Original Article

Adult Living Donor Liver Transplantation in Singapore: The Asian Centre for Liver Diseases and Transplantation Experience

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Abstract

Introduction: Living donor liver transplantation (LDLT) has progressed dramatically in Asia due to the scarcity of cadaver donors and is increasingly performed in Singapore. The authors present their experience with adult LDLT. Materials and Methods: Adult LDLTs performed at the Asian Centre for Liver Diseases and Transplantation, Singapore from 20 April 2002 until 20 March 2006 were reviewed. All patients received right lobe grafts and were managed by the same team throughout this period. Data were obtained by chart review. This study presents both recipient and donor outcomes in a single centre. Results: A total of 65 patients underwent LDLT. Forty-three were genetically related while 22 were from emotionally-related donors. The majority were chronic liver failure while 14% were acute. The most common indication for LDLT was end-stage liver disease due to hepatitis B virus. A total of 22 patients with hepatoma were transplanted and overall 1-year disease specific survival was 94.4%. The mean model for end-stage liver disease (MELD) score was 17.4 ± 9.4 (range, 6 to 40). Six patients had preoperative molecular adsorbent recycling system (MARS) dialysis with 83% transplant success rate. The mean follow-up was 479.2 days with a median of 356 days. One-year overall survival was 80.5%. There was 1 donor mortality and morbidity rate was 17%. Our series is in its early stage with good perioperative survival outcome with 1-month and 3-month actuarial survival rates of 95.4% and 87.3% respectively. Conclusion: The study demonstrates that LDLT can be done safely with good results for a variety of liver diseases. However, with dynamically evolving criteria and management strategies, further studies are needed to maximise treatment outcome.

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Key words: Donor and recipient outcome, End-stage liver disease, Hepatitis, Hepatocellular carcinoma, Living donor liver transplantation

Introduction

Living donor liver transplantation (LDLT) has evolved dramatically over the past decade and it has continued to progress and expand with the realisation of the exponentially increasing waiting times and waiting list deaths in cadaveric liver transplants. With the scarcity of cadaveric liver donors in Asia, this therapeutic innovation has thrived in the region.

Adult LDLT using right lobe grafts is an effective procedure but is associated with a significant complication rate despite good survival outcomes.[1-4] Advances in operative technique as well as imaging technological developments have allowed for better safety of living donors and further justification for the donor's risk.[5-8] Liver-assist devices have improved our management of fulminant liver failure and have offered new treatment strategies.[9-11]

Paediatric liver transplantation using left lobe graft is well established in Singapore. It has shown a very reputable success as well as donor safety. However, the demand for a larger liver size for adult patients has encouraged the use of right lobe grafts in LDLT. This paper presents a single-centre experience with adult right lobe LDLT over a 4-year period.

Materials and Methods

A total of 65 right lobe adult LDLT were performed at the Asian Centre for Liver Diseases and Transplantation,

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Singapore from 20 April 2002 until 20 March 2006. The same team of surgeons and anaesthesiologists performed all the donor and recipient operations throughout this period. Preoperative and postoperative care was managed by the same transplant team.

Recipients

Both non-urgent and high-urgency hospital bound patients were considered for LDLT at our centre. Evaluation and management of the recipients were dependent on the underlying liver aetiology and the severity of liver decompensation as well as the presence of ongoing comorbid conditions. All hepatoma patients had computed tomography (CT) scan of the abdomen and chest as well as PET scan and were considered for full transplant evaluation after extrahepatic disease had been excluded. Vascular anatomy is also reviewed on CT-scan and patients should not have gross involvement of the major vessels (hepatic vein, portal vein and hepatic artery) for them to be considered for liver transplantation.

Donors

Potential donors who volunteered for the procedure underwent medical and psychological evaluation. Both related and non-related individuals who were emotionally connected to the recipient were considered for donation. Non-related donors who were emotionally connected to the recipient were only considered as donors if related (genetically or by marriage) donors were deemed unsuitable. The risks and benefits of the procedure, and our institutional experience were discussed at multiple stages during the evaluation. Donors were assessed for possible coercion and were informed that they could withdraw at anytime. All probable candidates for liver donation undergo an independent psychiatric assessment to ensure that they are of sound mind, fully understand the procedure that they have consented to and the risks thereof, and that this is voluntary. Psychosocial and economic issues were considered and continued follow-up for donors was ensured. After potential donors were found medically and psychologically fit, final approval for transplant was provided by an ethics committee composed of an independent body not in anyway involved with the transplant team. The ethics committee consisted of 2 doctors, 1 from the hospital not in any way involved with the transplant team and 1 outside practitioner not connected with the hospital, and 1 lay person.

Laboratory assessments included liver function tests, biochemistry, haematology and bleeding profile. Routine chest X-ray, electrocardiogram (ECG) and urinalysis were done for preoperative assessment. Once preliminary tests were normal, all donors undergo 2-dimensional echocardiography and treadmill test. If there are findings of increased cardiac risk then they do not qualify for donation. If findings are inconclusive then they undergo CT-coronary angiography or conventional angiogram to better stratify their risks. Serologies for hepatitis A, B and C, cytomegalovirus, Epstein-Barr virus, Venereal Disease Research Laboratory (VDRL) and human immunodeficiency virus (HIV) were tested.

Abdominal CT scans were obtained to estimate the volumes of the right and left lobes and to assess hepatobiliary anatomy. The standard liver volume (SLV) is computed as [body surface area (DuBois formula) multiplied by 706.2] + 2.4 and based on the right lobe volume a "donor" graft-to-"recipient" standard-liver-volume ratio is computed and the minimum value accepted is 35%. The remnant liver volume for the donor on the other hand should be at least 40% although 35% is acceptable. Liver biopsy was done whenever steatosis was suspected on CT scan. The degree of steatosis should be less than 30%. If these are not met, then the patient and family were advised to find another donor.

Raw CT scan data were further utilised for vascular reconstruction and vascular flow studies using the MeVis Distant Services AG technology – Bremen, Germany.

After donation, routine donor follow-up included visits at 1 week, 1 month, 3 months, 6 months and yearly thereafter.

Operative Technique

The timing of laparotomy was largely influenced by the presence of hepatocellular carcinoma (HCC). Laparotomy and exploration was first started in the recipients with hepatoma to confirm that the disease was limited to the liver and to avoid unnecessary laparotomy to the donor.

The donor procedure begins with intraoperative assessment of the donor liver after laparotomy. Liver biopsy with frozen section is done if there is doubt regarding the graft quality. A fatty liver with >30% steatosis on biopsy would exclude the donor and the transplant operation is aborted. This is followed by cholecystectomy and intraoperative cholangiography to delineate the biliary anatomy. Next, complete mobilisation of the right lobe is done with division of its diaphragmatic attachments. The right hepatic artery and right portal vein are then carefully dissected and intraoperative ultrasound is performed to define the hepatic venous drainage of the right lobe and to identify the middle hepatic vein which we routinely preserve to avoid outflow blockage to the remaining segment 4 in the donor. We utilise MeVis imaging technology (Fig. 1) and routinely identify significant middle hepatic vein tributaries which, if present, are anastomosed to the vena cava in the recipient procedure using saphenous vein jump graft. Retrohepatic caval dissection is then commenced and the

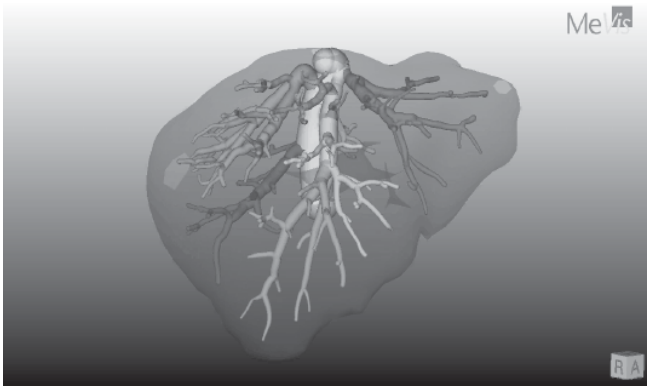

Fig. 1. Sample donor liver reconstruction and segmental venous flow analysis using MeVis.

right hepatic vein is isolated. A surgical nylon tape is passed along the medial border of the right hepatic vein which provides a guide to the plane of dissection. The right hepatic duct is then cut sharply near the confluence.

The hepatic parenchyma is divided along the Cantlie's line 1 cm to the right of the middle hepatic vein trunk using Cavitron Ultra-Sonic Aspirator (CUSA). Special attention is paid to the middle hepatic vein and its tributaries that drain the right lobe. The right lobe is removed and flushed with UW solution at 4ºC. After closure of the vascular stumps and hepatic duct stump, the cut surface of the liver and hilum are carefully checked for bile leak. Abdominal closure is performed in a standard fashion after placement of a tube drain.

We do not routinely use veno-venous bypass. Trial caval clamping is done with intravascular volume loading and, if the patient is stable, recipient hepatectomy is performed with preservation of the inferior vena cava. A Satinsky clamp is applied on the suprahepatic and infrahepatic vena cava with adequate spacing to allow hepatic venous anastomoses and the liver is removed with division of the bile duct, portal vein, hepatic artery and hepatic veins at the liver surface. The middle and left hepatic vein stumps are closed and the right hepatic vein orifice is utilised for end-to-end anastomosis after positioning of the right lobe liver graft in the right subphrenic space. Additional hepatic veins are sutured in an end-to-side fashion when present and significant segmental veins are anastomosed using jump graft. Portal veins are anastomosed and the graft is then reperfused. After hepatic artery anastomosis, biliary reconstruction is done in end-to-end fashion without a t-tube whenever possible. Hepatic ductoplasty is done when feasible to allow for a single anastomosis. We routinely utilise intraoperative Doppler ultrasound to assess graft perfusion and flow rates in all the vascular anastomoses prior to abdominal closure.

Results

Recipients

Sixty-five recipients (50 males and 15 females) with a mean age of 52.4 ± 8.75 years (range, 27 to 68) underwent right-lobe adult LDLT. Only 6 patients were from Singapore. The rest were predominantly from all over the Asia-Pacific region. Fifteen (23%) were from Indonesia, 13 were from India, 12 were from Malaysia, 4 were from Burma, 3 each were from Bangladesh, the United Arab Emirates and Pakistan, 2 each were from Philippines and Sri Lanka, and 1 each was from Brunei and Ethiopia.

Forty-three of the cases were from related donors (66%) and 22 were from non-related but emotionally connected donors. Of the living related liver transplants, 19 were donated by their children, 14 were from the nephew, 8 were from siblings, 1 was from the mother and 1 was from the cousin. Of the non-related donors, 5 were spouses or fiancée. All the remaining 17 unrelated donors where close family friends with established strong emotional relationship with the patient. They were only accepted because no relative was found suitable for liver donation.

The majority of the patients were chronic failure cases while 14% were acute, 33% of which were from the intensive care unit (ICU). Indications for transplantation were end-stage liver disease secondary to hepatitis B virus in 28 (43%) patients, with concurrent hepatitis C in 1 patient and HCC in 14 of these patients; hepatitis C in 15 patients, 47% of them with HCC; alcoholic cirrhosis in 6 patients, with HCC in 1 patient, concurrent hepatitis E in 1 patient and hepatitis B in another; cryptogenic cirrhosis in 8 patients, 1 of whom had HCC; chemical or drug-induced liver failure in 6 patients; autoimmune cirrhosis in 2 patients and polycystic liver disease with concurrent hepatitis B in 1 patient.

We had a total of 22 patients transplanted with HCC. One patient was transplanted due to hepatitis B cirrhosis and was noted to have hepatoma in the explanted liver. Fifteen (68%) had had previous treatment with the majority receiving hepatic chemoembolisation. Overall 1-year survival was 94.4% which was numerically better than that for non-HCC patients (85.1%) although their difference was not statistically significant with *P* value of 0.566 (Fig. 2). Thirty-two per cent fall within the Milan criteria (Table 1). Only 6 patients had tumour recurrence and the average time to recurrence was 7.6 months. All the recurrences were in patients beyond the Milan criteria and the most common site of recurrence was the lung followed by the transplanted liver. The median disease-free survival was 25months and the 1-year disease-free survival was 72.98% (Fig. 3). The median survival for the Milan group was 32.5 months and 32.25 months for those falling beyond the Milan criteria. Kaplan-Meier survival among these 2

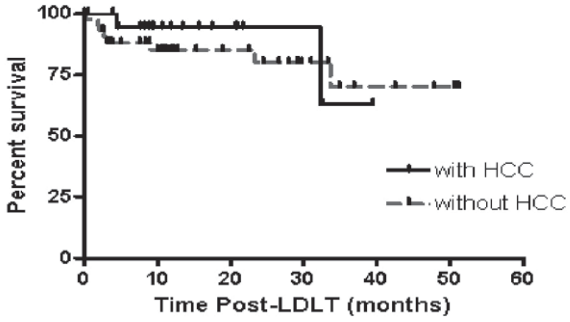

Fig. 2. Kaplan-Meier survival curve showing overall survival of patients with hepatocellular carcinoma (HCC) versus without HCC after living donor liver transplantation.

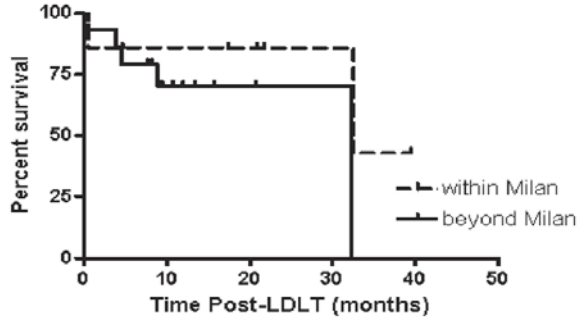

Fig. 4. Kaplan-Meier survival curve showing overall survival patients with hepatocellular carcinoma after living donor liver transplantation according to Milan criteria.

Table 1. The Milan Criteria for Liver Transplantation in Patients with Hepatocellular Carcinoma

No. of tumours	Criteria
Solitary	Should be ≤5 cm *
Multiple	Number of tumours at most 3 with none >3cm *

*There must be no major vascular involvement by the hepatocellular carcinoma

groups were not statistically significant ($P = 0.2457$) (Fig. 4).

The mean model for ESLD (MELD) score was 17.4 ± 9.4 (range, 6 to 40) with a median of 15.2 (Table 2). The majority of patients had a MELD score of greater than 10 (70%), the greater part of them (37%) having a score of 11 to 20 (Fig. 5). Thirty-four per cent had a MELD score of more than 20 and survival among these patients were similar to those with MELD scores of less than 20 (75% versus 78.1%). There were 30 patients with MELD scores of less than 15. Of these, 21 were transplanted with HCC while the remaining 9 (4 with hepatitis B, 2 with Hepatitis C, 2 with cryptogenic cirrhosis and 1 with alcohol-induced cirrhosis) were transplanted due to repeated episodes of encephalopathy and variceal bleeding.

A total of 7 patients received molecular adsorbent recycling system (MARS) dialysis perioperatively. Six

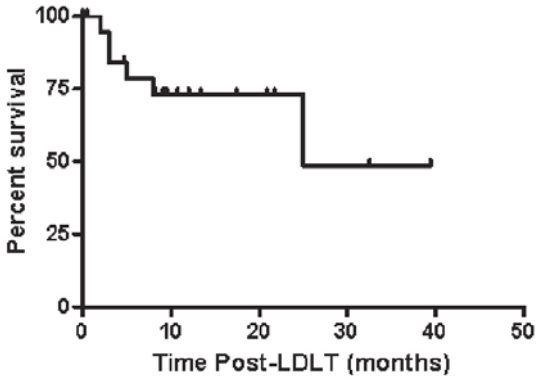

Fig. 3. Kaplan-Meier survival curve showing disease-free survival of patients with hepatocellular carcinoma after living donor liver transplantation.

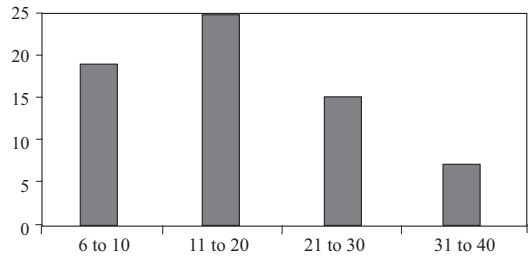

Fig. 5. Patient distribution according to MELD scores.

patients received dialysis preoperatively as a bridging strategy prior to transplantation. Improvements in bilirubin, ammonia, encephalopathy, renal function and cerebral oedema (Fig. 6) were noted in these patients and transplant success rate was 83% (5 out of 6). One patient had MARS dialysis post-transplant due to graft failure from hepatitis B reinfection 9 months after the liver transplantation and eventually expired while awaiting retransplantation.

We do not employ routine veno-venous bypass in our transplant programme and we have successfully transplanted the majority of patients (89.3%) without utilising it. A total of 6 patients required veno-venous bypass after being noted to be unstable during trial caval clamping. These patients were either elderly and could not tolerate trial clamping or had severe liver decompensation, as reflected by the high MELD scores.

The immunosuppression regimen used in our centre is primarily tacrolimus-based (80%). Simulect is also utilised for induction if there is renal impairment. Rapamune is used in all patients with hepatoma and is started 1 month post-transplant. The longest post-transplant survival in our series is 3 years and 11 months. The mean follow-up is 1 year and 4 months (479.2 ± 396.2 days) with a median of 356 days. The overall mortality rate is 24.6% (16 out of 65 patients). The 1-month mortality rate is 4.6% and the 3-month mortality rate is 12.7%. The majority of the mortalities were related to sepsis (50%) commonly from pneumonia.

Non-survivors in our series were significantly older than

Table 2. Recipient Age, Weight, Bilirubin, MELD Score and Graft-to-SLV Ratio Distribution

Recipient	Age (y)	Weight (kg)	Bilirubin	MELD	Graft-to-SLV ratio
Range	27-68	45-108	11-805	6.0-40	0.3059-0.9309
Median	52	67	62	15.2	0.5836
Mean	52.4	69.6	173.08	17.4	0.6019
SD	8.75	13.1	205.85	9.4	0.1158

MELD: model for end-stage liver disease; SD: standard deviation; SLV: standard liver volume

Table 3. Recipient Age, MELD Score, Graft Volume and Graft-to-SLV Ratio of Survivors vs Non-survivors

Recipient	Survivors	Non-survivors	*P* value*
Age	51 ± 9	56.8 ± 6	0.009
MELD score	17.4 ± 9.4	17.5 ± 9.6	0.957
Graft-to-SLV ratio	0.614 ± 0.120	0.565 ± 0.098	0.108

MELD: model for end-stage liver disease; SLV: standard liver volume
*Significant if $P < 0.05$.

the survivors (Table 3). However, MELD scores between these groups were not statistically significant. Although the mean graft-to-SLV ratio appeared to be higher among the survivors, this difference was not statistically significant. The principal cause of mortality in our series was sepsis and tumour recurrence.

A total of 3 patients died of HCC recurrence. We had 2 mortalities due to chronic rejection; one after using a generic immunosuppressant drug and one due to poor compliance. We had 1 case of primary graft non-function expiring on the second postoperative day. One patient died of portal vein thrombosis 2 weeks post-transplant. This patient presented as graft dysfunction with normal Doppler studies and portal vein thrombosis was seen intraoperatively on re-laparotomy. One patient died of intracerebral bleed on the fourth month post-transplant. One patient medicated with appetite stimulant containing cyproheptadine died with drug-induced graft failure.

Our series of 65 patients achieved an overall 1-year survival rate of 80.49% and a 2-year survival of 76.47% (Fig. 7). However, at least 1 complication was noted in 35% of patients (Table 4). The most common morbidity was Prograf toxicity occurring in 8 patients, 2 of whom presented with seizures. These patients improved after being shifted to a cyclosporine-based regimen. There were 5 cases of rejections (1 acute and 4 chronic), all of whom responded well to medical treatment. Two cases of chronic rejection were due to non-compliance. Four patients developed graft abscess, 2 required surgical evacuation of subcapsular abscess while the other 2 resolved with antibiotic treatment. We had 3 patients who developed bile leak, 2 of whom required stenting while the other resolved spontaneously.

Table 4. Living Donor Liver Transplantation Recipient Postoperative Morbidities

Postoperative morbidity	Incidence
Prograf toxicity	8
Rejection	5
Acute	1
Chronic	4
Graft abscess	4
Pleural effusion requiring drainage	3
Loculated intraabdominal fluid collection	3
Bile leak	3
Bilio-pleural fistula	2
Postoperative bleeding	2
Diabetic nephropathy	2
Incisional hernia	2
Small-for-size graft syndrome	1
CMV infection	1
Tuberculosis	1
Chemical-induced graft failure	1
Foot drop	1

CMV: cytomegalovirus

There were 2 cases of postoperative bleeding. One was a subphrenic bleeding from collateral varix while the other was a posterior wall leak of the hepatic vein-vena cava anastomosis. Another 2 patients developed bilio-pleural fistula which resolved with thoracostomy tube and abdominal drainage. One patient developed foot drop post-transplant with saphenous vein jump graft, which resolved with conservative treatment after 3 weeks. We had a 108-kg patient with a computed graft-to-SLV ratio of 0.42 who presented with small-for-size graft syndrome. He recovered with supportive care.

Donors

In our series, 2 prospective donor operations were aborted. One patient had fatty liver not picked up by CT scan with intraoperative liver biopsy of >40% steatosis and the other for lymphangiectasia and multiple lymphadenopathies noted

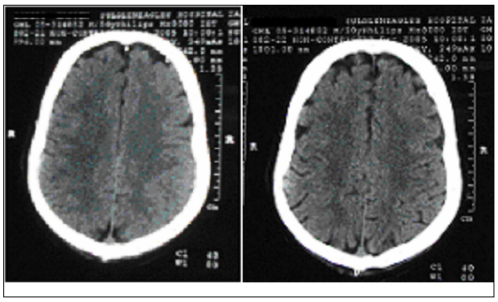

Fig. 6. Cranial CT scan showing improvement in cerebral oedema. (pre-MARS dialysis, left; and post-MARS dialysis, right).

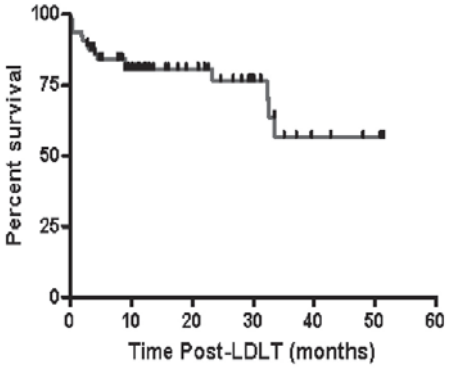

Fig. 7. Kaplan-Meier survival curve showing overall survival of patients who underwent living donor liver transplantation.

intraoperatively. Both patients were eventually discharged with unremarkable postoperative recovery. Right lobectomy for living donation was performed successfully in 65 patients (50 males and 15 females) aged 31.6 ± 8.7 years (Table 5). Graft volume was 745.7 ± 137.9 mL (range, 386 to 1091) and the donors' residual-liver-to-total-liver volume ratio was 0.4648 ± 0.0513 (range, 0.4021 to 0.5748).

Donors were routinely observed in the Liver ICU overnight. In the immediate postoperative period, the majority of the donors exhibited transient elevations of liver enzymes and bilirubin. Hospital stay was 6 to 8 days and routine ultrasound was done prior to discharge.

We had 1 donor who died due to acute myocardial infarction on the second postoperative day. The patient had good left ventricular motion on 2-D echo and tolerated treadmill test without any evidence of ischaemia on preoperative work-up. An emergency thoracotomy was done and an atherosclerotic lesion was noted involving the left anterior descending coronary artery. The patient died despite performing emergency coronary artery bypass graft. Post-mortem examination confirmed coronary artery disease with myocardial ischaemia. There was an overall complication rate of 16.9% (11/65). One patient was reoperated for bile peritonitis presenting on the third week post-hepatectomy. She had uneventful reoperative recovery. One patient underwent percutaneous drainage for loculated subphrenic collection. Two donors developed biliary strictures which were successfully managed with endoscopic retrograde cholangiopancreatography (ERCP) sphincterotomy and biliary stenting. There were 4 cases of superficial surgical site infection and 1 partial wound dehiscence. One patient developed transient median nerve palsy and another had ulnar nerve palsy which both resolved spontaneously. We had 1 donor, a smoker, who developed antral gastritis postoperatively. He responded well to medical treatment.

The majority of donors expressed inconvenience in going to Singapore so when their physical exam and liver ultrasound and liver function tests were normal after 9 to 12 months post-surgery, they are discharged from follow-up and advised to consult us on an as-needed basis when they have subjective complaints. The median follow-up is 10 months. There are donors, however, who still come to see us routinely; the longest being 41 months post-surgery. No long-term donor complications were encountered in our experience.

Discussion

The first adult LDLT using a right lobe graft was attempted in Japan in 1994. Given the near absence of cadaveric donor livers in Asia, adult LDLT with right lobe grafts has dramatically increased with the increasing success rates and lower donor morbidities.

The current report on our experience in adult LDLT shows viral followed by alcoholic induced liver failure to be the most common indications for liver transplantation. These findings are similar to those reported by the European Liver Transplant Registry.[12] Although hepatitis B infection

Table 5. Donor Age, Weight, Graft Volume and Residual-Liver-to-Total-Liver-Volume Ratio Distribution

Donor	Age (y)	Weight (kg)	Graft volume (mL)	Residual-liver-to-total-liver volume ratio
Range	21-59	47.7-137	386-1091	0.4021-0.5748
Median	29	68.5	747	0.4612
Mean	31.6	70.0	745.7	0.4648
SD	8.7	14.5	137.9	0.0513

SD: standard deviation

is the indication for transplantation in the majority of our patients (48%) as well as in Asia, it is noteworthy to mention that, although prevalent in the US and Europe, there have been a significant number of patients with hepatitis C cirrhosis transplanted (23%) and nearly half of them (47%) presented with HCC. The incidence of HCC was also less common in autoimmune and cryptogenic cirrhosis which can be explained by the lower cancer risk in these patients.[13]

Hepatoma patients appeared to have a better survival in our study (94.4% versus 85.1%) although their difference was not statistically significant ($P = 0.566$). The number of cases maybe too small to show statistical difference but the discrepancy in survival may be explained by a more timely surgery because of a live-donor transplant programme which has no waiting-time and the less hepatic dysfunction in these patients compared to those with end-stage cirrhosis which may influence the postoperative outcome.[14,15] These data suggest that an intensive screening for distant disease and early timing of surgery are beneficial in these patients, and with improved criteria, long-term survival may be further optimised. Liver transplantation is emerging as a potential treatment strategy for patients with HCC. Currently, however, the selection criteria is continuously evolving and there is no definite objective guide to provide measures for the proper timing of advising transplantation in these patients to effect the best cure and survival advantage.[16]

Liver-assist device (MARS) was used in 7 patients due to its recognised effects in published data.[9-11,17] Although improvements in bilirubin, ammonia, cerebral oedema and renal function were observed, the number of patients was too small to conclude a therapeutic benefit. This, however, offers a new strategy of management especially in patients with fulminant failure who have a clear indication for transplant but no potential donor is available.

Overall survival was 75.4% and MELD scores among survivors and non-survivors did not show statistically significant difference. This finding was similar to other published data that MELD scores, computed as [3.8 x log (e) (bilirubin mg/dL) + 11.2 x log (e) (INR) + 9.6 log (e) (creatinine mg/dL)], although predictive of waiting list mortality, is a poor predictor of postoperative outcome.[18] Graft-to-SLV ratio between these 2 groups was statistically similar but age was noted to be higher among non-survivors, and this has been identified as an independent factor affecting transplant outcome in other studies.[19]

Biliary complications remain a significant concern in liver transplant surgery. There were 2 donors who developed bile duct strictures at the level of the bifurcation. These have occurred early in the series and are cases with common hepatic duct bifurcation very near the parenchyma of the liver that we had to transect the duct near the confluence. We currently give at least 2 mm allowance to avoid compromising the remaining ducts in the donor patient and had no further incidence of bile duct strictures encountered in the rest of the series. The majority of these complications were managed non-operatively with good results and we feel that with improved experience and radiologic technology, the rate of surgical intervention will continue to decline. However, prevention is still the dictum and operative technique during transplantation can never be overemphasised.

Cardiac complications associated with any major surgery remain a significant concern in liver transplantation. We feel that a systematic assessment should be carried out especially for seemingly fit patients who volunteered for liver donation. We had 1 donor death and this serves as a realisation of this risk. However, it should be made clear that patients undergoing this phenomenal operation should understand that this risk will always remain even under appropriate care. We strongly believe that this does not warrant invasive assessment with routine angiography in all patients going for this procedure.[20] The accuracy of exercise testing for detecting coronary artery disease depends on the severity of stenosis, sensitivity and specificity may approach 100% in patients who reach maximum levels of exercise, and this limitation was reached in our patient. In the absence of symptoms, the indications for angiography are controversial and must be individualised. This invasive strategy is considered beneficial only if the estimated mortality rate of the proposed operation is substantially higher than 5%. We believe that this invasive cardiac procedure should be considered only when a high risk of cardiac complication is evident, as it may lead to the very same cardiac complication that it is designed to prevent. Death after an elective surgery may often pose a question of how far should we go with regard to cardiac evaluation and further studies would be needed to better address this concern of donor safety. We also look forward to accuracy data on other new diagnostic modalities that we may include in the pre-operative evaluation in the future.

Donor morbidity in our series is comparable to published data.[21-23] It is important to note that these morbidities were not associated with long-term dysfunction and these data show that this is a relatively safe procedure.[24,25] We are doing an average of 3 to 4 liver tranplants per month and with more experience, improved surgical techniques, and meticulous donor evaluation, the morbidity and mortality for recipients and living liver donors will be improved.

Liver transplantation has offered new treatment options for a variety of liver diseases and a remarkable transformation has occurred in the management of patients with liver disease over the last decade. It is now apparent

that liver transplantation offers the only chance for improved survival for patients with end-stage liver disease and selected patients with HCC.

Cadaveric liver transplantation is always a preferred procedure especially considering the risks to the donor. Unfortunately, the demand for cadaveric liver transplantation has continued to increase and the waiting list is ever increasing. The long waiting time has been recognised all over the world and as such, measures to prioritise cadaveric liver allocation have been established. The MELD scoring system has been utilised for organ allocation.[26,27] It has dramatically helped in improving transplant outcome but donor liver shortage has continued to be a concern. Both graft and patient survival are similar between adult LDLT and cadaveric liver transplant, and published data show that living donor transplant programme is a reasonable alternative, especially in Asia, where there is an extreme scarcity of cadaveric liver donors.

Transplantation is also not widely available in many countries and it is fortunate that this treatment option is offered in Singapore. However, considerable controversy still remains about some aspects of liver transplantation that must be settled convincingly, given the scarcity of donor organs available for transplantation. Clearly, further research is needed to settle controversies such as immunosuppression regimen and the use of steroids especially with hepatitis C, transplant criteria for HCC beyond tumour size and number, as well as aggressiveness in the live donor cardiac evaluation, and controlled clinical trials may be required to further improve treatment outcome.

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