

Living Donor Liver Transplantation with Dual Grafts - A Case Report

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Rezumat

Transplant hepatic de la donator viu cu graft dual - prezentare de caz

Introducere: Transplantul hepatic de la donator viu (THDV) expune la riscuri atât donatorul, datorită potențialului de a rămâne cu un volum hepatic rezidual insuficient, cât și primitorul, cu risc de inducere a sindromului de small-for-size. Folosirea a două grefe de la donatori diferiți poate evita riscurile mai sus menționate. Această lucrare prezintă un caz de THDV cu grefă duală folosind un hemificat drept și o secțiune hepatică laterală stângă de la donatori înrudiți.

Prezentare de caz: THDV cu grefă duală a fost efectuat la o pacientă în vârstă de 14 ani, diagnosticată cu insuficiență hepatică prin boala Wilson (scor MELD de 25), folosindu-se hemificatul drept cu venă hepatică medie reconstruită donat de soră și secțiunea hepatică laterală stângă recoltată de la mamă. Nici una din grefe nu avea un raport al greutateii grefă-receptor (RGGR) corespunzător (1%), dacă ar fi fost implantate independent. RGGR combinat a fost de 1,1%. Donatoarele și receptoarea au fost urmărite post-transplant timp de peste 1 an.

Rezultate: Nu s-a înregistrat nici o complicație postoperatorie la donatoare, care au fost externate după 8 zile. Receptoarea

a fost externată în ziua 19 postoperator. La 12 luni postoperator, pacientele sunt în viață, cu stare de sănătate optimă.

Concluzii: THDV cu grefă duală este o soluție terapeutică fezabilă pentru evitarea riscului de sindrom small-for-size.

Cuvinte cheie: transplantul hepatic de la donator viu, grefe duble, boala Wilson

Abstract

Background: Living donor liver transplantation (LDLT) exposes to risks both the donor, due to a potential small residual liver volume, and the recipient, who faces the risk of small-for-size graft syndrome. In order to overcome these drawbacks, liver grafts from two different donors can be used. This paper presents a case of dual graft LDLT using a right hemiliver and a left lateral section from related donors.

Case presentation: A 14-year old female diagnosed with chronic hepatic failure due to Wilson's disease with Model-for-End-Stage-Liver-Disease score of 25, underwent a dual graft LDLT, receiving a right hemiliver with a reconstructed middle hepatic vein from her sister, and a left lateral section from her mother. None of the grafts complied with a satisfactory graft-to-recipient weight ratio (GRWR), if they would have been independently transplanted. The combined GRWR was 1.10. The donors and the recipient have been followed-up for over 1 year.

Results: The donors had no postoperative complications. The donors and the recipient were discharged 8 and 19 days after surgery, respectively. After 12-month follow-up, both donors and the recipient were alive, with normal graft function.

Conclusion: Dual graft LDLT can be a feasible solution to overcome the risk of small-for-size graft syndrome.

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Abbreviations: BSA = body surface area, GRWR = graft-to-recipient weight ratio, GV/SLV = recipient standard liver volume, HA = hepatic artery, HD = hepatic duct, HV = hepatic vein, LDLT = Living donor liver transplantation, LL = left lobe, LLS = left lateral section, MELD = Model for End-Stage Liver Disease, POD = postoperative day, PV = portal vein, RL = right lobe, SFS = small-for-size graft, SLV = standard liver volume, WD = Wilson's disease

Key words: living donor liver transplantation, dual grafts, Wilson's disease

Introduction

Living donor liver transplantation (LDLT) is a well-established treatment for end-stage liver disease. LDLT exposes to risks both the donor, due to a potential small residual liver volume, and the recipient, who faces the risk of small-for-size graft (SFS) syndrome. The transplantation of SFS grafts may cause an unbalance between liver regeneration and an increase demand of liver function, which leads to a severe graft dysfunction known as SFS syndrome (1). Presently, its mechanisms are not yet fully understood, but SFS syndrome appears to be primary linked to graft overperfusion (2). Thus, SFS graft represents one of the main issues of LDLT. This problem has been partially solved by using a right lobe (RL) graft (3), but still small-size donors willing to donate to a large-size recipient are encountered in the clinical practice. If the small-size grafts would be denied liver transplantation, patients with end-stage liver disease could face the risk of death due to donor shortage. In order to overcome these limitations and to expand the donor pool, dual graft LDLT using left lobe (LL) graft and left lateral section (LLS) has been designed and performed by Lee et al in 2000 (4). Kaihara et al described the details of dual RL graft and LLS transplantation in 2002 (5). This paper presents a case of dual graft LDLT for Wilson's disease (WD) with severe liver failure, using a RL and a LLS from related donors.

Case Report

Patients

Recipient

The recipient was a 15-year old female affected by Wilson's disease, weighing 78 kg (BMI=26.1). The patient was admitted about 3 months before surgery in the Intensive Care Unit of our Institute for acute liver failure, with a MELD score of 37, and grade I-II hepatic encephalopathy. After conservative treatment and 5 sessions of liver dialysis using an artificial extracorporeal liver support - Prometheus system (Fresenius Medical Care, Bad Homburg, Germany), the MELD score decreased to 25. The patient was sub-sequently placed on the liver transplant list.

Donors

The first donor was the recipient's sister, a 19-year old female,

who donated the right hemiliver (Donor 1). The second donor was the recipient's mother, a 38-year old female, who donated the LLS of the liver (Donor 2). Donor candidates did not have any significant medical diseases.

Pre liver transplant work-up

Recipient

The recipient's blood type was Rh positive AII. Preoperative MELD score was 24.

Wilson's disease was diagnosed based on the clinical examination and specific tests:

- laboratory tests: ceruloplasmin = 0.08 g/L (normal value >0.2 g/L); blood copper = 36 µg/dl (normal range 80-155 µg/dl); urinary copper = 1314/24h (normal range 15-70 µg/24h); haemoglobin 8.6g/dl; present anti-erythrocytes antibodies; negative Coombs test.
- cerebral MRI: hyperintensity on T2 phase in the peri- and supraventricular region.

The liver anatomy was evaluated by contrast-enhanced CT and MRI cholangiography which showed an accessory left hepatic artery (HA) emerging from the left gastric artery, the HA emerging from the celiac trunk, and modal distribution of portal and biliary tree.

Donors

The donors and recipients were blood group identical (Rh positive AII).

Clinical examination and the laboratory tests were within normal range.

Abdominal imaging (contrast-enhanced computed tomography, contrast-enhanced MRI, MRI cholangiography, and abdominal Doppler ultrasonography) ruled out any abdominal focal lesions and assessed the liver anatomy: both donors had an accessory left HA from the left gastric artery, HA from the celiac trunk, with modal distribution of portal and biliary tree. Donor 1 had a right inferior hepatic vein (HV) >5 mm in diameter.

The volumetric CT measurements of the liver were as follows:

- in Donor 1 - Total liver volume: 1234.60 cm³; RL liver volume: 553.03 cm³; remnant liver volume: 681.57cm³;
- in Donor 2 - Total liver volume: 1093.87 cm³; LLS liver volume: 209.25 cm³; remnant liver volume: 884.62 cm³.

The remnant liver volume was intended to be at least 35% of the total liver volume (6): in Donor 1 it was 55.2%, while in Donor 2 it was 80.8%.

Dual grafts management

The recipient's standard liver volume (SLV) was calculated using the following formula based on the body surface area (BSA) (7):

$$SLV(ml) = 706.2 \times BSA(m^2) + 2.4 = 1351.24$$

The BSA was calculated using the following formula based on the weight (W) (78kg) and the height (H) (1.72m) of the recipient (8):

$$BSA(m^2) = W(kg)^{0.425} \times H(cm)^{0.725} \times 0.007184 = 1.91m^2$$

Then, the ratio of graft volume to recipient standard liver

volume (GV/SLV) was calculated:

- for the RL graft, the GV/SLV would have been 40.9%;
- for the LLS graft, the GV/SLV would have been 15.5%;
- The combined GV/SLV was 56.4%.

The graft-to-recipient weight ratio (GRWR) was also calculated:

- for the RL graft, the GRWR would have been 0.76%;
- for the LLS graft, the GRWR would have been 0.33%;
- The combined GRWR was 1.10%.

Based on literature, the optimal % SLV was considered at least 50% (7), while the optimal value of GRWR was set to at least 1% (9).

Surgery

After discussing the risks and benefits of the operations with both the donors and the recipient, informed consent was obtained from the patients. Both donors volunteered to donate part of their livers. The procedure was approved by the Ethical Committee of our hospital. All three patients were taken to the operating room simultaneously. All three operations were carried out under general anesthesia with orotracheal intubation. The surgical approach was through a bilateral subcostal incision extended vertically in the midline to the xiphoid process (the so-called "Mercedes" incision).

Surgery was performed in March 2012 and consisted in a dual graft LDLT: the recipient received a right hemiliver with a reconstructed middle hepatic vein from her sister, and the LLS from her mother.

Grafts harvesting

From Donor 1, the RL was harvested (right hepatectomy). In order to ensure the safety of the donor, the middle hepatic vein was not retained in the RL graft. From Donor 2, the LLS of the liver was harvested (left lateral sectionectomy). The harvested graft weights were 600g (the RL) and 260g (the LLS), respectively. The RL graft was harvested along with the right HA, right portal vein (PV), right hepatic duct (HD), right HV, and the right inferior HV. The LLS graft was harvested along with the left HA, left PV, left HD and left HV. The procedure time was 205 min and 335 min, respectively, with a blood loss of 800ml and 440ml, respectively. No significant intraoperative incidents were recorded.

Back table

The V5 and V8 tributaries of the anterior section of the RL graft were >5 mm in diameter, thus the re-establishment of its venous drainage was mandatory and it was consequently reconstructed on the back table by suturing a Y shaped cadaveric iliac vein graft to the V5 and V8 tributaries. No arterial, portal or biliary reconstruction was needed.

Dual graft liver transplantation

The RL graft without the middle hepatic vein of the recipient's sister was orthotopically implanted in the right-lobe position of the recipient. The following anastomoses were performed (Fig. 1):

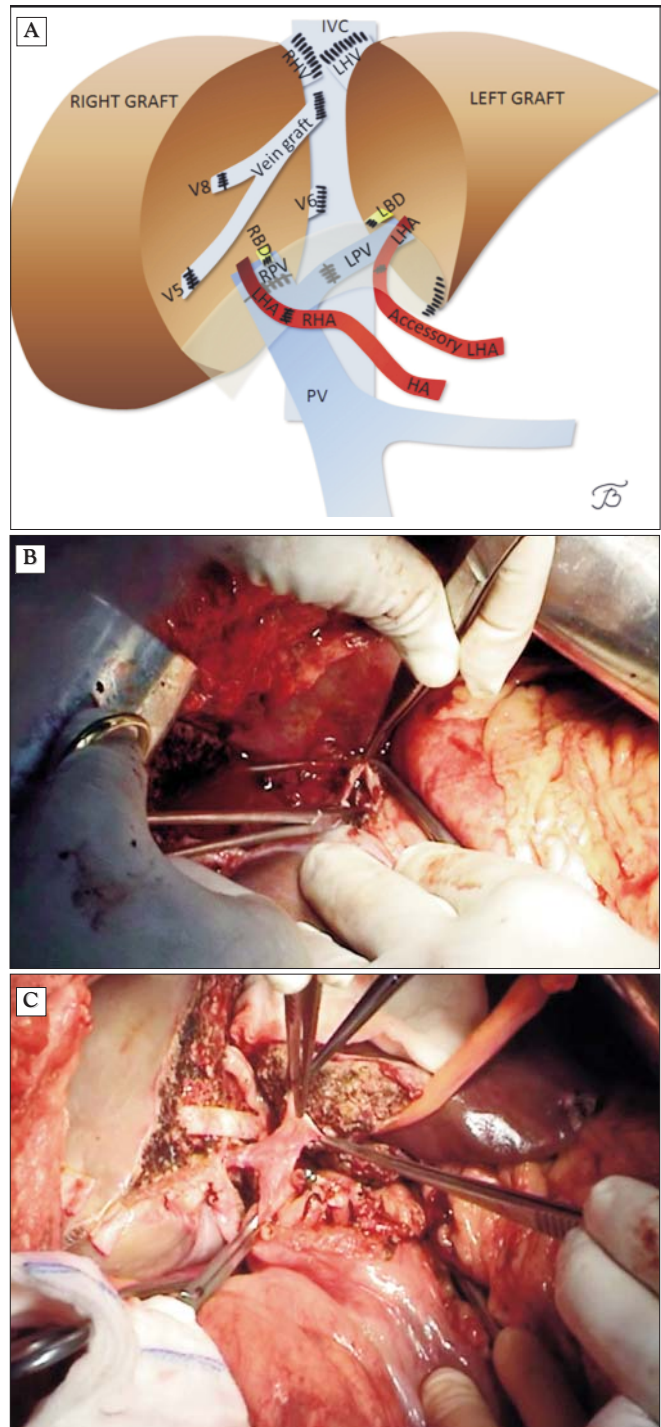


Figure 1. Technical aspects of the dual graft LDLT. (A) Schematic illustration of the procedure (HA – hepatic artery, PV – portal vein, BD – bile duct, HV – left hepatic vein, IVC – inferior vena cava, L – left, R – right); (B) intraoperative aspect during hepatocaval anastomosis for the left graft (left lateral section), with the right graft (right lobe) in place and re-vascularized; (C) intraoperative aspect of the preparation for porto-portal anastomosis of the left graft; the iliac vein graft reconstructing the venous drainage from V5 and V8 can be seen on the cut surface of the right graft

- the right HV of the donor graft was anastomosed end-to-side to the inferior vena cava (IVC) at the level of the right HV opening of the recipient;
- the right inferior HV of the donor graft (>5 mm in diameter) was anastomosed end-to-side to the recipient's IVC using a 6-0 polypropylene continuous suture;
- the Y shaped cadaveric iliac vein graft used to reconstruct the venous drainage of the right anterior section was anastomosed end-to-side to the recipient's IVC using a 6-0;
- the right PV of the graft was anastomosed to the corresponding PV of the recipient using a 6-0 polypropylene continuous suture;
- the right HA of the graft was anastomosed to the corresponding HA of the recipient, using microsurgical technique under operative microscope.

Then the LLS from the recipient's mother was orthotopically implanted to the left lobe position of the recipient. The subsequent anastomoses were performed (Fig. 1):

- an end-to-side anastomosis between the left HV of the graft and the recipient's VCI at the level of the common orifice of the middle and left HVs, using a 6-0 polypropylene continuous suture;
- end-to-end anastomosis between the left PV of the graft to the corresponding portal vein of the recipient, using a 6-0 polypropylene continuous suture;
- and end-to-end anastomosis between the left HA of the graft and the corresponding accessory HA of the recipient, using microsurgical technique under operative microscope.

The biliary drainage of the right hepatic duct (HD) and the HD of the LLS was reconstructed through a Roux-en-Y hepatico-jejunostomy protected by two biliary stents exteriorized through a jejunal loop. The stents were removed 12 months after surgery.

The procedure time was 620 min, with a blood loss of 9800 ml. No significant intraoperative incidents were recorded.

Immunosuppression therapy

The immunosuppression was induced by Simulect (Basiliximab) (POD 0 and 4), and continued from POD 5 with Tacrolimus (Prograf®, Astellas Pharma, Italy), and mycophenolate mofetil (CellCept®, Roche, United Kingdom) (discontinued after 3 months).

Patient follow-up

Recipient

The recipient was followed-up monthly for the first 3 months, and then every 3 months by the same team, using the same protocol (physical examination, abdominal ultrasound, liver function tests).

Donors

The donors were followed-up monthly for the first 3 months, and every 3 months for the following months by an expert liver transplantation team of our institution who performed physical examination and checked the liver function tests, and abdominal ultrasound alternately.

Results

Recipient's outcome

The immediate postoperative course was almost uneventful. The levels of total bilirubin, aPTT and INR decreased starting with the 1st postoperative day (POD), while in the POD 14 total bilirubin, AST, ALT, albumin, aPTT, INR and thrombocyte count were within range or close to normal levels. The sole postoperative complication was recorded on the 6th POD, when fever was recorded (38°C), the abdominal ultrasound and contrast-enhanced CT scan (Fig. 2) finding an effusion between the two grafts. The patient recovered completely after an ultrasound-guided puncture of the effusion performed in the POD 8, with aspiration of approximately 20ml of clear liquid (negative microbial cultures). The repeated Doppler exam of the graft vessels was regular, both intra and postoperatively, with a resistance index of the hepatic arteries varying between 0.66 and 0.68. The patient was discharged on the 19th POD, in good general condition and with normal graft function. The long-term outcome, evaluated after a 12-month follow-up, was optimal, with good general condition, normal graft function, and good quality of life.

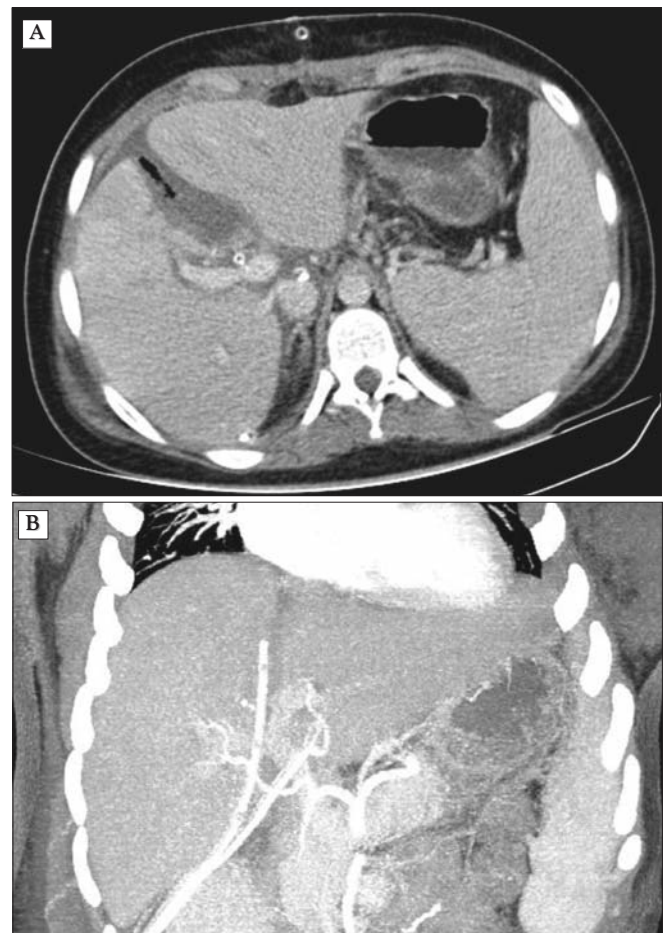


Figure 2. Postoperative CT scan (POD 6): patent grafts with small effusion in between

Donor's Outcome

There was no postoperative donor morbidity or mortality. Both donors were discharged in POD 8 and returned to their daily lifestyle and work within 1 month.

Discussions

The initial experience with LDLT yielded generally poor results (10), many of them having as cause the under evaluation of the importance of size matching between donors and recipients. Often, recipients with relatively small grafts developed a severe condition that became known as small-for-size (SFS) syndrome, characterized by synthetic dysfunction, elevated aminotransferases, and prolonged cholestasis (11,12), and approximately 50% of liver recipients died of sepsis 4 to 6 weeks after transplantation. To avoid this problem, two methods have been developed in order to predict an adequate functional hepatic mass of the graft. The first method involves the calculation of the graft-to-recipient weight ratio (GRWR). Its optimal ratio is 1%-3% and should not be inferior to 0.8% (9) in order to achieve graft and patient survival of 90% (13, 14). The GRWR has repeatedly been identified as independent prognostic factor of survival after LDLT (9, 15-19). The second method involves the calculation of the liver volume as a percentage of the standard liver volume (SLV) (% SLV), with an optimal value of $\geq 50\%$ (7). In recipients without cirrhosis and portal hypertension, even grafts with 30% of SLV can be successfully transplanted. Inversely, in the presence of severe portal hypertension, at least 40-45% of SLV is usually required (19). Kiuchi et al (9) demonstrated a nearly linear correlation between these two estimation procedures, and that both methods can therefore be used interchangeably.

Although successful graft function has been obtained with grafts as small as 0.6% GRWR (25% SLV) (20-22), other authors have reported increased risk for postoperative morbidity and mortality with the use of grafts $< 1.0\%$ of GRWR ($< 50\%$ SLV) (7, 9, 11). Grafts with GRWR between 0.8%-1.0% or "small-for-size grafts" usually showed poor graft function marked by manifest cholestasis and prolonged coagulopathy (11). The RL of the liver represents approximately 60% of the hepatic parenchyma and in most adults would provide at least 1% of GRWR (23). In our case, the RL graft had a GV/SLV of 40.9% and a GWRW of 0.76. The presence of liver cirrhosis associated with portal hypertension in recipient determined us to consider this graft as insufficient. In order to avoid the risk of a SFS syndrome, a supplementary graft was considered (the LLS donated by her mother). This way, both the GV/SLV and the GWRW were raised within optimal range (55.4% and 1.10, respectively), and thus the risk of SFS graft was eliminated.

Dual graft LDLT proved to be an efficient method to avoid the SFS grafts. Since the first case was published in 2001 by Lee SG et al (4), to date a total of 243 cases were reported worldwide, demonstrating its efficiency and becoming an established procedure in liver transplantation. Two indications for dual graft LDLT were described: the first indication (4), was

in cases when two donors were rejected for RL donation due to anatomical variations of the liver hilum or insufficient remnant liver volume, but they could successfully donate their left lobe (LL) or left lateral section (LLS) for dual graft LDLT; the second indication was in cases in which a RL graft was available but considered insufficient as volume or had significant liver steatosis, and therefore supplemented with a LL or a left lateral section from a second donor (24,25). In the first indication, the LL from the first donor is orthotopically implanted in the recipient, while the second graft (a LL or a left lateral section) is rotated at 180° and heterotopically implanted in the right lobe position of the recipient (4); the bile duct reconstruction is carried out by duct-to-duct anastomosis before the graft revascularization. In the second indication both grafts are orthotopically implanted using the standard technique for LDLT (24,25). The group of Lee SG has by far the largest experience in dual graft LDLT, with 226 reported cases (25). The remaining 17 published cases are divided among 7 other centers worldwide. The present case is the first in Romania and the fourth in Europe, only 3 other similar cases being reported from Germany (2 cases) and Turkey (1 case) (26,27).

Dual graft LDLT has some specific complications reported in the literature. One is the atrophy of one of the grafts due to the particular hemodynamics that creates a competition in blood supply between the two grafts (24). Also the immune environment becomes more intricate, and the risk of rejection is not anymore only between the grafts and the recipient, but also between the grafts (24). Survival time is difficult to report due to incomplete data.

The main drawback of this procedure is the increased cumulated donor risk of the two donors. This issue can be partially overcome by expert transplantation teams. Another solution is the use of a combination of cadaveric and living grafts (24), but the split liver grafts yield inferior results. While the donor mortality was estimated to be approximately 0.1% after left lateral sectionectomy (28), the risk of death for donors of a right lobe ranges from 0.4% to 0.5% (29). For this reason, left grafts (LL or LLS) are preferred in dual graft LDLT (24). In our case, the LL could not be harvested from none of the donors due to the anatomical arterial variations present in both donors and recipient that would have put the arterial reconstruction of the potential grafts at high risk of failure (accessory left HA coming from the left gastric artery, with the artery for the left medial section emerging from the HA). Another drawback of this procedure may be the higher costs of the surgical procedure, but this is balanced by the higher costs of postoperative management in case of SFS syndrome after a LDLT with a SFS graft, which involves complex and costly postoperative care, and even retransplantation. Nevertheless, the dual graft LDLT proved to be a feasible solution to the organ donor shortage, along with the split liver transplantation, use of marginal donors, and domino liver transplantation (30,31), thus reducing the mortality on the waiting list (32).

In conclusion, although complex and expertise demanding, dual graft LDLT has proven to be a safe procedure

and a feasible solution to overcome the risk of small-for-size graft syndrome due to volumetric (insufficient graft volume), anatomical (anatomical variations of the liver hilum), or morphological (hepatosteatosis) reasons, when the selection of an optimal single donor fails.

Conflict of Interest Statement

All authors have no financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work.

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