

# Experience with 122 consecutive liver transplant procedures at King Faisal Specialist Hospital and Research Center

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**BACKGROUND:** Saudi Arabia is a leading country in the Middle East in the field of deceased-donor liver transplantation (DDLT) and living-donor liver transplantation (LDLT). We present our experience with DDLT and LDLT at King Faisal Specialist Hospital and Research Center (KFSHRC) for the period from April 2001 to January 2007.

**PATIENTS AND METHODS:** We performed 122 LT procedures (77 DDLTs and 45 LDLTs) in 118 patients (4 re-transplants) during this period of time.

**RESULTS:** The number of adult and pediatric procedures was 107 and 11, respectively. The overall male/female ratio was 66/52 and the median age of patients was 43 years (range, 2-63 years). In the DDLT group, the median operating time was 8 hours (range, 4-19), the median blood transfusion was 6 units (range, 0-40), and the median hospital stay was 13 days (range, 6-183). In the DDLT group, after a mean follow-up period of 760 days (range, 2-2085), the overall patient and graft survival rate was 86%. In the LDLT group, the median operating time was 11 hours (range, 7-17), the median blood transfusion was 4 units (range, 0-65), and the median hospital stay was 15 days (range, 7-127). In the LDLT group, and after a mean follow-up period of 685 days (range, 26-1540), the overall patient and graft survival rates were 90% and 80%, respectively with no significant difference in patient and graft survivals between groups. Biliary complications were significantly higher in LDLT compared to DDLT ( $P < 0.05$ ). Vascular complications were also significantly higher in LDLT compared to DDLT ( $P < 0.05$ ).

**CONCLUSIONS:** Both DDLT and LDLT are being successfully performed at KFSHRC with early experience indicating a higher rate of biliary and vascular complications in the LDLT group.

The Kingdom of Saudi Arabia is the leading country in the Middle East in the field of deceased-donor liver transplantation (DDLT).<sup>1-5</sup> Since the first DDLT in 1990, more than 300 DDLTs were performed in Saudi Arabia, divided mostly between two main liver transplantation (LT) centers. More recently, living-donor liver transplantation (LDLT) has been introduced in Saudi Arabia in an attempt to overcome the severe shortage of cadaveric organs in the Kingdom. To date, more than 200 LDLTs have been performed in Saudi Arabia, divided between three main LT centers.<sup>6-9</sup> Along with Egypt, Saudi Arabia was one of the leading countries in the field of LDLT in the Middle East.<sup>10-12</sup> The LT program at King Faisal Specialist Hospital and Research Center (KFSHRC)

was first established in 1994. At that time, 45 DDLTs were performed by a visiting LT team from abroad, but unfortunately that program was suspended in 1996 due to logistical difficulties (Figure 1). In April 2001, the LT program at KFSHRC was re-started by a local team in an attempt to meet the rapidly growing need for LT in Saudi Arabia.<sup>13</sup> We present the KFSHRC experience in the last 6 years with both DDLT and LDLT.

## PATIENT AND METHODS

In the period between April 2001 and January 2007 122 liver transplant procedures (77 DDLTs and 45 LDLTs) were performed in 118 patients (including 4 re-transplants) at KFSHRC. All 77 DDLTs procedures were performed by the local team using cadav-

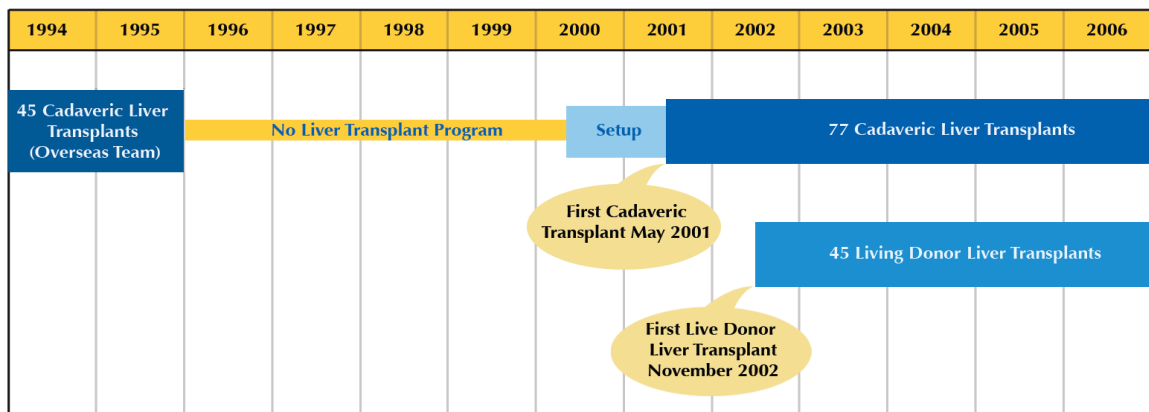


Figure 1. Evolution of the liver transplant program at KFSHRC.

eric organs retrieved from brain-dead heart-beating cadaveric donors who fulfilled the strict clinical criteria for brainstem death diagnosis set by the Saudi Center for Organ Transplantation. Almost all DDLT recipients were adults; only 3 pediatric patients underwent DDLT. Double veno-venous bypass was used in six of the DDLT recipients. Roux-en-Y hepaticojejunostomy was used for biliary reconstruction in 12 DDLT recipients while duct-to-duct anastomosis was used in the remaining 65 DDLT recipients.

For the LDLT group, outside assistance was required in the first two LDLTs, while the local team alone without outside assistance performed all the following 43 LDLT procedures. The left lateral segment (segments 2-3) was used in 8 pediatric LDLT recipients, the entire left lobe without the caudate (segments 2-4) was used in one pediatric LDLT recipient, and the whole right

lobe (segments 5-8) was used in the 36 adult LDLT recipients. The middle hepatic vein was included with the right liver graft in only 3 LDLT recipients. In all LDLT procedures, microvascular surgeons performed the hepatic artery anastomosis using a microscope. Roux-en-Y hepaticojejunostomy (REY) was used for biliary reconstruction in 6 LDLT recipients, duct-to-duct anastomosis was used in 38, and combined REY and duct-to-duct anastomoses were performed in one patient. All biliary anastomoses were performed using interrupted 6/0 absorbable sutures without stenting. Re-transplantation using a cadaveric organ was necessary in 4 LDLT recipients.

All donors for LDLT were related to their recipients. The graft-recipient weight ratios ranged from 0.8% to 1.7%; the remaining liver volume in all donors was  $\geq 30\%$  of the calculated whole liver volume; and macrovesicular steatosis in all grafts was  $\leq 20\%$  (estimated by routine percutaneous liver biopsy in all donors). All donors were carefully assessed and approved by a social worker, a psychologist, and at least one senior member of the surgical team.

Our postoperative immunosuppression regimen was mainly FK506 and steroids. Mycophenolate mofetil was used in conjunction with FK506 for various indications, including renal impairment, neurotoxicity, autoimmune etiology, and hepatitis C virus (HCV) recurrence. In most cases, steroids were stopped after 3 months, but continued in those with autoimmune etiology. A few patients were converted from calcineurin inhibitors to sirolimus for various reasons including nephrotoxicity, neurotoxicity, and posttransplant lymphoproliferative disorders. Lamivudine and hepatitis B virus (HBV) immunoglobulins were used in four patients who had HBV infection-related cirrhosis.

A Kaplan-Meier analysis was used to measure the

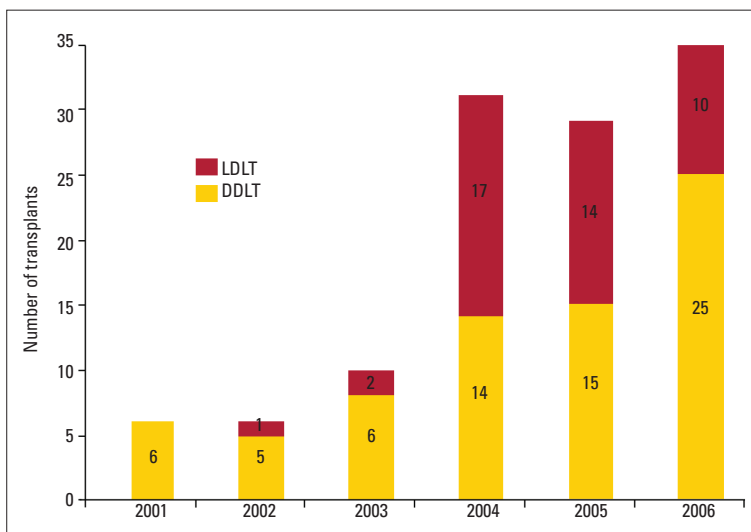


Figure 2. Number and types of liver transplants performed each year since April 2001.



**Figure 3.** Liver explant showing hepatitis C virus-induced liver cirrhosis and small hepatocellular carcinoma.

**Table 1.** Indications for liver transplantation in 122 recipients.

Indication	No	%
Hepatitis C virus	35	29%
Viral hepatitis + hepatocellular carcinoma	21	17%
Hepatitis B virus	10	8%
Autoimmune hepatitis	15	12%
Cholestatic liver disease	11	9%
Cryptogenic cirrhosis	10	8%
Primary hyperoxaluria	4	3%
Wilson's disease	5	4%
Glycogen storage disease	2	2%
Budd-Chiari syndrome	1	1%
Re-transplantation	4	3%
Others	4	3%
<b>Total</b>	<b>122</b>	

survival function, the log-rank test was used to compare between the survivals in different groups, and the Chi-square test was used to compare the frequency of complications in different groups. SPSS software was used for statistical analysis. A P value of < 0.05 was taken as significant.

## RESULTS

The numbers of LTs performed per year is shown in Figure 2. The overall male/female ratio was 66/52; the adult/pediatric ratio was 107/11, and the median age was 43 years (range, 2-63 years). Indications for liver transplantation in 122 LT recipients are shown in Table

1. Liver cirrhosis due to viral hepatitis with or without hepatocellular carcinoma (HCC) was the main indication for LT in our study group (Figure 3).

In the DDLT group, the male/female ratio was 38/39; the adult/pediatric ratio was 74/3; the median age was 44 years (range, 11-63 years); the median operating time was 8 hours (range, 4-19), the median blood transfusion was 6 units (range, 0-40), and median hospital stay was 13 days (range, 6-183). The overall patient and graft survival rate was 86% after a mean follow-up period of 760 days (range, 2-2085). The 11 deaths in the DDLT group were due to primary graft non-function in 4 patients, central pontine myelinolysis in 3 patients, recurrent hepatitis C virus cirrhosis in 3 patients, chronic rejection in one patient, recurrent HCC in one patient, and recurrent cholangiocarcinoma in one patient.

In the LDLT group, the male/female ratio was 29/16; the adult/pediatric ratio was 36/9; the median age was 47 years (range, 1.5-63 years); the median operating time was 11 hours (range, 7-17), the median blood transfusion was 4 units (range, 0-65), and the median hospital stay was 15 days (range, 7-127). The overall patient and graft survival rates were 90% and 80%, respectively, after a mean follow-up period of 685 days (range, 26-1540). Re-transplantation using cadaveric organ was necessary in 4 LDLT recipients. Graft failure and patient deaths were due to hepatic artery thrombosis in 2 cases, biliary complications in one patient, uncontrollable bleeding in one patient, portal vein thrombosis in 2 cases, and small-for-size syndrome in 3 patients.

For the live liver donors, the male/female ratio was 34/11; the median age was 25 years (range, 18-42), the median hospital stay was 6 days (range, 4-14), and only two donors required intra-operative blood transfusion. After a median follow-up period of 529 days (range, 8-1354), a total of 28 morbidities were encountered in 17 donors (37.8%) of which 9 donors (20%) had serious complications (Table 2). No donor death was encountered in our experience.

Biliary complications were significantly higher in the LDLT group compared to the DDLT group—25.6% vs. 2.6% respectively ( $P < 0.05$ ). Vascular complications were also significantly higher in the LDLT group compared with the DDLT group—8.9% vs. 2.6% respectively ( $P < 0.05$ ).

The overall (DDLT and LDLT) patient and graft survival after a mean follow-up period of 736 days (range, 6-2089) were 90% and 86%, respectively (Figure 4). The overall and actuarial survival rates in both DDLT and LDLT groups are summarized in Table 3. In the short-term follow-up there was significantly

**Table 2.** Donor morbidities in 45 live liver donors.

Recorded Complication	No.	Graft Used	Management	Outcome
Sever liver dysfunction	2	Rt Lobe	Supportive	Recovered
Incisional hernia	2	Rt Lobe(1); LLS (1)	Laparoscopic mesh repair under GA	Recovered
Bad scar	3	Rt Lobe	Scar revision	Satisfied
Bile leak, collections, and sepsis	1	Rt Lobe	ERCP and stenting under sedation	Recovered
Biloma	1	LLS	Percutaneous drainage	Recovered
Skin dehiscence	1	Rt Lobe	Secondary closure under local anesthesia	Recovered
Pressure-induced alopecia areata	3	Rt Lobe	None	Recovered
Neurapraxia of the right arm	1	Rt Lobe	Physiotherapy	Recovered
Bad scar	2	Rt Lobe(1); LLS (1)	Refused scar revision	Satisfied
Incisional pain	4	Rt Lobe	Pain control	Responded
Abdominal discomfort	5	Rt Lobe(4); LLS (1)	Symptomatic treatment	Responded
Depression	3	Rt Lobe	Psychological counseling	Responded

LLS: left lateral segment; GA: general anesthesia; Rt: Right.

**Table 3.** Overall and actuarial survival rates in 122 liver transplant recipients.

Type	No.	Overall survival	Actuarial survival May 2001 – Jan 2007					
			Patient survival			Graft survival		
			1 yr	3 yr	5 yr	1 yr	3 yr	5 yr
DDLT	77	86%	91%	79%	79%	91%	79%	79%
LDLT	45	89%	88%	87%	87%	79%	79%	79%
<b>Overall</b>	<b>122</b>	<b>87%</b>	<b>90%</b>	<b>83%</b>	<b>83%</b>	<b>86%</b>	<b>79%</b>	<b>79%</b>

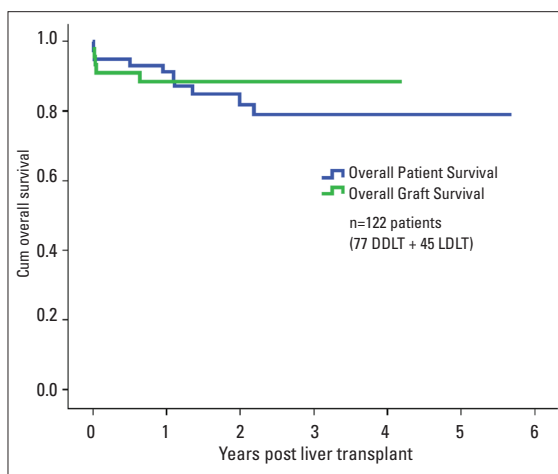
DDLT: deceased donor liver transplantation; LDLT: living donor liver transplantation.

poorer graft survival rate in the LDLT (log-rank test,  $P < 0.05$ ); however, in long-term follow-up there was no statistical significant difference between the two groups in either patient survival or in graft survival (Figures 4-6). This can be simply explained by the use of cadaveric organs to re-transplant failed LDLT grafts.

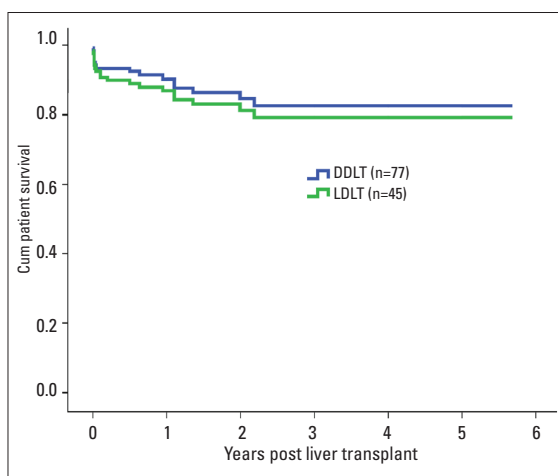
## DISCUSSION

The Saudi Center for Organ Transplantation was successfully established in 1985,<sup>14</sup> and this paved the way for the launch of DDLT programs in our country. The first DDLT in Saudi Arabia was performed in 1990, and to date more than 300 of these operations have been performed with good success.<sup>1</sup> As mentioned, the LT program at KFSHRC lapsed for a period, and was reactivated by our current surgical team in 2001. We have since performed 77 DDLT procedures with excellent outcomes and a survival rate that is comparable to

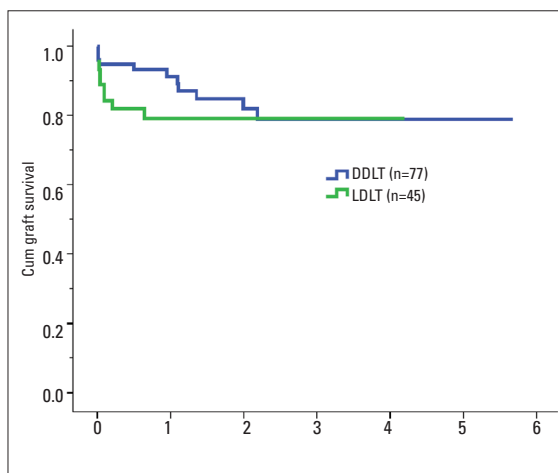
rates at other experienced LT centers. However, soon after restarting our DDLT program, we were faced with the major barrier of a severe cadaveric organ shortage for LT in Saudi Arabia. This shortage is due to many complex logistical problems in all steps of the cadaveric donation process, including donor identification, reporting, diagnosis, management, documentation, and obtaining consent.<sup>14-20</sup> This distressing scarcity of cadaveric donor organs, together with the increasing number of patients dying on our LT waiting list has significantly limited our ability to expand our LT program. Therefore, we were forced to consider adopting LDLT, which seemed the only logical way forward in our situation. Our initial reluctance to undertake LDLT was fueled by the many ethical questions that are generated by the concept of live liver donation: Is it ethical to ask a person to donate part of his or her liver to save the life of a loved one? Can the donor truly give



**Figure 4.** Overall patient and graft survival after mean follow-up of 736 days.



**Figure 5.** Cumulative patient survival in deceased-donor and live-donor transplantations.



**Figure 6.** Cumulative graft survival in deceased-donor and live-donor transplantations.

informed consent under such circumstances? Would it not be considered “emotional blackmail”? Is it ethical to subject a healthy person to a major operation with potential morbidity and mortality in order to save the life of another? Another major concern about live donation is the likelihood of organ trafficking, which cannot be ignored, especially in regions with high poverty rates. Despite these moral dilemmas, the team came to the conclusion that our patients have the right to be offered all available treatment options, including LDLT, and that, as a team, we must take all necessary precautions to respect donor interests and ensure donor safety. To date, we have performed 45 LDLTs and our overall survival rates are comparable to other international LDLT programs, especially when the learning curve process is considered.<sup>21-24</sup> The rate of biliary complications in the LDLT group was significantly high when compared to DDLT, which again has been reported by other centers that perform LDLT.<sup>23,25</sup> Despite this higher rate of biliary and vascular complications in the LDLT group, the overall 1-, 3-, and 5-year graft and patient survival rates are similar to the DDLT group, which reflects the successful management of those complications by a multidisciplinary team approach.

In our early experience with LDLT at KFSHRC, we were astonished by how difficult it is to find living donors who fulfill our criteria for liver donation. Many candidates have been rejected for a variety of reasons, including unexpected pathology (steatosis and viral disease) and failure to pass psychosocial evaluation.<sup>26</sup> Therefore, we have come to the conclusion that LDLT is not the answer to all of our challenges, and that this procedure can help alleviate the problem of organ shortage, but cannot replace DDLT in Saudi Arabia. We believe that we should focus our efforts on identifying and fixing the different problems that have led to the decline in the number of available cadaveric donors. By doing so, we hope to considerably increase the cadaveric organ pool for LT in our country.

In conclusion, both DDLT and LDLT are being performed successfully at KFSHRC. The shortage of cadaveric donors and the difficulty of finding suitable donors for LDLT remain the main factors that limit expansion of our emerging LT program. Therefore, efforts should be directed toward increasing the number of available cadaveric donors. Until the number of cadaver donors rises, expansion of the LDLT component of our program may be the only way to save patients from dying on the waiting list.



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