Early Outcome of Donors in Living-Donor Liver Transplantation at King Hussein Medical Center

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ABSTRACT

Objectives: To evaluate the safety and early outcome of donors who underwent partial hepatectomy for Living donor- related Liver Transplantation at King Hussein Medical Center (Amman- Jordan).

Methods: We retrospectively reviewed 28 living donors who underwent liver resections (21 right lobes, 5 left lobes, 2 left lateral lobes) for living donor liver transplantation at King Hussein Medical Center. The procedures were performed over a period of four years from June 2004 till August 2008.
Donor characteristics, operative times, blood loss, hospital stay, and complications as graded by Clavien's classification were recorded. Donors were followed- up for a mean period of 8.5 ± 1.91 months (range 6-12 monthes). Simple descriptive statistical methods (frequency, mean and percentage) were used to describe the study variables

Results: A total of 54 potential candidates for living-donor liver transplantations were evaluated. Of these, 28 underwent successful hepatectomy for donation. Male to female ratio was 21:7. The mean age was 28.89 ± 1.30(range 19- 49) years. A total of 26 potential donors (48%) were excluded at different points of the work-up. The mean operative times were 6.07 ± 1.12 (rang = 4-8 hours). The mean intraoperative blood loss were 428.5 ±296.9 (range: 50 to 1500ml), (intraoperative blood transfusion was required for one donor).

Conclusion: Donor hepatectomy in living-donor liver transplantation is a safe procedure. Meticulous and comprehensive selection protocols are a prerequisite for a good outcome.

Key words: Early outcome, Donor hepatectomy, Liver transplantation.

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Introduction

Living Donor Liver Transplantation (LDLT) is the treatment of choice and the hope for patients with end-stage liver disease in Jordan where the waiting mortality is high and the availability of deceased donor is almost absent due to the presence of strong cultural, traditional and religious beliefs.[1]

The history of liver transplantation dates back to 1963 when Starzl in Colorado first attempted Cadaveric Liver Transplantation (CLT) in humans. Following this failed trial, the first successful CLT was also performed by Starzl in 1967 and long-term results were then reported.[2] The first successful LDLT in an adult recipient was performed in Japan in 1994 because of limited availability of cadaveric grafts in this country.[3]

A left-lobe graft could provide only 30 to 50% of the required liver volume for adult recipients and thus tended to be too small for adult recipients to sustain their metabolic demands.[4]

Recently, right-lobe donation has become the standard procedure to overcome the graft size problem, with good initial results reported in both donors and recipients. The concept of left-lobe donation for adult recipients has now been almost completely abandoned. To solve these size

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Table I: Current donor evaluation protocol

Basic: 20–60 years
Requirements Relationship: relatives or unrelated volunteers
Blood type: identical or compatible
Step I Clinical evaluation: initial informed consent, history and physical examination
Laboratory: blood group, liver and renal function
Serology: HBsAg, HBsAb, HBcAb, anti-HCV, anti-HIV
Step II Clinical examination: psychological evaluation
Laboratory: hematology, coagulation profile, blood sugar, electrolytes, cross-matching, alpha-1- antitrypsin, ferritin, tumor markers (AFP, CEA,CA199), arterial blood gas, urine and stool analysis, pregnancy test (female)
Serology: HBV DNA, RPR, antibody for CMV, EBV, HSV, varicella and rubella viruses
Imaging study: Chest radiograph, abdominal ultrasound, ECG
Step III Imaging study: CT angiography and volumetry, MRC

problems, especially in Western countries, right lobes accounts for approximately 2/3 of the entire liver volume, and provides a graft capable of size-for size, donor-to-recipient weight ratio or even smaller donors to donate to larger recipients.[5] Moreover, it has been suggested that a graft-to-recipient weight ratio of 1.0% appears to be a safe limit for adult recipients, regardless of the cause of disease.[5] Nonetheless, the overwhelming benefit of LDLT for critically ill patients with end-stage liver disease should not undermine our concern for the safety of donors.

The first role in medicine is "first do no harm". On the surface, adult-to-adult LDLT disagrees with this principle, because a healthy individual undergoes a major operation for no direct, physical benefit.[6]

The primary barriers of Deceased Donor Liver Transplantation (DDLT) in Asian countries are the cultural and religious beliefs of people for organ donation after death. Therefore most the patients with liver diseases died while waiting for liver transplantation.[7]

Still there is considerable debate concerning donor safety despite great results with LDLT. Risks to the donor include those associated with invasive pre-surgical testing and the surgical procedure. These risks are accepted by potential donors when they know that the patient's life may be saved without the uncertainty of a cadaveric waiting list. This study was conducted to evaluate the safety and early outcome of donors who underwent partial hepatectomy for Living donor- related Liver Transplantation at King Hussein Medical Center (Amman- Jordan).

Methods

Between June 2004 to August 2008, a total of 54 candidate donors underwent multistep evaluation at King Hussein Medical Centre after obtaining approval from Royal Medical Services Ethical Committee and a written informed consent.

Twenty-six (48%) were excluded at one step of the evaluation. A total of 28 consecutive LDLTs (21 right lobes, 5 left lobes and 2 left Lateral lobes) were performed.

Evaluation and Selection of Donors

The donor evaluation protocol was designed for testing. It started from simple and noninvasive to more complex and invasive, assuming continued donor willingness and lack of contraindications to donation. Testing assured the donor safety and then evaluated the quality of graft. The minimal age accepted for consideration was 19 years with the upper age limit 55 years.

The donor-recipient pair must be blood-group identical or compatible. The donor evaluation protocol followed at our center is outlined in Table I.

When a potential recipient came to our center, he and his family members were informed of the need for an early liver transplantation, and they agreed to receive LDLT, and then the risks and benefits of the procedure would be explained in general. The written informed details focused on the evaluation protocol, with concentration on invasive testing, surgical procedure, and all possible risks of the donor hepatectomy. The donor should make the decision voluntarily, without any emotional pressure.

To reduce the pressure on potential donors, informed consent was obtained in the absence of other family members. The donor can withdraw at any time, with the assurance that an excuse would be provided by the transplant team.

The evaluation of donors for medical or surgical suitability could be continued only after informed

Fig. 1: Liver volumetry (RT Lobe)

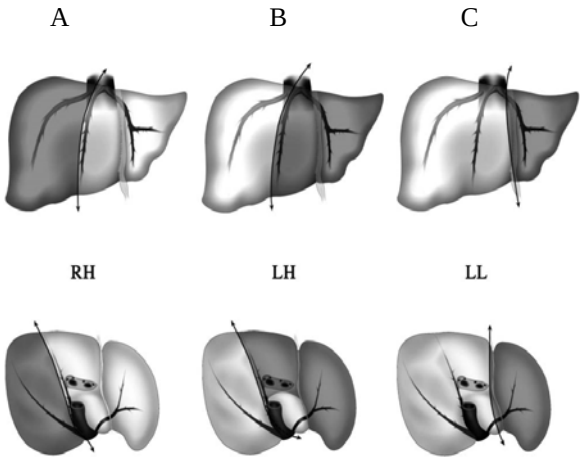

Fig. 2: (A) Right-lobe graft. (B) Left-lobe graft. (C) Left lateral segment graft.

consent was made. Acute or chronic medical illness was excluded by a detailed history and physical examination, and all donors were screened by laboratory tests including complete blood cell count, liver and renal biochemistry values, and viral serologic studies. Positivity of Hepatitis B surface antigen, Human Immunodeficiency Virus antibody, or hepatitis C virus antibody constituted an outright ineligibility of the potential donor. Donors with Diabetes Mellitus or hypertension even under regular control were rejected. The psychological status of the potential donor was assessed by a clinical psychologist. Abdominal ultrasonography (US) was performed to evaluate the quality of liver parenchyma, exclude the presence of tumors, and confirm the patency of blood vessels. Chest radiography and Electrocardiography were performed to exclude cardiopulmonary disease. Computed tomography (CT), CT volumetry, multiple detector three-dimensional CT angiography, and three-dimensional Magnetic Resonance Cholangiography (MRC) were performed to assess liver volume and identify unsuspected intra-abdominal pathology and anomalous vasculature incompatible with donation. Liver biopsy was not routinely performed in our center. If there was radiographic evidence of fatty infiltration or parenchymal liver disease, even with normal liver function, echo-guided liver biopsy of the segments to be donated was performed (it was for five donors to rule out steatohepatitis).

After completion of each step, the donors' statuses were reevaluated and a decision of whether to proceed was made by the transplant team.

Donor evaluation continued in the operating room with intraoperative cholangiography and ultrasonography.

Liver Volumetry:

Volume studies were performed pre-operatively using CT volumetry images. The volume of each graft was calculated (Fig. 1).

Overall, the total volume of the liver resected was highly correlated to the predicted liver volume. The Right Hepatic (RH) graft volume is usually significantly higher than Left Hepatic (LH) or Left Lateral (LL) as well as LH compared with LL.

The most important issue for the donor is the mean residual volume after RH and was estimated to be 41%, 71% after LH and 82% after LL. The smallest remnant observed after RH was 30%, accounting for 0.6% of body weight. The largest remnants of the RH group accounted for 0.9% of body weight. In contrast, all remnants for the LH and LL were greater than 1% of body weight. So, highly significant differences in parenchyma resection were observed between RH and LH or LL.

Donor Hepatectomy:

Donor hepatectomy was performed under general endotracheal anesthesia and monitored by a single transplant anesthesia team. A long midline incision was used for Left Lobectomy (LL) with a standard (J) liver transplant incision for the left and Right Hepatectomies (RH) and in some donors Mercedes incision.

Three hepatectomies were defined according to the segmental anatomy of Couinaud.[8] LL for resection of segments II and III, left hepatectomy (LH) for segments II, III and IV, and RH for segments V, VI,

Table II: Evaluated donor demographic characteristics (No. = 28)

Donor Demographics	Evaluated and accepted donors
Age	19-49 (mean 28.89 ± 1.30)
Gender	Male 21, Female 7
Relationship to recipient	Mother 1 Father 4 Wife 1 Sister 5 brother 6 son 10 Nephew 1

Table III: Underlying diseases of transplant recipients

Recipients Diseases	Number
Hepatitis B Virus (HBV)	7
HBV+ Hepatocellular carcinoma (HCC)	1
Auto Immune Hepatitis (AIH)	6
Cryptogenic	3
Primary Sclerosing Cholangitis (PSC)	1
Progressive Familial Intrahepatic Cholestasis (PFIC)	2
Hepatitis C Virus (HCV)	3
Congenital Hyperbilirubinemia	1
Histocytosis	1
Primary Hyper Oxalosis	1
Biliary Atresia	1
Hepatoblastoma	1

Table IV: Causes of donor's exclusion

Causes of exclusion	Number
ABO incompatibility	9
Positive hepatitis serology	7
Liver anatomy anomalies	5
Effects from family, relatives and society	3
Fatty liver	2

Table V: Overall donor complications

Overall Complications (28.5%)	Number	Clavien's classification
Atelectasis	2	Grade I:-4(14%)
Infection	2	
Pneumonia	1	Grade II: 2 (7%)
Bleeding (no re-op)	1	
Pleural eff. (drain)	1	Grade III: (7%)
Biliary leak (drain)	1	
		Grade IV : 0 Grade V : 0

VII and VIII resection. There were 2 LL, 21 RH and 5 LH. In most cases of RT hemihepatectomies the parenchyma was transected to the right of the middle hepatic vein. We used the ultrasonic dissector (CUSA) for parenchymal transecting and then the vascular pedicle was divided after transection of the liver parenchyma. Right hepatectomy was conducted by dissecting the RT triangular ligament of the liver with ligation of the short hepatic veins and then passing a tape behind the liver and between the right and middle hepatic veins (hanging) in the plane of transection, thereby guiding the parenchymal division. Cholecystectomy; right hepatic artery identification; right portal vein identification; biliary ducts dissection; finally parenchymal transection and pedicle division. Left hepatectomies were conducted with first dissection of left and middle hepatic veins; cholecystectomy; left hepatic artery identification; left portal vein identification with mobilization of the caudate lobe portal veins and dividing the bile ducts. For LL, left hepatic vein was dissected; left hepatic artery; left portal vein identification with mobilization of all branches.

The three hepatectomies are shown in (Fig. 2): right hepatectomy, left hepatectomy, and left lateral lobectomy.

Follow-up:

Outcomes related to complications and ongoing symptoms were defined according to Clavien's classification.[9]

A specific research assistant was in charge of the whole follow-up. The methods were taken including record table, telephone follow-up and return visit.

Simple descriptive statistical methods (frequency, mean and percentage) were used to describe the study variables

Results

A total of 54 candidate donors were evaluated for LDLT at our center. Of these, 28 underwent successful hepatectomy for living donation. The mean age of donors 28.89 ± 1.30 (range 19 to 49) years. Twenty-eight donors fulfilled relationship with the third degree of consanguinity. Demographics characteristics of evaluated donors are listed in Table II. The mean age of transplant

recipients 35.04 ± 15.58 (range: 3-57 years). The underlying diseases of transplant recipients are listed in Table III.

A total of 26 potential donors (48%) were excluded at different points of the work-up. Positive hepatitis serology and ABO incompatibility were the main contraindications to donation. After the first step, volunteers withdrew from donation due to effects from family, relatives and society, with society being some of the reasons for exclusion. The reasons for exclusion listed in Table IV.

The mean duration of the operation from skin incision to closure was 6.07± 1.12 (range 4 - 8) hours and the mean intraoperative blood loss was 428.57 ± 297.96 (range 50- 1500) ml. Intraoperative blood transfusion was required for one donor. The mean stay of donors in the intensive care unit (ICU) was 1.2 ± 0.4 d and the mean hospital stay was 6.43 ± 1.32 (range 5 - 9) days for left lobe and left lateral donation, and 9.68 ± 2.93 (range 8-20) days for right lobe donation.

In the immediate postoperative period, all donors exhibited a significant transient elevation of liver enzymes and hyperbilirubinemia on postoperative day one.

Normalization of serum transaminases and total bilirubin was accomplished by postoperative days 5 to 7. In contrast, prothrombin time exhibited a mild postoperative elevation that declined to normal level within 3 days.

The mean follow-up time was 8.54 ± 1.9(range 6-12) months. Follow-up was not lost for anyone. The mean recovery time of 28 donors who were followed up for more than 6 months, was 2.875 ± 0.715 (range 2- 4) months, the mean time to return to work was 5.0 ± 1.0 months, and 13 of them returned to normal work even earlier.

No re-operation was performed and no deaths occurred in this series, while morbidity rate was 8 (28.5%). Four experienced grade I (minor) complications, two experienced grade II, two experienced grade III, none had grade IV or grade V according to Clavien classification. Donor complications are shown in Table V.

Discussion

Liver transplantation is the only life-saving treatment for patients with end-stage liver disease. Because of the rarity cadaveric donor organs in Asia, (due to the cultural and religious beliefs of people with acceptance of brain-death criteria), and variable shortages in most other parts of the world, the idea of partial liver donation to help save the life of a family member has considerable appeal, but reliable information about risks must be provided to prospective donors. The development of LDLT in Jordan experienced two stages: Pediatric Living Donor Liver Transplantation (PLDLT) and Adult-to-Adult Living Donor Liver Transplantation (ALDLT). To ensure the safety of donors, we identified three basic principles for the selection of donors: independent decision on donation, no contraindication for donation, and avoidance of obligation in the process of donation. These principles were strictly fulfilled with no exceptions.

LDLT was performed on the premise that the donor liver could be divided into two separate parts, the remnant liver in the donor would regenerate quickly, and the donor would not be injured operatively.[10] An essential part of LDLT is to perform donor hepatectomy with minimum risk while preserving graft viability.[11] Our operative time was 6.07± 1.12 (range 4-8 hours) and is nearly comparable to the other center 7.6±0.8 hours (range 6.8-10.3 hours).[10]

The adult-to-child living liver transplantation was first successfully performed in 1989 and accounts for 10% of pediatric liver transplants in the United States, while ALDLT was first performed in 1993 and accounts for approximately 3% of adult liver transplants in the United States.[12] Applying the principle of justice to LDLT is also complex, and nobody knows whether a procedure that violates the principle 'above all, do no harm' can be justified.[13] Exposing a healthy volunteer to operative insults can be justified only when donor risk is minimized to an acceptable degree. In practice, complete prevention of donor complications is not feasible, but many of them appeared to be prevented or ameliorated.[14]

To the authors' knowledge, there have been 12 deaths of right-lobe donors and three deaths of left-lobe donors worldwide. Additionally, two donors have required liver transplantation themselves as the result of operative complications.[15] The overall mortality is 0.2% in relation to the total number of liver donations worldwide and the risk of death for donors of a left lateral segment or a left lobe is estimated to be approximately 0.1%, whereas the risk for donors of a right lobe is estimated to be approximately 0.4 to 0.5%.[8,16] Donor death has occurred in both experienced and inexperienced centers. Lack of vigilance and loosening of acceptance criteria are the major reasons for the

donor mortalities. To avoid further donor death, the transplant surgeon should maintain his role as the gatekeeper in preventing unjustified and risky donor operations. Finally, he should have full commitment of life-long and holistic care of the donors.

A right lobe hepatectomy has a major issue of concern for LDLT to the donors because of the greater extent of resection and the higher expected risk, and it is known that the risks associated with right hepatectomy vary and that they depend primarily on the volume of the remnant left liver, which must be sufficient so that the donor is not at risk of developing liver failure post-donation.[5, 17]

Selection and evaluation of a living liver donor for adult recipients is a complex process that involves optimizing graft size in relation to the safety of donors and recipients, technical details of liver procurement, and ethical problems of using nonrelated live donors, so partial liver donation can be performed safely with a relatively low-risk of major perioperative morbidity.[1,18]

No effort should be spared in avoiding complications by appropriate patient selection, controlling blood loss, meticulous surgical technique, and postoperative care.[19] However, donor hepatectomy in a healthy population, should be taken as a situation different from that encountered in the oncologic field.[20]

In our center, we strictly followed our protocol; a careful and comprehensive work-up for selection and evaluation of the donors was made to decrease mortality and morbidity rate to the range of the other centers in the world. All our donors returned to their normal life and work.

Conclusion

Donor hepatectomy in living-donor liver transplantation is a safe procedure. Meticulous and comprehensive selection protocols are a prerequisite for a good outcome.

References

1. **Li F, Yan L, Zeng Y, Yang J, *et al.*** Donor safety in adult living donor liver transplantation using the right lobe: Single center experience in China. *World J Gastroenterol* 2007; 13(27): 3752-3755.
2. **Ng K, Lo C.** Liver transplantation in Asia: past, present and future. *Ann Acad Med Singapore* 2009; 38:322-331.
3. ***Broering DC, Wilms C, Bok P, et al.*** Evolution of donor morbidity in living related liver transplantation, single-center analysis of 165 cases. *Ann Surg* 2004; 240: 1013-1026
4. **Soejima Y, Shimada M, Suehiro T, *et al.*** Outcome analysis in adult-to-adult living donor liver transplantation, using the left lobe. *Liver Transplantation* 2003; 9(6): 581-586.
5. **Cho J, Suh K, Kwon C, *et al.*** Outcome of donors with a remnant liver volume of less than 35% after right hepatectomy. *Liver Transpl* 2006; 12:201-206.
6. **Robert S Jr, Brown SR.** Live donors in liver transplantation. *Gastroenterology* 2008; 134(6): 1802-1813.
7. **Sobhonslidsuk A, Intaraprasong P, Tongprasert S.** Evaluation of donors for living donor liver transplantation (LDLT). *J Med Assoc Thai* 2010; 93(5): 637-641
8. **Renz J, Reichert P, Gordon S, Emond J.** Surgical anatomy of the liver. In: R Busuttil and G Klintmalm, editors. Transplantation of the liver.2nd ed. RD546.T643 2005, and ch 26, Outcomes of living donor liver transplantation. eg: network Philadelphia: Elsevier, 2005:713-724.
9. **Chan S, Fan S, Lo C, *et al.*** Toward current standards of donor right hepatectomy for adult-to-adult live donor liver transplantation through the experience of 200 cases. *Ann Surg* 2007; 245: 110–117.
10. **Wen T, Chen Z, Yan L, *et al.*** Measures for increasing the safety of donors in living donor liver transplantation using right lobe grafts. *Hepatobiliary Pancreat Dis Int* 2007; 6: 590-595
11. **Sugawara Y, Makuuchi M, Takayama T, *et al.*** Safe donor hepatectomy for living related liver transplantation. *Liver Transplantation* 2002; 8:58-62.
12. **Bramstedt K.** Living liver donor mortality: where do we stand? *Am J Gastroenterol* 2006; 101:1-5.
13. **Nadalin S, Bockhorn M, Malago´ M, *et al.*** Living donor liver transplantation. *HPB* 2006; 8: 10-21.
14. **Hwang S, Lee S, Lee Y, *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: 920-927.
15. **Florman1 S, Miller C.** Live donor liver transplantation. *Liver Transpl* 2006, 12: 499-510.
16. **Walter J, Burdelski M, Bröring C.** Chances and risks in living donor liver transplantation. *Dtsch Arztebl Int* 2008; 105(6): 101-107.
17. **Ibrahim S, Chen C, Wang C, *et al.*** Small remnant liver volume after right lobe living donor hepatectomy. *Surgery* 2006; 140: 749-755.
18. **Patela S, Orloffa M, Tsoulfasa G, *et al.*** Living-Donor liver transplantation in the United States: identifying donors at risk for perioperative complications. *Am J Transpl* 2007; 7: 2344–2349.
19. **Azzam A, Uryuhara K, Taka I, *et al.*** Analysis of complications in hepatic right lobe living donors. *Ann Saudi Med* 2010; 30(1):18-24.
20. **Burcin Taner C, Dayangac M, Akin B, *et al.*** Donor safety and remnant liver volume in living donor liver transplantation. *Liver Transplantation* 2008; 14: 1174-1179.