Special Article

Evaluation of Donors for Living Donor Liver Transplantation (LDLT)

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Liver transplantation has been the last resort of definite treatment for decompensate cirrhosis, early-stage of hepatocellular carcinoma, and acute liver failure. Organ shortage is the major obstacle of deceased-donor liver transplantation. Since the first case of living-donor liver transplantation (LDLT), many centers around the world started the LDLT program. Living donors should be informed about the possible risk of morbidity and mortality, and later give consent for liver donation without coercion. Donor selection and evaluation have become one of the important steps prior to LDLT, aiming to exclude donors who may have high risks from LDLT and to assure that LDLT recipients will receive perfect liver grafts. In Thailand, living donors must have been blood relatives or be legally married with recipients for at least three years. Donor evaluation can be divided into three step-by-step phases. Psychological evaluation of living donors is also included in pre-transplant assessment.

Keywords: *Evaluation, Liver transplantation, Deceased donor, Living donor*

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Regular alcohol consumption, hepatitis B, and hepatitis C viral infection are three major causes of cirrhosis and hepatocellular carcinoma in Thailand. Liver transplantation is the recommended treatment for decompensate cirrhosis, early stage of hepatocellular carcinoma, and acute liver failure. Since the first case of deceased-donor liver transplantation (DDLT) done in 1984, the number of DDLT has been proliferated worldwide[1]. However, the progress of DDLT in Asia has been hampered by the shortage of brain-dead donors[1]. The primary barriers of DDLT in Asian countries are the cultural and religious beliefs of people for organ donation after death[1]. Numerous patients with liver diseases died while waiting for liver transplantation[1]. The first case of living donor liver transplantation (LDLT) was performed in Asia in 1989. Until now, LDLT has been done in more than 12,000 cases[2]. At the beginning of the LDLT programs, only left lobe grafts were transplanted to pediatric recipients. Left lobe graft is such a small-sized graft for adult recipients to meet their metabolic and energy demand. The first right-lobe LDLT in adult recipients was reported from Japan in 1994[3]. Since then, right-lobe LDLT has been widely performed not only in Asian but also in Western countries. A recent report from a large US liver-transplant database revealed that patient survival following LDLT was slightly better than that of DDLT[4].

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Advantages and potential risks of LDLT

The decision of LDLT should only occur when the outcome after LDLT is at least equal to the outcome after DDLT, and more importantly, the chance of recipient death on the waiting list is higher than the potential risks and harms of the living donors and recipients[5]. Patients who are destined for LDLT should have indications similar to the ones who are planned for DDLT except that recipients in LDLT will receive liver grafts much sooner than those in DDLT. Similar to DDLT recipients, morbidity and mortality can occur in LDLT recipients and living donors as well. Before LDLT, living donors should be informed in details about the potential risks and complications that can happen to the living donors and recipients, and alternative treatment for recipients if LDLT is not feasible[6-10]. From previous reports, recipient complication rates tend to

be greater following LDLT than DDLT[11]. Right lobe LDLT is related to increased morbidity and more severe complications than left lobe LDLT[12]. Mortality approaches 0.5% for the right lobe donors and was 0.1% for the left lobe donors[12]. The objectives of donor selection are to exclude donors with medical or psychological problems that may be harmful to donor health and well-being from live liver donation. Donor selection with appropriate evaluation guarantees that recipients will receive high-quality and suitable liver grafts, and there were minimal risks on donors and recipients from LDLT. Short waiting time is one of the important advantages from LDLT. Patients with decompensate cirrhosis or hepatocellular carcinoma do not need to be on the long waiting list of liver transplantation, especially in a country like Thailand that has had the problem of organ donation scarcity. Small children with end-stage liver diseases, liver cancer, or acute liver failure may never have liver transplantation from DDLT mainly because of the mismatch between body size and liver grafts from deceased donors. Liver grafts with high quality can be selected through the process of donor selection and evaluation before LDLT. Operating time can be scheduled electively if LDLT is chosen[6-10]. Living donation creates mutual feeling and relations between donors and recipients such as parents and their children, husbands and wives, etc.

Evaluation of donors for living donor liver transplantation

In Thailand, potential living donors must have very close ties with recipients such as having true biological relationship or having been legally married for more than three years. Furthermore, they must not have financial benefit from organ donation. Potential donors must be healthy people aged between 18 and 55 years old[6]. The use of older donor livers is one of the important risk factors for the poor outcome after liver transplantation[13]. Body size matching between donors and recipients is a key preliminary consideration in the donor evaluation process. The lower limit of liver graft acceptability is about 0.8% for graft-recipient body weight ratio (GRBW) and 40% for the percentage of standard liver mass[6,8,9]. Living donors should be healthy subjects without medical and psychological problems. The primary purpose of a donor evaluation process is to identify donors who are likely to have a high risk of morbidity and mortality if LDLT is done. Only 30% of the potential recipients for LDLT in a dedicated liver transplant program can identify potential living donors[14]. Furthermore, only 40-65% of the potential living donors who had formal evaluation were found to be acceptable living donors[14-16]. The characteristics of donors associated with the acceptance for LDLT were younger age; lower body mass index and having biological or spousal relations with the recipients [15]. The process of donor evaluation can be divided into 3 phases, starting from basic laboratory investigation to advanced but invasive investigation as following (Table 1).

The first phase

Potential donors are told of the details of indications for liver transplantation, the risk of donor and recipient morbidity and mortality, and alternative treatment of recipients. Then, they will be asked without coercion, whether they are willing to donate a part of

Table 1. Proposed phases of donor evaluation

Phase 1	Having biological relationship or legally married for more than three years
	Age 18-55 years
	Blood group identical or compatible
	Fully informed of potential risks (of both donors and recipients) and alternative treatment for recipients
	Willing to donate without coercion
	Physical examination
	Basic laboratory tests (: blood group, complete blood count, liver function and biochemical test)
Phase 2	Serologic tests (HBsAg, anti-HBc IgG, anti-HCV, anti-HIV, VDRL, FTA-ABS, EBV, CMV, HSV)
	Chest x-ray
	EKG
	Psychosocial evaluation
Phase 3	Multidetector computed tomography (MDCT) whole abdomen (with CT volumetry and CT angiogram)
	Liver biopsy (if indicated)
	Magnetic resonance cholangiopancreatography (MRCP) (if indicated)

their liver. Living donors and recipients should have compatible blood groups[1]. Nevertheless, the use of incompatible blood groups may be allowed in infants who are younger than 1 year old with emergency indications[2].

The second phase

Blood tests were done for serologic work-up of viral hepatitis, syphilis, herpes simplex virus, Cytomegalovirus and Epstein-Barr virus. Psychosocial evaluation is aimed to assess psycholosocial well-being and emotional stability of living donors and to consider if living donors give informed consent for liver donation voluntarily[17]. Potential living donors are usually the family members of recipients, thus living donors may feel subconsciously compelled to donate parts of their livers. Furthermore, living donors may face some stress on direct and indirect cost of surgery including the cost of living during a short period of inability of work. Formal psychosocial evaluation by expert psychiatrists, and financial evaluation by social workers play an important part of the living donor evaluation process[18].

The third phase

More sophisticated and invasive investigations are included in the third or last phase. Nowadays, multidetector computed tomography (MDCT) abdomen (with CT volumetry and CT angiogram) is the standard investigation in the process of living donor evaluation. Magnetic resonance cholangiopancreatography (MRCP) and liver biopsy are only recommended in living donors who have exceptional indications. Pre-liver transplant imaging study of the living donors is important in exclusion of focal lesions (a large liver mass, etc) and diffused parenchymatous liver diseases (fatty liver diseases), evaluation of vascular and biliary anatomy and its variants[17,19]. The imaging study can also assess liver volume before liver transplantation[17,19]. Arterial and portal venous variants are found in about 42% and 10% of cases, respectively[19]. CT angiography or MR angiography allows a comprehensive assessment for hepatic arterial and portovenous system[17,19]. The variants of biliary system are more common than those of vascular anatomy, but they do not generally affect candidacy for liver donation[9]. Although postoperative biliary complications are common in 15-40% of living liver transplant recipients and in 4-13% of living donors, the evaluation of biliary anatomy is not always required during the process of living donor evaluation[9]. MR cholangiography (MRCP) is an alternative study of non-invasive imaging for evaluation of biliary tract anatomy pre-operatively instead of intraoperative cholangiography, which is the invasive gold standard[17]. Ideally, radiologic work-up with 'all-in-one' imaging protocol (for instance CT scan, CT angiography, CT volumetry and CT cholangiography) are helpful, cost-effective and time-saving[20]. The minimal liver volume of 40% of the total liver volume with the estimated graft liver volume to a recipient body weight ratio (GBWR) of an at least 0.8-1.0 would provide enough liver function for the LDLT recipients[17,19]. In LDLT, small-for-size graft syndrome is one of the important causes of graft dysfunction due to inadequate functional mass of the liver graft and excessive portal perfusion[17,19]. The correlation between liver volume by CT volumetry and the actual weight of liver graft is reported to be high[17,19,21]. Furthermore, the virtual hepatectomy done by CT volumetry is helpful for pre-transplant plan for LDLT. Steatosis was found in 9-26% of liver donors[22]. Conditions frequently relating to steatosis include obesity, diabetes mellitus, regular alcohol drinking, drugs, steroids, female, and metabolic disorders[22]. Steatosis in liver grafts leads to primary non-function, graft dysfunction, and impaired regenerative capacity of the liver by reducing a functional hepatic mass and increasing ischemia-reperfusion injury risk[8,22]. Poor graft survival is frequently seen in liver transplantation with liver grafts with moderate or severe steatosis. The result from a previous study suggested that the degree of steatosis increases as BMI increases[23]. The reports of the accuracy of imaging studies to quantify the degree of hepatic steatosis showed conflicting results[24,25]. Thus, liver biopsy remains the gold standard for assessing the amount of steatosis despite its risks of complications and mortality in a few cases[22]. Liver biopsy is recommended in living donors with abnormal liver function tests or imaging studies, body mass index more than 28 kg/m^2, history of substance abuse or family history of genetic or immune-mediated liver diseases[8,9,12,26]. The Vancouver Forum suggested that liver biopsy should be done for the presence of abnormal liver function tests, steatosis on imaging studies or with body mass index higher than 30 kg/m^2[8,12]. By following the Vancouver Forum recommendation, liver biopsy can be avoided in 78% of living donors[26]. The maximal acceptable amount of steatosis in living donor livers among several transplant centers varies from 10% to 30%[9]. The other conservative approach was reported from a Taiwan group[8]. For living donors found to have steatosis from non-invasive investigation, they would be encouraged to be enrolled in a weight reduction

program first in order to have better control of blood glucose and lipid levels and to increase exercise because short-term weight reduction program for living donors is proved to clear hepatic steatosis[27]. The Taiwan group performs liver biopsy if ultrasound or CT scans show hepatic steatosis or in people with BMI greater than 28 kg/m^2[8].

In conclusion, living donor evaluation, one of the most important processes in living donor liver transplantation, is carried out to assure the donor safety and the high-quality of liver grafts for recipients. It consists of medical, radiological, and psychological assessment. Furthermore, voluntary donation with understanding of live donation is strongly enforced along the entire process.

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การประเมินผู้บริจาคตับเพื่อการผ่าตัดปลูกถ่ายตับจากผู้บริจาคมีชีวิต

อาภัสณี โสภณสฤษฎ์สุข, พงษ์ภพ อินทรประสงค์, ศศิณี ทองประเสริฐ

การผ่าตัดปลูกถ่ายตับได้รับการยอมรับว่าเป็นการรักษาขั้นสุดท้ายของโรคตับแข็งระยะปลาย โรคมะเร็งตับระยะต้น และโรคตับวายเฉียบพลัน ปัญหาการขาดแคลนอวัยวะเป็นอุปสรรคที่สำคัญของการผ่าตัดปลูกถ่ายตับจากผู้บริจาคสมองตาย หลังจากการผ่าตัดปลูกถ่ายตับจากผู้บริจาคที่มีชีวิตเป็นครั้งแรก จากนั้นมาโรงพยาบาลต่าง ๆ ทั่วโลกได้เริ่มทำการปลูกถ่ายตับจากผู้บริจาคที่มีชีวิตจนเป็นที่แพร่หลาย ก่อนการผ่าตัดปลูกถ่ายตับ ผู้บริจาคที่มีชีวิตควรได้รับข้อมูลอย่างครบถ้วนเกี่ยวกับโอกาสเสี่ยงของการเกิดภาวะแทรกซ้อนที่อันตรายจนอาจสูญเสียชีวิตในบางครั้ง และให้ความสมัครใจบริจาคตับบางส่วนโดยไม่มีการบังคับ การคัดเลือกและประเมินผู้บริจาคที่มีชีวิตกลายมาเป็นขั้นตอนที่สำคัญของการปลูกถ่ายตับจากผู้บริจาคที่มีชีวิต โดยมีจุดประสงค์เพื่อคัดกรองผู้บริจาคที่คาดว่าจะมีความเสี่ยงจากการผ่าตัดปลูกถ่ายตับออกไป และเพื่อให้ผู้ป่วยได้รับตับจากการบริจาคที่มีคุณภาพสมบูรณ์ ในประเทศไทยมีข้อกำหนดไว้ว่าผู้บริจาคที่มีชีวิตจำเป็นต้องมีความสัมพันธ์ทางสายเลือดกับผู้ป่วย หรือ ได้สมรสอย่างถูกต้องตามกฎหมายเป็นเวลาอย่างน้อยสามปี การประเมินผู้บริจาคที่มีชีวิตอาจแบ่งได้เป็นสามระยะตามลำดับขั้นตอน การประเมินสภาพของจิตใจของผู้บริจาคที่มีชีวิตได้ถูกจัดไว้ในขั้นตอนการประเมินการผ่าตัดปลูกถ่ายตับเช่นเดียวกัน