

case report

The first two cases of living donor liver transplantation using dual grafts in Saudi Arabia

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The concept of dual-graft liver transplantation was introduced to overcome the discrepancy between liver transplantation demand and liver donation. Dual-graft transplantation also mitigates cumulative family risk by decreasing individual donor risk through minimization of the resected liver volume from each donor. Here, we describe the first two cases performed in Saudi Arabia wherein a dual-graft living donor liver transplantation was facilitated by the use of one left lobe graft and one left lateral segment in both cases. These are the first two cases of dual-graft liver transplantation reported from Saudi Arabia and the Middle East.

SIMILAR CASES PUBLISHED: Nine on the same subject in other parts of the world (Korea, Japan, Germany, China, and Brazil).

Liver transplantation (LT) is considered the most effective treatment for acute and chronic liver failure patients, and is the only definitive treatment for hepatocellular carcinoma (HCC) in the setting of significant liver disease. With the increased demand for LT, an ever-expanding discrepancy has developed between liver transplantation demand and liver donation. This increases the waiting time, which exposes the potential liver transplant recipient to the hazards of disease progression beyond the limits of curability. This situation has stimulated those who work in the transplantation field to find new ways to increase the donor pool.¹ An unacceptable wait list mortality and limited access to deceased donor livers has led to the development of living donor and split liver transplantation as well as dual graft liver transplantation. The concept of dual-graft liver transplantation was proposed to avoid the exclusionary size mismatching that is a major challenge in adult-to-adult living donor liver transplantation (LDLT). This mismatching predicament emanates from the fact that up to one-quarter of all potential liver donors are disallowed as right hepatectomy donors due to insufficient remnant liver volume, yet are unable to provide adequate liver volume to the intended recipient with their left lobe.^{2,3} The target is to have a balance between donor safety in regards to the remnant liver volume while providing the recipient with adequate graft volume for metabolic demands.^{2,4} Dual-graft living donor liver transplantation was performed for the first time by Lee in 2001 at the Asan Medical Center in South Korea^{5,6} and for first time in Europe in 2005 by Broering at the Hamburg University Hospital.⁷ Dual-graft living donor liver

transplantation maximizes donor safety by minimizing the resection volume from each donor, which correlates with post-hepatectomy mortality rates; the worldwide donor mortality estimate for left lateral segmentectomy is 0.1% while for right lobe donors it is 0.4%-0.5%.^{8,9} Currently, five types of dual-graft pairs have been used to carry out dual-graft living donor liver transplantation: 1) two left lobes grafts, 2) two left lateral segments, 3) one right lobe graft and one left lobe graft, 4) one right lobe graft and one left lateral segment, and lastly 5) one left lobe graft and one left lateral segment.^{5,6,10} We report the first two cases of dual-graft adult-to-adult LDLT in Saudi Arabia performed at the King Faisal Specialist Hospital and Research Centre using one left lobe graft and one left lateral segment graft in both cases.

CASES

First case was done on June 2016 with a 16-month follow-up. Second case was done on December 2016 with a 10-month follow-up.

Case 1

In the first case, LDLT was planned for a 54-year-old male patient (weight 72 kg) with cryptogenic liver cirrhosis with HCC involving segments 7 and 8, which had been down-staged with complete response via trans-arterial radio-embolization 6 months before transplant. He had well-compensated Child A cirrhosis with a MELD score of 22 based on HCC exception criteria. Two sons of the recipient, 19-year-old non-identical twins stepped forward for donation. Donor #1 had an estimated remnant left lobe volume of 25%, and was accordingly excluded as a right lobe donor per program policy (requisite remnant liver volume $\geq 30\%$ of total liver volume). Likewise, donor #2 was excluded for right lobe donation as his remnant left lobe volume of 34% was coupled with a liver biopsy demonstrating 10% macro-steatosis; this degree of steatosis also precluded him as a full left lobe donor. After discussions with the family about the inherent risks and benefits of the procedure, we elected to proceed with dual-graft donation. Left hepatectomy (segment 2, 3, 4) from donor #1 with an estimated graft volume of 394 cc and a remnant liver volume of 75% and a left lateral segment procured from donor #2 yielded an estimated graft volume of 224 cc with a remnant volume of 85%. The cumulative 618 cc of liver tissue represented a graft-to-recipient-weight ratio (GRWR) of 0.86 (**Table 1**).

Case 2

In the second case, a 36-year-old male patient (weight 62 kg) with autoimmune hepatitis classified as Child B

with a MELD score of 21 was assessed for LDLT. His brother volunteered to donate, but his estimated remnant left lobe volume was only 26.6% and the GRWR of the left lobe was estimated to be 0.62; therefore, he was excluded as an isolated, unilobar donor. After inquiring about a second donor, a cousin agreed to come forward with the stipulation that he undergo the least morbid procedure possible. We therefore suggested taking the left lobe from the first donor (brother) and performing a left lateral segmentectomy from the second donor (cousin), which carries with it substantially less risk. By coupling these donors in that manner, we exposed the second potential donor (cousin) to the least morbid donor operation and simultaneously provided the recipient tenable access to an otherwise unobtainable liver transplant. The left lobe graft was estimated to be 386 cc and the left lateral graft was 210 cc, which provided a GRWR of 0.96; the remnant liver volume for each donor was almost 74% (**Table 1**).

Operative procedures

Case 1

The operation was started by resecting the two liver grafts (**Table 2**). During hepatectomy, we found an ablated HCC tumor in segment 8 that was adherent to the overlying diaphragm so the diaphragm was resected and followed by immediate repair. A portocaval shunt was not required and we started to implant the first graft. The left lobe was placed into its normal, orthotopic position and the sequence of anastomoses were completed as follows: 1) extended recipient confluence of the left/middle hepatic vein (L/MHV) with confluence of L/MHV of the graft, 2) recipient left portal vein (LPV) to LPV of the graft. With clamps secured to the recipient right portal vein, right hepatic vein, and common hepatic artery, reperfusion of the first graft was carried out by declamping of the IVC clamp followed by declamping of the main portal vein. The left lobe implantation was then completed as the arterial anastomosis was performed by connecting the recipient left hepatic artery (LHA) with LHA of the graft.

After reperfusion, assessment of the portal flow by flowmeter (MediStim VeriQ system; MediStim Oslo, Norway) showed a high portal flow confirmed by an absent diastolic flow in a hepatic artery Doppler sonogram, so we decided to partially occlude the portal vein via a circumferential, external band until implantation of the second graft. This transient inflow modulation protected the left lobe graft from portal hyperperfusion and simultaneously allowed for sufficient venous drainage to avoid any bowel edema. The spleen was not

Table 1. Donor characteristics.

	Case 1		Case 2	
	Recipient body weight: 72 kg		Recipient body weight: 62 kg	
	Donor 1	Donor 2	Donor 1	Donor 2
Relationship	Son	Son	Brother	Cousin
Age (years)	19	19	26	37
Gender	Male	Male	Male	Male
Body weight (kg)	68	75	60	99.4
Type of graft	Left lobe	Left lateral segment	Left lobe	Left lateral segment
Expected graft volume (cc)	394	224	386	210
Total graft volume (cc)	618		596	
Graft- to recipient-weight ratio	0.86		0.96	

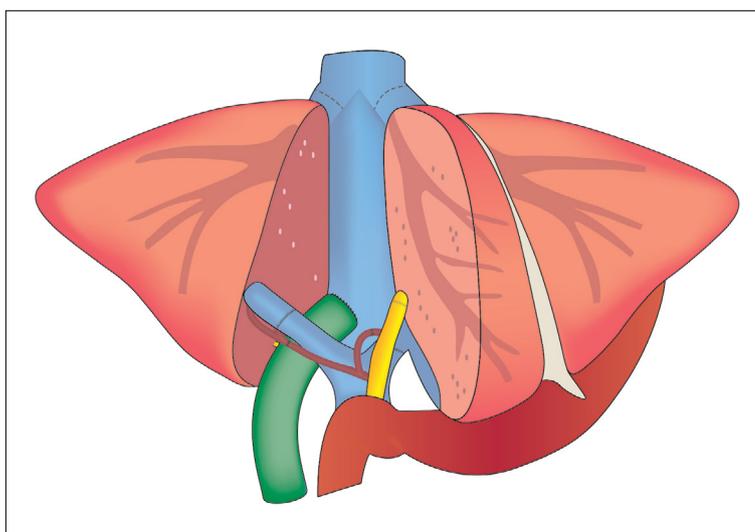


Figure 1. Diagram showing dual grafts liver transplant using one left lobe graft (on the left side) and one left lateral segment (on the right side) rotated 180° on the sagittal axis.

splenic artery to decrease the portal flow. The arterial continuity of the second graft was then established by anastomosing the LHA of the graft to the right hepatic artery (RHA) of the recipient.

After adequate arterial and portal flow was documented by Doppler ultrasound and flowmeter and after satisfactory hemostasis was confirmed, the bile ducts were reconstructed. The left hepatic duct of the first graft (in the orthotopic position) was anastomosed end-to-end with the recipient common hepatic duct. Two bile ducts were present in the second graft (left lateral graft); these were approximated with interrupted sutures (ductoplasty) and anastomosed to a jejunal Roux limb as a single anastomosis. The posteriorly positioned biliary anastomosis was carried out by gently retracting the graft to the left in order to expose the bile ducts lying posterior to the hilar vascular structures (**Figure 1**). Total operative time was 587 minutes, blood loss was 5 liters and 11 units of packed red blood cells were transfused.

enlarged and the GRWR of the first graft was only 0.4, so we did not ligate the splenic artery as a portal vein modulation technique.

The left lateral segment (segments 2, 3) graft was then placed into the right upper quadrant after rotating it upon its sagittal axis 180° from its normal anatomic position. Implantation was started by anastomosing sequentially, 1) the LHV of the graft to the extended RHV of the recipient, 2) the LPV of the graft (located anterior to the bile duct in this position) to the RPV of the recipient. After reperfusion of the second donor graft, the portal flow was still high in both grafts so we ligated the

Case 1 outcome

Both donors spent one night in the recovery room, and were subsequently discharged on postoperative day 4 without complication. The recipient stayed in the intensive care unit (ICU) for 5 days and was then moved to the regular ward and discharged on the 58th postoperative day. This protracted course was due to the development of a biloma in the space between the two grafts and a mild, right-sided pleural effusion. Both were managed non-surgically by percutaneous drainage; the bile leak resolved after three weeks, and the effusion abated after 8 days. At 16 months follow up,

the patient was alive with good allograft function, no HCC recurrence and had developed no further morbidity.

Case 2

In the second case, we started by resecting the two liver grafts (**Table 2**). The recipient operation was started by hepatectomy of the cirrhotic liver followed by implantation of the first graft, the left lobe. The graft was placed into the orthotopic position, and vascular reconstructions were performed as in Case 1. Then the second graft (left lateral segment) was implanted as in Case 1, with reperfusion of the second graft coming after declamping of the RHV and RPV. Biliary reconstruction was started by approximating the two bile ducts in the left lobe graft via interrupted sutures then anastomosing them as a single anastomosis with the recipient common hepatic duct. Likewise, the two bile ducts in the left lateral segment graft were approximated and subsequently anastomosed to the jejunal Roux limb in one anastomosis. The operative time was 535 minutes, blood loss was 2 liters and blood transfusion was only 2 units of packed red blood cells.

Case 2 outcome

Both donors spent the night in the recovery room and then were moved to the regular ward where the left lateral segment donor (second donor) was discharged on postoperative day 3, while the left lobe donor (first donor) was discharged on postoperative day 4 without complication.

The recipient stayed in the ICU for 3 days and was discharged on the 15th postoperative day in good physical condition and with excellent graft function. Four months later he developed a strangulated umbilical hernia which was repaired; he was discharged after 2 days without further morbidity. At 10 months post liver transplant, the patient and graft are in a satisfactory condition. Surveillance computed tomography showed well-perfused grafts with patent vessels and an absence of abdominal fluid collections (**Figure 2**).

DISCUSSION

In most Middle Eastern countries including Saudi Arabia, the concept of deceased donor liver transplant is not well established due to cultural obstacles. This limitation renders LDLT as the only option for the majority of patients with life-threatening liver disease, and stimulates constant surgical innovation to maximize this finite donor pool. In the case of imbalance between the potential donor remnant volume and recipient required liver volume, dual-graft liver transplant is an apex level combination of surgical techniques resulting in a completed transplant in a situation previously deemed to be exclusionary, without exposing a single donor to augmented risk.

The early experience with adult-to-adult LDLT was done using left lobe grafts in an effort to achieve the highest level of donor safety by minimizing the resected liver volume.¹¹ Unfortunately, the outcome was unsatisfactory due to inadequate graft volume for the recipient resulting in inferior outcomes.^{12,13} Therefore,

Table 2. Intraoperative characteristics of the liver grafts.

	Case 1		Case 2	
	Donor 1	Donor 2	Donor 1	Donor 2
Type of the graft	Left lobe Seg. 2, 3, 4	Left lateral segment Seg. 2, 3	Left lobe Seg. 2, 3, 4	Left lateral segment Seg. 2, 3
Vascular anatomy	No vascular abnormality	No vascular abnormality	No vascular abnormality	No vascular abnormality
Biliary anatomy	1 bile duct	2 bile ducts	2 bile ducts	2 bile ducts
Actual graft weight (gm)	310	270	361	287
Cold Ischemia time (min)	136	23	230	31
Warm Ischemia time (min)	26	18	21	17
Blood loss (mL)	300	200	200	350
Operation time (min)	360	220	190	285

right lobe graft donation, became the default procedure in LDLT by directly addressing the problem on the recipient side. However, this practice inherently has increased liver donor risk as it is felt to be directly proportional to the amount of resected liver as evidenced by the variable mortality rates noted among the various types of donor hepatectomies. This may manifest in the form of inadequate remnant liver volume, which in a few extreme cases has led to liver failure, resulting in death or the need for liver transplantation in the liver donor.^{7,14} The balance between the recipient graft volume requirement to avoid small-for-size syndrome (SFSS) and the donor's safety is considered to be a crucial factor in the era of LDLT.¹⁰

To optimize recipient outcome, the minimum graft size should be at least 40% of standard liver volume to produce a GRWR of ≥ 0.8 ; this is the minimal graft volume that can withstand the metabolic demands of the recipient and avoid SFSS. Furthermore, grafts with macrosteatosis of 10%-30% may need to reach GRWRs of ≥ 1 to overcome the diminished quality of the graft.^{4,15} In regards to the donor, the remnant liver volume should not be less than 30% of the estimated total liver volume.

In most cases right lobe graft donation provides sufficient volume to the recipient, but carries higher donor risks and morbidity than the left lobe and left lateral segment donations, which have lower complication rates.^{13,16} In some populations such as that in Korea, a sizeable portion (up to one-quarter) of liver donors have an insufficient right lobe liver volume to facilitate acceptable LDLT recipient outcomes. Total reliance on unilobar grafting would therefore be lethal for that cohort of potential LT recipients who find themselves without a single donor able to provide the requisite amount of liver. In 2001, Lee and his group outlined their approach in circumventing this problem by coupling two donors (both excluded as isolated, right lobe donors) to provide the necessary liver volume with the attractive option of concurrently minimizing individual risk.^{5,6} Dual-graft donation has generated ethical questions in regards to the appropriateness of exposing not just one but two healthy liver donors to the contingencies of major surgery. It can be justified when we focus on the cumulative family risk which is affected not just by the number of donors involved but also by the inherent risk incurred by each individual. As previously stated, there is a marked diminishment of donation-related mortality when involving non-right lobe donation. Most surgeons feel that left lateral sectionectomy should carry a near zero postoperative mortality. These safer donor operations therefore result in a comparable or



Figure 2. CT scan of recipient 2 after transplantation. Six months after transplant.

even lower overall mortality risk to a family despite the addition of a second donor. Our two cases provide a small but concrete example of this, wherein we harvested two left lobes grafts and two-left lateral segments grafts with a hospital stay of 4 days in three donors and 3 days in one donor, with no reported morbidity or complication. By definition, LDLT recipients benefit immeasurably from this innovation; without it, they would simply be relegated to the ever-expanding deceased donor list waiting list, which in many countries confers near universal mortality.

Our recipients received sufficient liver volumes with satisfactory graft function with no complication directly related to the dual graft technique itself (**Table 1**). Bile leak, a relatively common LDLT complication, which we faced in the first case, was managed non-surgically by percutaneous drainage in the same manner as in unilobar LDLT. This complication directly led to the 58-day postoperative stay, which we were able to avoid in the second case which had a smooth, complication-free course resulting in discharge in just over 2 weeks.

Despite the advantages and benefits of dual graft liver transplant, the procedure has remained unpopular and not adopted by many centers, especially in the West and Middle East. We believe this could be due to the logistical challenges introduced by the requisite need for three experienced surgical teams in separate operating rooms. We addressed this issue by prioritizing simplicity and streamlining of the procedure. No vascular interposition grafts or veno-venous bypass were used to avoid unnecessary lengthening of the procedure. The use of a tissue expander to support the second (right side) graft to avoid tension on the hilar structures was not deemed to be essential. We elected to close the space between the diaphragm and

the Gerota fascia with interrupted sutures. This formed a platform to stabilize the second graft. Moreover, one of the challenging points in dual-graft liver transplant is rotation of the second graft 180 degrees in the sagittal plane, which places the hilar structures in a reversed position. Some recommend performing the posteriorly positioned bile duct anastomosis before the PV anastomosis to take advantage of the favorable exposure of the ducts. The cost incurred is of course the additional warm ischemia time prior to reperfusion, which inevitably will occur despite attempts at topical in-situ cooling maneuvers. Therefore, in our cases we preferred biliary reconstruction after reperfusion. Access to the duct was optimized by gently retracting the graft toward the left shoulder thus bringing the duct into better view.

From our early experience in dual graft liver transplant, we recommend the following:

- 1) The combination of left lobe graft and left lateral graft for dual graft adult living donor liver transplant is very safe on the donor side as it minimizes the resected liver volume which lowers morbidity. As mentioned, the second donor of the second recipient agreed to donate on a condition that we minimize the possible risks, which

we achieved by resecting only the left lateral segment only from him.

- 2) Technical planning must be in place to address the reversed nature of the hilar structures in the heterotopic graft after subsequent to the 180° axial turn. This makes the biliary anastomosis more challenging as it becomes more posterior. We prefer jejunal Roux limb anastomosis with the biliary system in the left lateral segment as it is easier to flip it upward and to the left to have more exposure of the bile ducts, which may be more difficult in a left lobe graft. This flipping of the graft may require more distance, which could be achieved by jejunal Roux anastomosis.

In conclusion, we consider dual-graft liver transplantation to be a feasible way to expand the donor pool, especially in countries that depend mainly on living donors, as is the case in Saudi Arabia. Despite the technical and logistical challenges, dual-graft liver transplantation should be assimilated into the armamentarium of a mature LDLT center as it has been shown to facilitate the completion of a LDLT while jointly prioritizing safety in the individual donors, which results in acceptable overall cumulative family risk.

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