[14] Testa G, Malago M, Nadalin S, Hertl M, Lang H, Frilling A, et al. Right-liver living donor transplantation for decompensated end-stage liver disease. Liver Transpl 2002;8:340–346.
[15] Shah JN, Ahmad NA, Shetty K, Kochman ML, Long WB, Brensinger CM, et al. Endoscopic management of biliary complications after adult living donor liver transplantation. Am J Gastroenterol 2004;99:1291–1295.
[16] Gondolesi GE, Varotti G, Florman SS, Munoz L, Fishbein TM, Emre SH, et al. Biliary complications in 96 consecutive right lobe living donor transplant recipients. Transplantation 2004;77:1842–1848.

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Living donor liver transplantation in Japan and Kyoto University: what can we learn?

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The first living donor liver transplantation (LDLT) was reported by Raia in Brazil in 1988 [1] and the first case in Japan was performed by Nagasue in Shimane Medical College in 1989 [2]. Subsequently, LDLT developed rapidly in Japan because of the virtual absence of deceased donors. This procedure was initially utilized only for pediatric recipients using the left hepatic lobe (or one or more of its segments). However, with the introduction of right hepatic lobe LDLT, adult recipients were able to undergo successful transplantation. In this review we will address some of the critical issues related to the evolution of LDLT in Japan and Kyoto University Hospital.

1. Overview of LDLT in Japan and Kyoto University Hospital

According to the registry of the Japanese Liver Transplantation Society, 2249 liver transplants have been performed until the end of 2002 in 49 institutions in Japan. One and three year survival in LDLT are 80.8 and 78.5%, respectively [3].

LDLT was first introduced in Kyoto University Hospital in June 1990. By June 2004 the number of LDLT reached 1000 including 387 adults and 613 children (Fig. 1). In pediatric recipients, the etiology of liver disease was: cholestatic disease (72%), metabolic disease (8%), acute liver failure (6%), and liver cirrhosis (3%). In adult recipients, the etiology of liver disease was: cholestatic disease (28%), liver cirrhosis (24%), neoplastic disease (23%), acute liver failure (12%) and metabolic disease (5%). Patient and graft survival rates are depicted in Fig. 2.

2. Donor morbidity and mortality

The Japanese Liver Transplantation Society has published donor morbidity and mortality rates through data obtained via a questionnaire sent to the 46 liver transplant centers where the operations have been performed [4]. Data were obtained anonymously so as not to invade donor privacy. Approval for the study was granted by the society's ethics committee. From November 1989 to April 11, 2002, 1852 LDLT donors were registered in the database and no perioperative donor deaths have been recorded since introduction of LDLT in Japan. After April 11, 2002, one donor died 4 months after donation probably due to non-alcoholic steatohepatitis and a small remnant liver (estimated 27%). A total

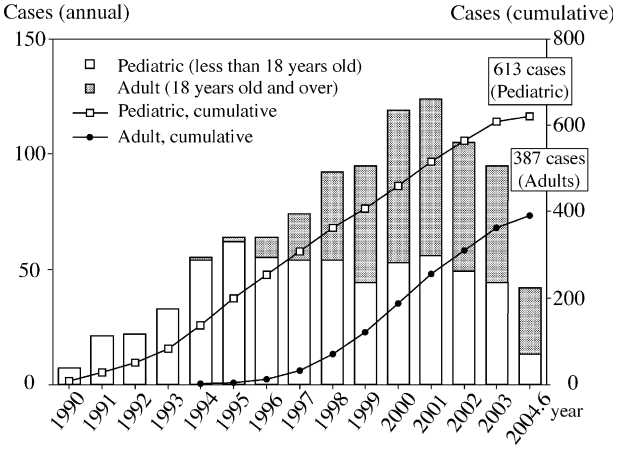

Fig. 1. Annual and cumulative number of LDLT in Kyoto University Hospital according to pediatric and adult recipients.

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Abbreviations: LDLT, living donor liver transplantation; HAT, hepatic artery thrombosis; DDLT, deceased donor liver transplantation; GRWR, graft-to-recipient weight ratio; APOLT, auxiliary partial orthotopic liver transplantation; RHV, right hepatic vein; MHV, middle hepatic vein; LHV, left hepatic vein.

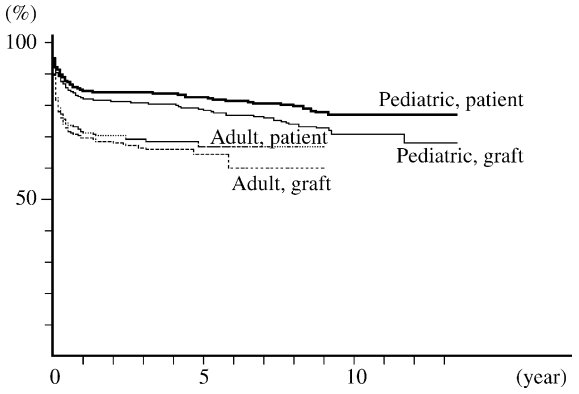

Fig. 2. Actuarial patient and graft survival rates in Kyoto University Hospital.

of 244 post-operative complications were reported in 228 (12%) donors. The frequency of complications was significantly higher in donors of the right lobe liver than in those involving the lateral segment, and left lobe graft. Following right lobectomy, 18.5% of donors developed surgical complications and 3.2% experienced non-surgical complications. In addition, the post-operative hospital stay was significantly longer in right lobe donors compared to patients donating the lateral segment, left lobe or left lobe with caudate lobe. Re-operation related to donor hepatectomy was required in 23 donors.

3. Development of surgical techniques

We have developed many innovative techniques for LDLT since the inception of this procedure. Initially, LDLT was restricted to pediatric recipients. Lateral segmentectomy was performed because it carried less risk for the donor and the volume of lateral segment provided adequate hepatocyte mass for pediatric patients [5]. The incidence of hepatic artery thrombosis (HAT) in pediatric liver transplantation was reported to range between 15 and 20% [6], most of whom would require re-transplantation with a deceased donor (DD) graft. However, in Japan, re-transplantation with a DD graft was impossible because deceased-donor liver transplantation (DDLT) was not accepted until 1997. Therefore, prevention of HAT was a key factor for the success of LDLT in Japan. In the third case at our center, we encountered a donor whose arterial anatomy would have required arterial anastomoses to two diminutive hepatic arteries (1.2 and 1.5 mm). Since arterial reconstruction was performed using a loupe at that time, the possibility of HAT after hepatic artery reconstruction was very high. Therefore, we decided to use the right hepatic artery for hepatic artery reconstruction, which required removal of the right hepatic lobe. This case is the first right lobe graft liver transplantation in the world [7].

In Kyoto, the hepatic artery reconstruction under high magnification was introduced with the seventh case [8]. Microsurgical techniques allow successful hepatic artery reconstruction in the case of diminutive or multiple arteries. This technique reduced the incidence of HAT to 1.5–2% which is comparable to that of DDLT. Consequently, it was decided not to perform perioperative angiography in consideration of the risk to the donor's safety. With improvements in the technical success of the procedure and favorable recipient outcomes, the number of pediatric LDLT's increased accordingly. The next major challenge was application of the procedure to larger teenagers and adults. The greatest initial challenge in applying LDLT in physically larger recipients was obtaining a graft of sufficient size.

We found that the patient outcomes were closely related to graft size [9]. There are two different ways to show graft size relative to recipient size. One is to express graft weight as percentage of expected liver size, often designated as 'standard volume', for each patient [10] and another is to express graft weight simply as percentage of recipient body weight (GRWR) [9]. The negative impact of small-for-size graft is not an all-or-none phenomenon. We reported, through a large single-center series of LDLT's, a stepwise reduction of graft survival relative to graft size. In this series, graft survival in patients with a graft-to-recipient weight ratio (GRWR) of 1.0–3.0% was not affected by relative graft size. However, it decreased by approximately 20% when GRWR was reduced to 0.8–1.0%, and an additional 20% reduction was observed when GRWR was reduced to less than 0.8% (Fig. 3) [9]. As a result, LDLT recipients should have a GRWR of 0.8% or more to insure that the graft is of sufficient size to sustain the recipient. However, in many adults the GRWR is $<0.8\%$ when the left lobe is utilized. Therefore, auxiliary partial orthotopic liver transplantation (APOLT) was developed for adult recipients with non-viral related liver cirrhosis [11]. APOLT is the procedure of transplanting the donor's left lobe orthotopically after excising a recipient's left lobe. In this procedure, a part of the native liver compensates for the initial dysfunction until a small liver graft regenerates. Although it showed a certain degree of success, APOLT was unable to be adapted for viral liver disease which is common in adult patients.

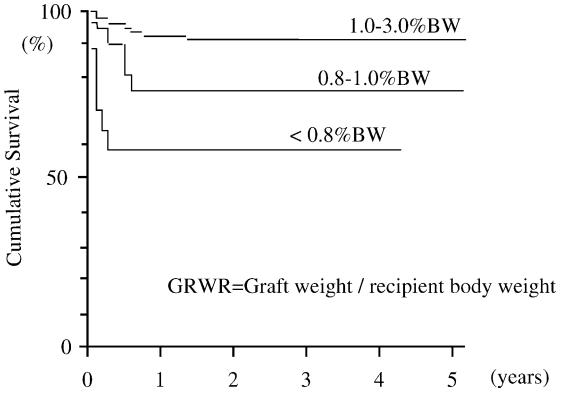

Fig. 3. Graft survival rates by graft-to-recipient weight ratio.