Impact of Portal Hemodynamic Changes in Partial Liver Grafts on Short-Term Graft Regeneration in Living Donor Liver Transplantation

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ABSTRACT

Background. Regeneration of partial liver grafts is critical for successful living donor liver transplantation (LDLT), especially in adult recipients. The purpose of this study was to investigate the intraoperative hemodynamic changes in partial liver grafts and characterize their potential impact on post-transplant liver regeneration in LDLT.

Methods. We examined the portal venous flow (PVF) and hepatic arterial flow (HAF) to partial liver grafts by means of ultrasonic transit time flowmeter of donors immediately before graft retrieval and of the corresponding recipients after vascular reconstruction in 48 LDLT cases. We evaluated post-transplant liver regeneration according to the changes in graft liver volume between the time of transplantation and the 7th post-transplant day.

Results. There was a significant increase in PVF to the partial liver grafts in recipients (rPVF) compared with that in donors. In contrast, graft HAF in recipients significantly decreased compared with that in donors. The rPVF inversely correlated with graft weight (GW)–recipient body weight ratio (GRWR), whereas HAF volume showed no significant correlation. The rPVF/GW positively correlated with the rate of liver regeneration (GRR), which inversely correlated with GRWR. The rPVF/GW was significantly higher, and GRR tended to be larger in the small graft group than in the non-small graft group.

Conclusions. Intraoperative portal hemodynamic changes in partial liver grafts strongly affect their post-transplant regeneration. In particular, in small liver grafts, an immediate and remarkable increase in graft PVF may contribute to rapid liver regeneration after LDLT if the increased PVF remains within a safe range.

LIVING DONOR LIVER TRANSPLANTATION (LDLT) has become an established method of liver grafting, especially in Japan, where cadaveric transplantation is rare. Despite recent advances in surgical techniques and immunosuppressive management, the unavoidable usage of a small liver for a large patient remains a major problem in terms of post-transplant patient recovery, although the introduction of right liver grafts has conferred substantial benefits [1]. From this point of view, regeneration of partial liver grafts is critical for successful LDLT, especially in adult recipients. Liver regeneration appears to be affected by several factors such as hemodynamics, humoral factors, and immunological responses [2] after liver resection or partial liver transplantation.

Previous studies have examined systemic and hepatic hemodynamic changes in cadaveric orthotopic whole liver transplantation [3–6], whereas in clinical partial liver

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transplantation, few relevant reports have been identified [7–11]. Several lines of evidence suggest that in cirrhotic patients, the grafted liver is exposed to high portal venous flow caused by disease-related persistent hyperdynamic splanchnic circulation [3,6,12,13]. Long-standing portal hypertension and several hormonal changes may account for this hemodynamic derangement [5,14]. However, fulminant hepatic failure (FHF), another major indication for liver transplantation, is characterized by an elevated cardiac output and a resultant increase in the portal venous flow [15,16].

In LDLT, the small size of the liver graft appears to have an additional impact on its hemodynamic changes during and after transplantation. High blood flow volume into a small liver graft is frequently observed in LDLT and is implicated in postoperative graft injury leading to small-for-size (SFS) syndrome [10,17–19]. However, to our knowledge, very few studies have investigated the relationship between graft-recipient size mismatch and hemodynamic graft changes in LDLT. Furthermore, most studies that have focused on graft hemodynamics in LDLT examined either a small number of patients or only adult cases, using right liver grafts [7–11,20].

Several studies have described liver regeneration after LDLT [9,11,21–23]. The grafted liver has been shown to regenerate more rapidly than the corresponding remnant liver in the hepatectomized live donor, although the 2 separate liver sections share the same parenchymal condition [21]. Furthermore, the rate of liver regeneration is suggested to be higher in small grafts than in large livers [9,23].

We hypothesized that remarkable hemodynamic changes in the graft would occur when a partial liver was grafted from a donor to a recipient, and the changes would have a strong impact on the rapid regeneration of the graft. Therefore, we examined the hepatic blood flows to the same partial liver sections in both donors and corresponding recipients. We previously quantified the intraoperative changes in the hepatic blood flow in 19 LDLT cases, and those results emphasized the significance of the increased portal venous flow to the liver graft during rapid post-transplant liver regeneration [9].

In this medium-sized study on hemodynamics in LDLT, we have updated our data to further elucidate the hemodynamic changes in liver grafts and their implications in post-transplant liver regeneration.

METHODS

Clinical Profiles of Donors and Recipients

Between April 1995 and August 2002, 57 LDLTs were performed at Keio University Hospital. Among these, we retrospectively reviewed 48 cases in which data on intraoperative flowmetry and/or post-transplant liver volume were available. All the donors were adults related to the recipients. The medical criteria for donor selection were based mainly on liver function tests, ABO blood type compatibility, and estimated volume of the potential liver graft, using computed tomography (CT) scans [24]. The ages of recipients (23 men and 25 women) ranged from 2 months to 60 years (median, 24.5 years) and consisted of 22 children under 16 years old and 26 adults. The primary diseases of recipients were biliary atresia (n = 19), FHF (n = 11), primary biliary cirrhosis (n = 8), hepatitis B–related cirrhosis associated with or not associated with hepatocellular carcinoma (n = 5), cryptogenic cirrhosis (n = 2), primary sclerosing cholangitis (n = 1), Wilson disease (n = 1), and familial amyloid polyneuropathy (n = 1).

For further research purposes, adult patients were divided into 2 groups, those with liver cirrhosis (LC, n = 17) and those without liver cirrhosis (NLC, n = 9). The mean ± standard deviation (SD) of MELD score in LC patients was 20.7 ± 7.4 (range, 13–35; median, 22.0). Also, adult patients were divided into 2 groups: those with small grafts in which GRWR was <0.8 (n = 6) and those with non-small grafts in which GRWR was ≥ 0.8 (n = 20). Among the patients of this study, we never observed the symptoms of SFS syndrome such as prolonged hyperbilirubinemia, prolonged coagulopathy, or ascites, the definition of which was described by Dahm et al [17] or Yagi et al [18].

The study protocol was approved by the Institutional Liver Transplant Indication Committee, the study protocol conformed to the guidelines of the 1975 Declaration of Helsinki, and written informed consent was obtained from each patient and family member.

Surgical Techniques of LDLT

During the partial hepatectomy of donors, we avoided blocking the hepatic blood inflow during hepatic parenchymal transection and attempted to adjust the timing of graft retrieval to coincide with completion of the recipient hepatectomy to render cold ischemic duration as short as possible. Several types of partial liver grafts were extracted: left lateral sections (LLS, n = 14), extended left lateral sections (ELLS, n = 5), left livers with the middle hepatic vein (LL, n = 13), left livers with caudate lobe (LLC, n = 4), or right livers (RL, n = 12). We included the middle hepatic vein in LL or LLC grafts but left it with the donor in cases of hepatectomy to obtain ELLS or RL grafts. Graft weight (GW, g) was measured after washout with a preservation solution but before cold storage. In this setting, the absolute value of graft volume (GV, mL) was assumed to be equal to that of GW. The standard liver volume of recipients (SLV) was calculated by use of the formula postulated by Urata et al [25]. The degree of the graft-recipient size mismatch was represented by the ratio of GW to the corresponding rBW (GRWR, %) or by the ratio of GV to the corresponding SLV (G/S ratio, %). GW ranged from 166 g to 854 g (median, 388 g) and GRWR from 0.64% to 5.53% (median, 1.21%).

In all recipient operations, the inferior vena cava was preserved by use of the so-called "piggy-back method." The middle hepatic vein was not reconstructed in any of the RL graft cases. The portal vein was reconstructed in an end-to-end fashion, or with some modification using vascular grafts. The hepatic artery was anastomosed with microsurgical techniques. All NLC patients underwent a temporary veno-venous bypass or an end-to-side portocaval shunt to reduce portal hypertension during portal clamping, whereas LC patients and pediatric patients did not undergo these supportive measures.

All of the 48 recipient operations were successfully accomplished without any severe intraoperative complications. One patient died in the hospital within 1 postoperative month, but no patient died during the first postoperative week.

Measurement of Blood Flow to Liver Graft

Blood flow to the liver graft was measured intraoperatively with the use of an ultrasonic transit time flowmeter (Transonic, New York,