Original Articles/นิพนธ์ต้นฉบับ

Outcome of Living Donor Hepatectomy for Pediatric Liver Transplantation: Report of 100 Cases at Ramathibodi Hospital

Nuttapon Arpornsujaritkun[1], Surasak Leelaudomlipi[1], Abhasnee Sobhonslidsuk[2], Somkit Mingphruedhi[3], Sutipong Jongjirasiri[4], Pongpop Intraprasong[2], Panuwat Lertsithichai[5], Bundit Sakulchairungreung[1], Goragoch Gesprasert[1], Veeravorn Ariyakachorn[1,6], Suthus Sriphojanart[1]

[1] Vascular and transplant Unit, [3] Hepato-Pancreato-Biliary Surgery Unit, [4] Breast and Endocrine Unit, Department of Surgery, [2] Division of Gastroenterology and Hepatology, Department of Medicine, [5] Department of Radiology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, [6]Bamrungrad International Hospital, Bangkok, Thailand

Abstract

Background: Liver transplantation (LT) is the standard treatment for end-stage liver disease, early-stage hepatocellular carcinoma and acute liver failure in adults and children. The shortage of donor organ is a barrier of decease donor LT, resulting in a high waiting-list mortality. Living donor liver transplantation (LDLT) has been performed in Thailand for 15 years to solve this problem.

Objective: We evaluated the clinical outcomes after living donor hepatectomy.

Methods: A retrospective study of living donor who underwent LDLT between 2001 and 2015 was performed. Clavien scoring system was used to grade the severity of complications.

Result: One hundred living donors donated their parts of the livers, left lateral segment or left lobe, to their children. The operation was performed by one operative team. Complications did not occur in 91 donors. The common complications were wound problems (6%), bile leakage (2%) and bile duct injury (1%).Two donors required hospital readmission. Donor mortality is zero in 100 cases.

Conclusions: Living donor hepatectomy for pediatric recipients was associated with a low complication rate in an experience team. Good operative planning may decrease the complication rate.

Keywords: living donor, liver donor, pediatric liver transplantation, complication

Corresponding Author: Nuttapon Arpornsujaritkun
Vascular and Transplant Unit, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital
270 Rama VI Road, Ratchathewi, Bangkok, Thailand 10400
Telephone: 662-201-1304, 087-003-4787 Fax: 662-201-1304
E-mail: Arpornsujaritkunn@gmail.com

Introduction

The most common cause for pediatric liver transplant from worldwide reports is biliary atresia. Incidence of biliary atresia in Thailand is about 1 per 5,000-15,000 birth which is similar to worldwide reports[1,2]. The calculated annual incidence rate of biliary atresia in Thailand was about 50-150 cases per year. Pediatric patients who need liver transplant must be shared on a waiting list with adult liver patients. Few numbers of donations and quality of donors are the major problems, Pediatric patients need partial liver graft, therefore a good quality of deceased donor is required. Therefore, pediatric liver patients have a small chance for deceased donor LT, especially in pediatric patients with acute liver failure who had very little chance to undergo emergency deceased donor LT.

In similar to the other Asian countries, Thailand suffers from an organ shortage problem. Living donor liver transplantation (LDLT) becomes an option[3,4]. Donor risks which depend on the graft type. Right lobe liver graft has highest risk of morbidity and mortality and left lateral graft has a low risk[5-7]. Because of the organ shortage in Thailand and a low risk complication of living donor LT from adult to pediatric with good outcome[7-11], pediatric LDLT program is needed to solve this problem. The first LDLT in Thailand was initiated at Ramathiodi Hospital in 2001. Since then, the pediatric LDLT program has been continuing in our institute. We followed the rules of Thai Red Cross and Thai Medical Council, potential living donors are their parent, spouse and relatives. Donor safety should be considered as a priority. Therefore, we carried out a retrospective review of the outcome of the first 100 living donors in our institute to identify donor safety and complications.

Patients and methods

From January 2001 to December 2015, 100 LDLT were performed in Ramathibodi Hospital, Mahidol University. All of these were operated from adult to pediatric patients. Medical records of all living donors were reviewed.

Definition and data collection

Data collection was based on the Clavien grading system[12]. Intraoperative hypotension, was defined as systolic blood pressure < 100 mmHg.

Clavien grading chart

Clavien System for Classification of Negative Outcomes in General Surgery and Solid Organ Transplantation[12]

Grade 1: Any alteration from the ideal postoperative course, with complete recovery or which can be easily controlled and which fulfills the following general characteristics:

(a) Not life threatening;

(b) not requiring use of drugs other than immunosuppressants; analgesics; antipyretics; anti-inflammatory agents; antiemetics; drugs required for urinary retention or lower urinary tract infection, arterial hypertension, hyperlipidemia, or transient hyperglycemia;

(c) requiring only therapeutic procedures that can be performed at the bedside;

(d) postoperative bleeding requiring >3 units of blood transfusion; and

(e) never associated with a prolongation of intensive care unit stay or total hospital stay to more than twice the median stay for the procedure in the population of the study.

Grade 2: Any complication that is potentially life threatening or results in intensive care unit stay

>5 days, hospital stay >4 weeks for the recipient, but which does not result in residual disability or persistent disease

Grade 3: Any complication with residual or lasting functional disability or development of malignant disease

Grade 4: Complications that lead to retransplantation (grade 4a) or death (grade 4b)

Results

Donor characteristic

One hundred donors, aged 17-54 years, enrolled. The characteristic of donors was shown in Table 1. Most liver donors were female. Living liver donors usually had BMI within 35 kg/m^2. However, two liver donors with BMI more than 30 kg/m^2 underwent liver biopsy before surgery. Ninety-four percent of donors were the recipients' parents.

Table 1 Donor characteristics

Parameter	N (%)	Mean (SD)
Age (year)		29.55 (6.81)
Sex		
Female	62 (62)	
Male	38 (38)	
Height (cm)	100	160.98 (8.08)
Weight (kg)	100	58.14 (10.51)
Body mass index (kg/m^2)	100	22.69 (3.73)
<20	23 (23)	
≤20 to <25	57 (57)	
≤25 to <30	17 (17)	
≥30	3 (3)	
Biologically related to recipient		
Parent	94 (9)	
Sibling	6 (6)	
Alkaline phosphatase (U/L)		
≤58	16 (17.4)	
>58 to ≤69	13 (14.1)	
>69 to ≤86	32 (34.8)	
>86	31 (33.7)	
Bilirubin (mg/dL)		
≤0.5	43 (46.2)	
>0.5 to ≤0.7	23 (24.7)	
>0.7 to ≤0.9	16 (17.2)	
>0.9	11 (11.8)	
Blood group		
A	9 (9)	
B	24 (24)	
O	64 (64)	
AB	3 (3)	

Types of liver graft for pediatric recipients

All living donor hepatectomy was performed using two graft types, left lateral segment or left lobe (Table 2). The most common graft type is left lateral segment (93%). Liver volume ranged from 100 to 740 grams with the mean weight of 249.75 (85.27) grams.

Donor hospitalization

Length of hospital stay for the surgery was shown in table 3. The mean duration of hospital stay was 7.8 (4.8) days. The maximum hospital stay was 32 days after surgery due to bile leakage, which required surgical intervention. Two cases were readmitted duet to unrecognized common bile duct injury.

Operation in donor

One hundred donors were operated by one transplant team (Table 4). 71 percent of donor hepatectomy did not require blood transfusion. Five case (5%) needed blood transfusion of more than 3 units. Mean blood transfusion was 0.6 (1.2) units. Fifteen cases (15%) had intraoperative hypotension (systolic BP<100 mmHg) The mean operative time was 403.9 (±77.8) minutes. The mean blood loss was 872.2 (648.0) mL.

Donor morbidity and mortality

Clavien grading system defined types and severity of surgical complications as shown in table 5. The majority of donor complications were wound infection and wound dehiscence, which was defined as clavien grade 1. Two cases with bile duct leakage that could be controlled by endoscopic therapy. Serious complication defined as clavein grade 3 or higher was not found in this study. The mortality was not seen in our 100 donor hepatectomy.

Discussion

Our report is a retrospective study conducted in a single center. It shows that partial hepatectomy from adult for pediatric recipients can be performed

Table 2 Graft characteristics

Parameter	N (%)
Liver weight (g)	
<200	25 (30.9%)
200-250	29 (35.8%)
251-300	14 (17.3%)
>300	13 (16%)
Liver graft type	
Left lateral	93 (93%)
Left lobe	7 (7%)

Table 3 Length of hospital stay of the donors

Length of hospital stay (day)	No. (%)
≤2 to <6	49 (49)
≤6 to <7	19 (9)
≤7 to <8	5 (5)
≥8	27 (7)

Table 4 Intraoperative and postoperative data of the donor

Parameter	N (%)
Units of transfused blood	
0	71 (71%)
1-2	24 (24%)
≥3	5 (5%)
Blood loss (mL)	
150 to ≤450	23 (23.2%)
>450 to ≤750	30 (30.3%)
>750 to ≤1,050	22 (22.2%)
>1050 to 3,500	24 (24.2%)
Operative time (min)	
<165 to ≤358	29 (29%)
>358 to ≤424	39 (39%)
>424	32 (32%)

Table 5 Type and severity of complication based on clavien grading

Complication	No. (%)s	Grade 1	Grade 2	Grade 3	Grade 4
Wound dehiscence/wound infection	6 (6)	-	-	-	-
Bile duct leakage	2 (2)	2	-	-	-
Bile duct injury	1 (1)	1	-	-	-
Abdominal collection	1 (1)	1	-	-	-

safely. The results may guide the clinicians to modify current practice to prevent future complications. In this study, bile duct, wound and other complications occurred in a similar rate comparing to other centers[5-7,9,10]. According to the previous reports from five Asian centers, the total complication rate was 9.3% with bile duct complication of 4.7% and wound complication of 4.7%.[6] In our study, serious complications such as portal vein thrombosis, liver failure, pulmonary embolism or death were not seen and there was no donor mortality. In similar to the study by Yamaoka et al.[13] evaluating the donor safety in 100 cases ofLDLT. The authors concluded that donor surgery is safe and less complications when the left lobe or the left lateral segment were used as the liver graft. Miller et al[14] studied one hundred cases of LDLT from adult to pediatric recipients and found that donor surgery is safe and can be done with minimal complications.

Large scale study by Hwang et al[15] with 1,000 cases living liver donors found a low complication rate in left lobe graft surgery and most major donor complications are avoidable by strict selection of living donors and graft types, intensive postoperative surveillance, and timely feedback of surgical techniques.

This study has found bile duct complication in 2 cases, first case diagnosed after discharge of 1 week. Second case diagnosed while admitted. In both cases, bile leaked from minor duct that was successfully controlled by endoscopic therapy. In fact, prevention of bile duct injury can be done by preoperative MRCP or intraoperative cholangiography and both techniques can reduce the incidence of bile duct injury. Before the operation, we evaluated bile duct of all donors by using magnetic resonance cholangiopancreatography (MRCP) but in an emergency liver transplantation we were unable to evaluate by MRCP due to insufficient time. We use intraoperative cholangiography in an emergency case or inadequate preoperative bile duct evaluation. Taketomi et al[16] has recommended the procedures to prevent bile duct complications as the following: use a real-time cholangiography by the C-arm, minimized dissection of the hepatic vessels, meticulous closure of the bile duct, and/or the use of Pringle maneuver during the parenchymal transection.

This study has shown LDLT for pediatric patients is safe for donors, and it should be considered as the option for pediatric LT in the transplant centers that face the problems of organ shortage. In fact, LDLT can reduce waiting list mortality, particularly for the young children who suffer from cirrhosis. Successful LDLT program requires experienced multi-disciplinary team including surgeons, adult hepatologists, pediatric hepatologists, nurse coordinators, radiologists, pathologists, anesthesiologists, psychiatrists and social workers. In our center, we have established the living donor evaluation program, including careful history taking, physical examinations, psycho-

logical evaluation, screening blood tests, viral studies, volumetric computerized tomography of liver and MRCP. Percutaneous liver biopsy, echocardiography and other investigations are performed if they have clinical indications. We have had a multi-disciplinary meeting for operative plan before LDLT in all patients for successful operations and minimized the complications.

The limitation of our study is a low number of donor cases and short-term follow-up. Further studies with larger number of cases and long-term follow-up data are required.

In conclusion, living donor hepatectomy for pediatric recipients is associated with a low complication rate in an experience team. Although LDLT has a low complication rate, it still has some risks for the donors. Therefore, careful discussion the potential donors and their families regarding operative risks and potential complications before written informed consent is essential.In addition, an experienced surgical team and good pre-operative plan can decrease the operative complication rate.

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References

1. Jimenez-Rivera C, Jolin-Dahel KS, Fortinsky KJ, Gozdyra P, Benchimol EI. 1387 international incidence and outcomes of biliary atresia: A systematic review of opultion-ased studiies. J Hepatol 2012;56: S544-5.
2. Jimenez-Rivera C, Jolin-Dahel KS, Fortinsky KJ, Gozdyra P, Benchimol EI. International incidence and outcomes of biliary atresia. J Pediatr Gastroenterol Nutr 2013;56:344-54.
3. Porret PM, Olthoff KM. Current state of living donor liver transplantation. Clinical Liver Disease 2013;2: 160-4.
4. Olthoff KM, Abecassis MM, Emond JC, Kam I, Merion RM, Gillespie BW, et al. Outcomes of adult living donor liver transplantation: comparison of the Adult-to-adult Living Donor Liver Transplantation Cohort Study and the national experience. Liver Transpl 2011;17:789-97.
5. Middleton PF, Duffield M, Lynch SV, Padbury RT, House T, Stanton P, et al. Living donor liver transplantation-adult donor outcomes: a systematic review. Liver Transpl 2006;12:24-30.
6. Lo CM. Complications and long-term outcome of living liver donors: a survey of 1,508 cases in five Asian centers. Transplantation 2003;75:S12-5.
7. Hashikura Y, Ichida T, Umeshita K, Kawasaki S, Mizokami M, Mochida S, et al. Donor complications associated with living donor liver transplantation in Japan. Transplantation 2009;88:110-4.
8. Ueda M, Oike F, Ogura Y, Uryuhara K, Fujimoto Y, Kasahara M, et al. Long-term outcomes of 600 living donor liver transplants for pediatric patients at a single center. Liver Transpl 2006;12:1326-36.

9. Saidi RF, Elias N, Ko DS, Kawai T, Markmann J, Feng S, et al. Live Donor Partial Hepatectomy for Liver Transplantation: Is There a Learning Curve? Int J Organ Transplant Med 2010;1:125-30.

10. Muzaale AD, Dagher NN, Montgomery RA, Taranto SE, McBride MA, Segev DL. Estimates of Early Death, Acute Liver Failure, and Long-term Mortality Among Live Liver Donors. Gastroenterology 2012;142:273-80.

11. Wan P, Yu X, Xia Q. Operative outcomes of adult living donor liver transplantation and deceased donor liver transplantation: a systematic review and meta-analysis. Liver Transpl 2014;20:425-36.

12. Dindo D, Demartines N, Clavien P-A. Classification of Surgical Complications: A New Proposal With Evaluation in a Cohort of 6336 Patients and Results of a Survey. Annals of Surgery 2004;240:205-13.

13. Yamaoka Y, Morimoto T, Inamoto T, Tanaka A, Honda K, Ikai I, et al. Safety of the donor in living-related liver transplantation--an analysis of 100 parental donors. Transplantation 1995;59:224-6.

14. Miller CM, Gondolesi GE, Florman S, Matsumoto C, Munoz L, Yoshizumi T, et al. One hundred nine living donor liver transplants in adults and children: a single-center experience. Ann Surg 2001;234:301-11

15. Hwang S, Lee S-G, Lee Y-J, Sung K-B, Park K-M, Kim K-H, et al. Lessons learned from 1,000 living donor liver transplantations in a single center: How to make living donations safe. Liver Transplantation 2006;12: 920-7.

16. Taketomi A, Morita K, Toshima T, Takeishi K, Kayashima H, Ninomiya M, et al. Living donor hepatectomies with procedures to prevent biliary complications. Journal of the American College of Surgeons 2010;211: 456-64.

Original Articles/นิพนธ์ต้นฉบับ

ผลการผ่าตัดตับของผู้บริจาคตับที่มีชีวิตเพื่อการปลูกถ่ายตับในเด็ก: รายงานผู้ป่วย 100 รายในโรงพยาบาลรามาธิบดี

ณัฐพล อาภรณ์สุจริตกุล[1], สุรศักดิ์ ลีลาอุดมลิปิ[1], อาภัสนี โสภณสฤษฎ์สุข[2], สมคิด มิ่งพฤฒิ[3], สุทธิพงษ์ จงจิระศิริ[4], พงษ์ภพ อินทรประสงค์[2], ภาณุวัฒน์ เลิศสิทธิชัย[5], บัณฑิต สกุลชัยรุ่งเรือง[1], กรกช เกษประเสริฐ[1], วีระวร อริยขจร[1,6], สุทัศน์ ศรีพจนารถ[1]

[1] หน่วยศัลยศาสตร์หลอดเลือดและปลูกถ่ายอวัยวะ [3] หน่วยศัลยศาสตร์ตับ ตับอ่อนและท่อน้ำดี
[5] หน่วยศัลยศาสตร์เต้านมและต่อมไร้ท่อ ภาควิชาศัลยศาสตร์, [2] หน่วยโรคทางเดินอาหารและตับ ภาควิชาอายุรศาสตร์,
[4] ภาควิชารังสีวิทยา คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล, [6] โรงพยาบาลบำรุงราษฎร์ กรุงเทพ

บทคัดย่อ

บทนำ: การผ่าตัดปลูกถ่ายตับเป็นการรักษามาตรฐานสำหรับโรคตับวายเรื้อรังระยะท้าย โรคมะเร็งตับระยะต้น ตับวายเฉียบพลันทั้งในเด็กและผู้ใหญ่ ปัญหาการขาดแคลนอวัยวะจากผู้บริจาคสมองตายเป็นอุปสรรคของการผ่าตัดปลูกถ่ายตับจากผู้บริจาคสมองตายดังนั้นการผ่าตัดปลูกถ่ายตับจากผู้บริจาคที่มีชีวิตจึงได้ถูกนำมาใช้ในประเทศไทยมานาน 15 ปี

วัตถุประสงค์: เพื่อศึกษาผลทางคลินิกของผู้บริจาคที่มีชีวิตภายหลังการผ่าตัดตับเพื่อการปลูกถ่ายตับแก่ผู้ป่วยเด็ก

วิธีการ: เป็นการศึกษาเก็บข้อมูลย้อนหลังในผู้บริจาคตับที่มีชีวิตที่ได้ทำการแบ่งตับบริจาคให้ผู้ป่วยเด็ก ระหว่างปี พ.ศ. 2544-2558 โดยใช้ระบบ Clavien scoring system มาใช้ในการประเมินระดับความรุนแรงภาวะแทรกซ้อน

ผลการศึกษา: ผู้บริจาคตับที่มีชีวิตให้ผู้ป่วยเด็กเข้าร่วมการศึกษาจำนวน 100 ราย ได้ถูกทำการผ่าตัดตับเพื่อบริจาคตับด้วยศัลย์แพทย์ทีมเดียวกันตลอดการศึกษา ผลการศึกษาไม่พบภาวะแทรกซ้อนจำนวน 91 ราย ภาวะแทรกซ้อนที่พบได้แก่ ปัญหาแผลผ่าตัดจำนวน 6 รายคิดเป็นร้อยละ 6 ปัญหาท่อน้ำดีรั่วซึมจำนวน 2 รายคิดเป็นร้อยละ 2 ปัญหาท่อน้ำดีได้รับบาดเจ็บจำนวน 1 รายคิดเป็นร้อยละ 1 และมีผู้ป่วยจำนวน 2 รายที่ต้องนอนโรงพยาบาลซ้ำรอบสอง

สรุป: การผ่าตัดตับบริจาคจากผู้บริจาคที่มีชีวิตให้กับผู้ป่วยเด็กมีภาวะแทรกซ้อนน้อยในทีมผ่าตัดที่มีความชำนาญ

คำสำคัญ: living donor, liver donor, pediatric liver transplantation, complication

Corresponding author: ณัฐพล อาภรณ์สุจริตกุล
หน่วยศัลยศาสตร์หลอดเลือดและปลูกถ่ายอวัยวะ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล
โทรศัพท์ 662-201-1304, 087-003-4787 โทรสาร: 662-201-1304