Liver Transplantation In Young Children: Japanese Experience

Mureo Kasahara

ABSTRACT
Organ transplantation center, Tokyo Japan reviews the experience of liver transplantation in young children. Based on 27 years experience, since the living donor liver transplantation was first performed in Japan, some of the newer developments necessity by paucity of organs and desire for decreasing mortality and morbidity are presented in this paper. From one transplant in 1989 the number has stabilized around average of 400+ every year. Children have formed significant number of these cases (Adults >18 Yr. n=4992; Children<18 Yr.= 2751). Indications for which these cases were performed are listed. The indications of pediatric liver transplantation have been refined and those are now followed in National Center for Child Health and Development. Technical refinements especially those decrease the parenchymal cell injury to liver meant for transplantation in children weighing less <5 kg receiving adult liver (large for size grafts) are illustrated in step wise manner. The modified left lateral segment reduction by which transplant could be done in very small infants. An algorithm proposed by our experience which takes into account factors like graft thickness and abdominal AP diameter is introduced. In our opinion further refinement of this algorithm is needed.

INTRODUCTION
It has been 27 years since living donor liver transplantation (LDLT) was first started in Japan as a life-saving procedure for a patient with end-stage liver disease. Shortage of diseased organ donors led to the development of unique technical, physiological and logistical innovations in LDLT. Experience with and technical improvements in living donor surgery led to the generalization of pediatric LDLT with excellent patient survival outcomes. These techniques have expanded to potential donor pool and decreased waiting list mortality in pediatric liver transplantation.

There have been technical refinements in the Japanese pediatric LDLT program, such as resolving graft size matching. We reported that the use of small-for-size grafts, defined as grafts with a graft-to-recipient body weight ratio (GRWR) less than 0.8%, is associated with small-for-size syndrome, the development of massive ascites, renal insufficiency, persistent cholestasis, coagulopathy and infectious complications in patients with lower grafts and reduced patient survival; especially in adolescents, most likely due to enhanced parenchymal cell injury and reduced metabolic and synthetic graft capacity. Meanwhile, large-for-size grafts are used in neonatal and infantile LDLT. The main problems associated with large-for-size grafts include the small size of the recipient’s abdominal cavity, size discrepancies between vascular calibers and insufficient blood supply to the graft. Further reducing the left lateral segment (LLS) to monosegment increases the possibility of supplying an adequate graft size, while monosegment has been introduced to mitigate the problems of large-for-size grafts with GRWRs estimated to be over 4%.

The indications for LT were varied, include cholestatic liver disease, metabolic liver disease, acute liver failure, neoplastic disease, vascular disease, graft failure and other indications. Specific diseases and preoperative patient conditions might be associated with transplantation outcomes. During the past 27 years, medical and surgical innovations have established pediatric LDLT to be the optimal therapy for patients suffering from acute and chronic liver disease. This has allowed expansion of the indications for LT to assess patient severity and body weight in association with various diseases. The profiles of current pediatric LT recipients differ significantly...
from those of earlier eras. Organ Transplantation Center of National Center for Child Health and Development, Tokyo, Japan, has been established in 2005 and based on these 10 years experiences in pediatric LDLT and liver surgery, we have demonstrated our innovative surgical procedure. These include standard technique and complicated case presentations with informative surgical videos, to standardize and continue to improve the quality of surgery for end-stage pediatric liver disease in this text. This text is useful in maintaining high quality surgery in all pediatric patients and in avoiding unrecognized changes in surgical strategy for all involved in this field.

CURRENT STATUS OF LIVER TRANSPLANTATION IN JAPAN AND NCCHD

The number of LDLTs performed in Japan showed an initial increase to a maximum of 562 in 2005 followed by a decrease approximately 400 annually (Figure 1). During a quarter of a century (November 1989 to December 2014) 7,673 LDLTs were performed in Japan with a minimum follow-up of two years. Of these cases 2,751 involved children less than 18 years of age (35.9%). The annual number of pediatric LDLT cases has been 110~140 over the past five years. During the same period, 354 deceased LTs, including 23 split liver transplantations (ex-situ) in pediatric patients were performed. Between November 2005 and December 2015, 380 children underwent LT in National Center for Child Health and Development (NCCHD). The annual case number of 2015 was 72 cases, which covers 70% of pediatric LT in Japan (Figure 2).

There were 166 male (43.4%) and 214 female (56.6%) recipients with a median age of 3.9 years (range: 18 days–17.9 years) and a median body weight of 14.7 kg (range: 2.6–96 kg). Figure 3 lists the indications for LDLT. Cholestatic liver disease was the leading indication for LDLT (49%), followed by metabolic disorders (18%), acute liver failure (15%) and neoplastic liver disease (5%). Biliary atresia (43.9%) was the most common indication in patients with cholestatic liver disease, followed by Alagille syndrome (1.8%). Ornithine transcarbamylase deficiency (3.7%) was the most common indication in patients with metabolic liver disease, followed by Methylmalonic academia (3.7%) as shown in Figure 4. Nearly 75% of the children who underwent LDLT for acute liver failure had disease of unknown etiology. Hepatoblastoma (3.7%) was the most common indication in patients with neoplastic liver disease. Retransplantation using living donors was indicated in 11 patients (2.9%). The patient survival in 1, 3, 5, 10 years are 92.3, 92.1, 91.7, 91.7%, respectively (Figure 4).
TO SAVE THE SMALL BABIES ON LIVING DONOR LIVER TRANSPLANTATION

Transplantation in children who weigh less than 5 kg remains a problem because the left lateral segment (LLS) from an adult may be too large when the graft-to-recipient weight ratio is greater than 4.0% and thus may result in a large-for-size graft and its associated morbidity. Further reduced LLS grafts that can be transplanted safely without compromise to patient survival have been introduced for these children to mitigate the problem of large-for-size grafts. In very small children (neonates) who have no portal hypertension, hepatomegaly, or ascites, the abdominal cavity may be small, and the anteroposterior thickness of the graft remains a problem. Abdominal closure may require a temporary Silastic mesh, and this is associated with complications. We have developed a modified LLS reduction by which the thickness of the graft is addressed and transplantation is allowed in very small infants.

After implantation of conventional Hyper reduced left lateral segment, there are significant thickness discrepancy between the graft and abdominal cavity.

In the donor operation, after the isolation of the donor’s left hepatic artery and left portal vein (LPV), the hepatic parenchyma was transected 3 mm to the right of the falciform ligament, just as in any standard donor heptectomy for children. The LLS was first reduced by the removal of the falciform ligament, care was taken to preserve the segment III branch of the left hepatic vein (LHV). Normally, main LHV is running between P2 and P3. As far as one preserve P3 branch, it never compromise out flow of the graft. Moreover, Segment II graft can be available with meticulous technique. Following the round ligament towards the hepatic parenchyma, and then each PV branch feeding to segment 3 was separately exposed.

Segment III Glisssonian sheath was encircled, and parenchymal dissection has been made according to the demarcation line between segment II and III.
According to the preoperative assessment of the anatomical patterns of the PV, the relevant PV branches feeding to the reduction part of segment 3 were occluded to make demarcation lines on the surface between segment 2 and 3. At that point, the intraoperative Doppler ultrasonography (US) could visualize the portal venous flow feeding to the graft, which planned to be preserved inside the liver. The further transection of hepatic parenchyma was horizontally performed, following those demarcation lines. During that procedure, the care was taken to preserve the drainage veins of the graft. If required the further reduction from perspective of the graft volume, the removal of the lateral part of segment 2 was added.8,9

Applying this reduction procedure makes primarily abdominal closure possible even in neonates.

Our series proposes a novel algorithm that can be used to select the graft type in LDLT for smaller children, which is simply framed in terms of the GRWR and the ratio of the thickness of the LLS to the AP diameter in the recipient’s abdominal cavity. Furthermore, performing a preoperative analysis using a 3D, computer generated model of the donor’s liver can provide valuable information for the decision-making process in regard to graft type selection. As shown in Figure 9, if the maximum thickness of the donor’s LLS is smaller than the AP diameter in the recipient’s abdominal cavity (ratio of thickness <1.0), then segment 2 grafts may not be necessary for the majority of recipients. However, if a recipient is associated with a profoundly ill status before the operation, and shows severe subcutaneous edema of the abdominal wall or edematous intestines, then a non-anatomically reduced LLS is unlikely to fit into the small abdominal cavity of the child. Therefore, the algorithm proposed in our experience should be refined through the further accumulation of experience, especially considering various preoperative conditions of the recipients as reference indices for graft type selection.10

Algorithm used for the preoperative assessment for graft type selection. GRWR, Graft-to-recipient weight ratio; LLS, left lateral segment; ratio of thickness, the ratio of the maximum thickness of the LLS to the anteroposterior diameter in the recipient’s abdominal cavity.
Figure 9: The algorithm for graft type selection in Pediatric liver transplantation.

ACKNOWLEDGEMENT

This work was supported in part by grants from the Scientific Research Fund of the Ministry of Education and a Research Grant for Immunology, Allergy and Organ Transplant, Rare and Intractable Disease from the Ministry of Health, Labor and Welfare, Japan (H24-08, H24-014, H25-06, H27-01) and the Foundation for Growth Science, Japan.

REFERENCES


10. Kasahara M, de Ville de Goyet J. Reducing left liver lobe grafts, more or less? Don't throw out the baby with the bath water. Pediatr Transplant. 2015; Nov 4.

Address reprint requests to: Mureo Kasahara, M.D., PhD., Organ Transplantation Center, National Center for Child Health and Development, 2-10-1 Okura, Setagaya-ku, Tokyo, Japan, 157-8535. TEL: +81-3-3416-0181; FAX: +81-3-3416-2222; E-mail: kasahara-m@ncchd.go.jp