Living Donor Liver Transplantation for Biliary Atresia

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Biliary atresia is the most common cause of chronic cholestasis in infants and children. The incidence is estimated at 3.7:10,000 among Taiwanese infants. Kasai hepatoportoenterostomy helps children survive beyond infancy. Liver transplantation is indicated when the Kasai procedure fails to work or when patients develop progressive deterioration of liver function despite an initially successful Kasai operation. Living donor liver transplantation was developed to alleviate organ shortage from deceased donors. It has decreased the waiting time for transplantation and, therefore, improves patient survival. One hundred living donor liver transplantations have been performed for biliary atresia at Chang Gung Memorial Hospital-Kaohsiung Medical Center with both 98% 1-year and 5-year actual recipient survival. *(Chang Gung Med J 2007;30:103-8)*

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Occurring at an incidence of 1:8,000 to 1:20,000 live births, biliary atresia (BA) is the most common cause of congenital chronic cholestasis in infants and children.[1-5] There is an increased incidence in populations in the Pacific rim and a female predominance in Orientals.[4] In Taiwan, its incidence is estimated to be 3.7:10,000 among newborn babies.[6] This obstructive cholangiopathy of undetermined pathogenesis leads to early development of secondary biliary cirrhosis.[2,3] Untreated, the prognosis of BA is poor with median survivals of less than 2 years.

Surgical management of BA

The current surgical management of BA involves Kasai hepatoportoenterostomy and liver transplantation (LT). The former remains as a reliable and effective first line procedure particularly if performed in children less than 90 days old.[7] However, it often serves as a bridge to LT when, despite an initially successful Kasai procedure, progressive deterioration of liver function occurs.[8-10] Sixty-seven percent of patients will continue to develop chronic liver disease and almost all will ultimately require LT before reaching adulthood. Visser,

in a review of 42 patients, demonstrated no increase in major perioperative complications, including unplanned explorations, in those LT recipients who underwent Kasai procedures.[10]

BA is the most common indication for pediatric LT.[11] As a result of advances in medical care, the demand for LT has increased tremendously in the past ten years[12] and there is a shortage of organ donation. Living donor LT (LDLT) was developed to alleviate organ shortage from deceased donors.[13] In Brazil and Chile, LDLT is performed in 22%-24% of all transplantations for BA, which has greatly reduced the waiting period.[14,15]

LDLT for BA

Large series of pediatric LT for BA usually report on combined results of deceased donor grafts, reduced-size grafts, split-liver grafts and LDLT.[5,14,16,17] These studies confirm the effectiveness of LT for the treatment of children with BA and a failed Kasai procedure, as reported by Wallot where a post-transplant survival rate of 90% was achieved.[18] Few series have focused on the results of pediatric LDLT for BA.[19-21] Refinements in surgical techniques, proper recipient and donor selection, judicious monitoring, and early recognition and treatment of complications have all led to high recipient survival with low donor morbidity. However, data concerning long-term outcome in these children are not well-documented, including schooling, renal and metabolic functions, and effects on use of immunosuppression. Data on the outcome of the live donor are also lacking.

Survival after transplant depends on multiple factors. The condition of the recipient, urgency of the operation, graft quality and difficulty of the operation are important. High blood loss index is associated with poor recipient survival.[22,23] The relationship between recipient survival and donor age is controversial.[23-25] The cold ischemia time has been proved to be crucial for graft and recipient survival.[23-25] Live organ donation reduces ischemia time in liver grafts[12] and, therefore, contributes to improved results. The left lateral segmentectomy imposes minimal trauma to the liver and remains the primary approach for obtaining a liver graft segment from a live donor for pediatric LDLT.[26]

Vascular complications are major causes of morbidity and mortality after pediatric LDLT. The vascular calibers are smaller. The portal vein is usually sclerotic due to recurrent cholangitis. Routine Doppler ultrasonographic evaluation is effective in detecting vascular complications. The use of color flow Doppler ultrasound allows earlier detection of vascular complications intra-operatively and during post-operative follow-up thereby increasing graft salvage. Immediate surgical intervention is necessary for acute vascular complications; late complications may be treated with interventional radiology procedures, such as balloon angioplasty and/or endoluminal stent placement,[27] and use of tissue plasminogen activators.

When poor portal and/or hepatic vein flows due to graft malposition are encountered during surgery, tissue expanders and Foley catheter are used to reposition the graft.[28,29] Heparinized saline infusion into the inferior mesenteric vein through a Broviac[R] catheter is a useful technique to augment portal inflow when malpositioning of the graft is not a problem. Polytetrafluoroethylene patch (Gore-Tex[R]) is used to approximate the anterior abdominal fascia when the abdominal wall is too tight to close to avoid compromising vascular flow.[30]

The improvements in medical care, and advances in immunosuppression and surgical treatments in pediatric LT, have improved recipient survival.[12] With these advances, the focus of LT has now been shifted to quality of life and low or drug-free immunosuppression. It has been reported that chronic liver diseases do not influence linear growth and sexual development in pediatric patients who have received orthotopic LT.[31] However, prolonged use of steroids, age at time of orthotopic LT and degree of initial growth delay might lead to growth failure in children after orthotopic LT.[32-34] Burdelski[35] and Fouquet[5] also observed regain of growth in height and weight after orthotopic LT in children. Despite development of new renal dysfunction in a few recipients, Fouquet[5] demonstrated adequate renal function in the majority of her orthotopic LT patients. Renal function may improve when the dose of immunosuppression is reduced in the long-term.

The academic achievements, based on school records, of the transplanted children were not inferior and was comparable with the normal population.[5] However, assessments of cognitive function in most series used non-specific outcome measures.

Therefore, a more standard tool with a longer follow-up is necessary.

LDLT for BA: Overview at Chang Gung Memorial Hospital-Kaohsiung Medical Center

Between June 1994 and September 2005, we performed a total of 319 LT and 122 were for BA. Of these 122, 100 were LDLT. There were 52 male and 48 female patients. The median age was 2 years and 5 months (range 6 months to 19 years), and the median weight was 12.2 kg (range 5.1-53 kg). Twenty-seven patients were under 1 year of age and 49 had weights less than 10 kg at the time of LDLT. Ninety-six had undergone Kasai operation prior to LDLT. The median Child-Pugh-Turcotte, Pediatric Model for End-Stage Liver Disease, and United Network for Organ Sharing scores were 9, 12.8 and 3, respectively. There were no differences in the median disease severity scores, mean preoperative serum creatinine or computed glomerular filtration rate in the patients based on gender or weight groupings.

The mean cold ischemia time was 57.3 minutes (range 17-144 minutes). The mean warm ischemia time was 41.8 minutes (range 26-59 minutes). The mean total surgery time was 628 minutes (range 423-1180 minutes). The mean surgery blood loss was 170 mL (range 10-1210 mL). Thirty-five recipients did not require blood or blood product transfusion. Veno-venous bypass was not used in any recipient. There were 27 surgical complications and 3 deaths. One recipient died 42 days after LDLT while he was still an in-patient due to early portal vein thrombosis. The second mortality occurred in a recipient who, despite undergoing re-transplantation, developed portal vein thrombosis during a second re-transplantation (survival 69.1 months). The third recipient died after 8.8 months due to post-transplant lymphoproliferative disorder.

Of the 9 portal vein complications, 5 were detected intraoperatively by routine use of Doppler ultrasound and were redone, and 4 recipients underwent reoperation. Three patients underwent intraoperative redo of the hepatic artery and 1 patient underwent reoperation. The 4 hepatic vein complications were successfully managed by balloon dilatation, of which 1 underwent vessel stenting. Of the 7 bile duct complications, 5 underwent reoperation. Table 1 summarizes the surgical complications.

Nineteen (20%) recipients had episodes of acute cellular rejection. The immunosuppression regimen consisted of cyclosporine as a mono-therapy agent in the majority of the recipients. There was no steroid-resistant rejection and muromonab CD3 (OKT3) was not used. Likewise, there was no chronic rejection case. The over-all 6-month, 1-year and 5-year actual recipient survival rates were 99%, 98% and 98%, respectively.

There were 68 female and 32 male adult donors. The donors' mean age was 32 years (range 20-57 years) and their mean weight was 59.7 kg (range 34-90.3 kg). The left lateral segment was the most common graft procured (Table 2). Twenty grafts underwent venoplasty prior to implantation (Table 3). The mean graft-to-recipient weight ratio was 2.7 (range 0.91-5.1). The mean intraoperative blood loss was 66.4 mL (range 10-280 mL). There was no mortality

Table 1. Surgical Complications Based on Recipient Weight

Surgical complications (n = 27)	< 10 kg	> 10 kg	Total
Reoperation for bleeding	1	2	3
Portal vein	7	2	9
Hepatic vein	2	2	4
Hepatic artery	1	3	4
Bile duct	3	4	7
Total	14	13	27

Table 2. Type of Living Donor Graft Used (n = 100)

Type of graft	Number used
Left lateral segment	64
Extended left lateral segment	29
Right lobe without middle hepatic vein	4
Left lobe	2
Left lobe with middle hepatic vein	1

Table 3. Form of Graft Venoplasty Performed (n = 20)

Form of venoplasty	Number performed	%
Left hepatic vein + Left superior vein	16	80
Left hepatic vein + Segment 3 vein	2	10
Left hepatic vein + Middle hepatic vein	1	5
Segment 2 + Segment 3 veins	1	5

but there were 3 complications. One donor developed bile leak, which spontaneously sealed-off; another donor had biloma and was successfully treated by percutaneous drainage. The third complication was a biliary stricture in a donor who had received cholecystectomy prior to donation and required a Roux-en-Y biliary reconstruction.

Conclusion

LDLT offers a good surgical option for BA patients with end-stage liver disease. Proper preoperative donor and recipient selection, meticulous surgical technique, early detection and prompt intervention of complications, and adequate follow-up contribute to improved long-term survival in recipients and low donor morbidity.[36]

Acknowledgement

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活體肝臟移植治療膽道閉瑣症

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膽道閉瑣症是嬰幼兒慢性膽汁鬱滯最常見的原因，台灣嬰兒的發生率估計約萬分之 3.7。葛西氏肝門腸吻合術雖已改善病童的存活率，但仍因肝功能逐漸惡化，終需接受肝臟移植手術，葛西氏手術做為移植前過渡之橋樑乃目前之共識。活體肝臟移植之發展乃為紓解大愛器官捐贈之極度短缺，藉由有效縮短需移植病童的等待時間，而大幅改善存活機率。吾等在長庚紀念醫院高雄醫學中心，共完成 100 例活體肝臟移植手術治療膽道閉瑣症，受肝病童實際一年及五年存活率皆達到98%。(長庚醫誌2007;30:103-8)

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