulness of RRT in LDLT and to determine prognostic risk factors for patients who received RRT after LDLT. This study also focused on evaluating the clinical characteristics and prognosis of patients who developed ARF and received RRT before or after LDLT.

PATIENTS AND METHODS

Patients

Among the 139 patients who underwent LDLT at Mie University Hospital from March 2002 to May 2013, 113 were adults. The indications for these 113 LDLT patients included hepatocellular carcinoma ($n = 48$), liver cirrhosis ($n = 35$), primary biliary cirrhosis ($n = 15$), acute liver failure ($n = 10$), and others ($n = 5$). The transplanted liver grafts included left lobe grafts ($n = 41$), right lobe grafts ($n = 53$), right lobe with middle hepatic vein ($n = 17$), and posterior segment graft ($n = 2$). All LDLTs were performed after obtaining full informed consents from the patients and were approval by the Liver Transplantation Committee of Mie University Hospital. The exclusion criterion for this study was LDLT patients who had undergone morphologic renal alteration for chronic renal insufficiency ($n = 1$). Graft selection process and the details of the surgery were described elsewhere [15]. The mean follow-up was 58.4 months (range, 3–132 months).

Immunosuppression

The immunosuppression protocol consisted of tacrolimus and low-dose steroids as described elsewhere [16]. The target whole-blood trough level for tacrolimus was 10–12 ng/mL during the first 2 weeks, ~10 ng/mL thereafter, and 5–10 ng/mL from the 2nd month after LDLT. Methylprednisolone (1 mg/kg/d, intravenously) was given on postoperative days 1–3, followed by 0.5 mg/kg/d on postoperative days 4–6. Steroid administration was then switched to oral prednisolone (0.3 mg/kg/d) on postoperative day 7, and the dose was reduced to 0.1 mg/kg/d at 1 month after LDLT. If their liver function was stable, recipients were weaned from steroids at 3–6 months after LDLT.

Renal Replacement Therapy

The RRT for pre- or post-transplantation patients in this study comprised continuous venovenous hemodiafiltration to treat patients with marked comorbidities and general hemodynamic instability. Vascular access was created in the internal jugular vein or the femoral vein with the use of an 11-Fr flexible double-lumen catheter (Argyle; Covidien, Shizuoka, Japan). A poly(methyl methacrylate) membrane hemofilter (Hemofeel CH; Toray Medical, Tokyo, Japan) was placed in the circuit. Nafamostat mesilate (Futhan; Torii Pharmaceutical, Tokyo, Japan) was used as anticoagulant, with the dose adjusted to maintain an activated coagulation time of 150–180 s. The operating conditions were set as follows: blood flow rate, 80–100 mL/min; dialysate flow rate, 500 mL/h; and filtration rate, 300 mL/h. The hemodiafiltration system was continuously monitored with a personal bedside console (ACH-10; Asahi Medical, Tokyo, Japan).

Statistical Analyses

Categoric variables were compared with the use of the chi-square test. Continuous data were compared with the use of the Mann-Whitney test. Patient survival after liver transplantation was analyzed with the use of the Kaplan-Meier survival method and the log-rank tests. Variables with a P value of $<.1$ in the univariate analysis were entered in a multivariate analysis using a stepwise forward Cox regression procedure. All statistical analyses were performed with Statview 5.0 (Hulinks, Tokyo, Japan).

RESULTS

Characteristics of Patients With and Without RRT

Among the 113 patients who received LDLT, RRT was introduced preoperatively and/or postoperatively in 33 (29.2%; RRT group) and was not in 80 (Non-RRT group; Table 1). Although there were no significant differences in recipients' age or sex, the Model for End-Stage Liver Disease (MELD) score (23.2 ± 13.3 vs 15.8 ± 7.5; $P = .0021$) and Child-Pugh score (11.0 ± 2.1 vs 9.0 ± 2.5; $P = .0003$) were higher in the RRT group, and this group included more cases with acute liver failure as the primary hepatic disorder (8/33 vs 2/80; $P = .0002$). Regarding the donor and

Table 1. Characteristics of the Patients With and Without RRT

	RRT (n = 33)	Non-RRT (n = 80)	*P* value
Recipient		S	
Age	51.8 ± 10.2	52.9 ± 11.1	n.s.
Gender (M/F)	18/15	51/29	n.s.
MELD score	23.2 ± 13.3	15.8 ± 7.5	.0021
C-P score	11.0 ± 2.1	9.0 ± 2.5	.0003
Indication			
HCC	10 (HCV 5, HBV 3, Alc 2)	38 (HCV 22, HBV 7, cryp 7, Alc 2)	n.s.
Liver cirrhosis	9 (HCV 5, cryp 3, Alc 1)	26 (HCV 13, cryp 5, HBV4, Alc 4)	n.s.
PBC	6	9	n.s.
Acute liver failure	8 (HBV 3)	2 (HBV 1)	.0002
Others	0	5	
Donor			
Age	36.1 ± 12.3	38.3 ± 12.6	n.s.
Gender (M/F)	20/13	42/38	n.s.
Graft type			
Left lobe	15	26	n.s.
Right lobe	13	40	n.s.
Ex. Right lobe	4	13	n.s.
Posterior segment	1	1	n.s.
Graft weight (g)	528 ± 143	613 ± 136	.010
GRWR (%)	0.857 ± 0.24	0.986 ± 0.19	.025

Abbreviations: RRT, renal replacement therapy; MELD, the model for end-stage liver disease; C-P, Child-Pugh; HCC, hepatocellular carcinoma; PBC, primary biliary cirrhosis; GRWR, the graft recipient weight ratio.