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Learning curve for living-donor liver transplantation in a fledgling cancer center

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Summary

Hepatocellular carcinoma (HCC) has become one of the main indications for liver transplantation. To keep abreast of the times, a comprehensive cancer center may have to perform liver transplantation as a treatment option for HCC. We introduce a learning curve for living-donor liver transplantation (LDLT) and present our initial experience in a new cancer center as an example to any center considering LDLT. A total of 51 consecutive adult right liver LDLTs performed from January 2005 to January 2008 were analyzed by comparing the first 17 transplants performed with the help of an outside experienced team (group 1) with the middle 17 (group 2) and the last 17 cases (group 3) performed in our center independently. There was no hospital mortality in donors and recipients. In a mean follow-up of 34 months (range: 12–48 months), there was only one case of late mortality in donor and recipient, respectively. A total of four donors and 12 recipients underwent re-operations. The warm ischemic time was significantly longer in group 2 than that in groups 1 and 3. Otherwise, there was no significant difference in the operative outcomes among the three groups. Thorough preparation and the assistance of an experienced liver transplantation team at the beginning can facilitate a more rapid learning curve and bring about a good outcome even in a small, newly established institution.

Introduction

Living-donor liver transplantation (LDLT) is an accepted therapeutic option for patients with end-stage liver disease when cadaveric donor organs are scarce. LDLT requires technical proficiency in major hepatectomy, familiarity with liver anatomy, and multidisciplinary support from a vast array of medical specialties, including hepatology, immunology, critical care, radiology, anesthesiology, nephrology, cardiology, pulmonology, infectious disease, and rehabilitation medicine. Therefore, this intensive surgery is almost entirely performed in major hospitals.

Hepatocellular carcinoma (HCC) has become one of the main indications for liver transplantation. A hypothetical study using a decision analytic model suggested that patients with HCC are the best candidates for LDLT because the operation could be performed earlier for these patients disadvantaged by the allocation algorithm for cadaveric donor grafts [1].

In a region lacking sufficient cadaveric donor organs, LDLT is an important method for meeting the demand for liver transplantation. To meet this demand, our small-scale hospital, with only 500 beds, instituted LDLT without any previous organ transplant experience. The aim of this study was to introduce a learning curve for LDLT by presenting the initial experience at the National Cancer Center of Korea as an example to any center considering LDLT.

Methods

Preparation for the first LDLT

We planned to start LDLT in an effort to provide all-encompassing care for patients with HCC. Before starting LDLT, our center had provided full service of hepatobiliary

and pancreatic surgery by two surgeons competent in major hepatectomy. Both of them visited renowned liver transplant teams at home and abroad, observed LDLT, and gleaned the information about the whole process, including the surgical technique of LDLT.

One of the most difficult parts of setting up a transplantation program was to establish a multidisciplinary approach and numerous subspecialties that are needed to take care of the patients harmoniously. Before everything else, the infection and rehabilitation clinics, which were previously absent in our center, were installed to meet the legal requirements of the hospital permitted to perform liver transplantation, and two closely linked operating rooms were built and dedicated to LDLT. Equipments of venovenous bypass, the cell saver, and the rapid infusion system were also installed to be set on standby. Intensive care unit facilities were expanded.

Living-donor liver transplantation protocols and guidelines were developed for pre-, intra-, and postoperative managements. Anesthetic protocols were also structured to provide optimum safe intra-operative anesthesia. Preliminary meetings for LDLT were held periodically to familiarize the whole team with every detail about liver transplantation based on an extensive core of reference materials. As the program grew, an educational training program was developed to expose all transplant team members, consisting of doctor, nurse, technician, and allied staff, to their related fields using an outside experienced LDLT program. Before the first LDLT, all processes required in LDLT were set up and all personnel and services were organized.

Study design

The Ethical Committee of our institution approved this study. The study included 63 subjects who had a potential living donor evaluated between January 2005 and January 2008 at our center. Three patients were excluded because of extrahepatic metastases of HCC detected by pre-operative work-up. Other nine patients did not find any suitable donor in 11 candidates because of insufficient liver remnant ($n = 3$), fatty liver ($n = 3$), ABO blood type incompatibility ($n = 2$), withdrawal of intention to donate ($n = 2$), and hepatitis B positivity ($n = 1$).

The initial 51 consecutive cases of adult-to-adult LDLT performed at our hospital from January 2005 to January 2008 were reviewed for this study. The first 17 cases (group 1) were performed under the direction of the outside experienced team, with one of their surgeons as the primary surgeon. Both in-house surgeons participated as the first assistants, one in the donor operation and the other in the recipient operation. The subsequent 34 operations were performed entirely by our own surgical team. These were divided into two groups of 17 patients each, group 2 (initial in-house LDLT patients) and group 3 (later in-house LDLT patients).

All donors and recipients had a minimum follow-up of 12 months. The primary outcome was mortality after LDLT. Secondary outcomes were warm ischemic time and operative outcome including complications. Any event that deviated from the normal expected course of recovery was reported as a complication.

Donors

All living-donor candidates were informed about the items deliberated by the Ethics Group of the Vancouver Forum [2]. A hepatologist shared in an assessment of donor suitability with a social worker and a psychologist, which corresponded to a 'donor advocate team' [3]. No potential donor with concomitant medical or psychological illness was allowed to undergo the donor operation.

There were 32 men and 19 women, with a mean age of 30.4 years (range: 17–51 years). The living donors comprised 26 sons, nine daughters, one husband, six wives, five brothers, one brother-in-law, one sister-in-law, and two unrelated people. All donors volunteered for the procedure and signed informed consent.

They underwent a full examination, including blood group verification, calculation of body mass index and standard liver volume, liver and renal biochemistries, complete blood count, coagulation profile, and virologic assays for hepatotropic viruses. Donor imaging evaluation included Doppler ultrasonography, computed tomography (CT) with volumetry, and magnetic resonance cholangiography. All donors were followed for a month after right hepatectomy, then every 3 months for a year, and thereafter every 6 months.

Recipients

The recipients consisted of 43 men and eight women, with a mean age of 51.9 years (range: 36–66 years). The indications for transplantation were HCC with cirrhosis in 36 patients, hepatitis B virus-related cirrhosis in eight, hepatitis C virus-related cirrhosis in two, alcoholic cirrhosis in two, and drug-induced fulminant hepatic failure, intra-hepatic cholangiocarcinoma, and epithelioid hemangioendothelioma in one patient each.

According to Child-Pugh classification, there were 16 class A cases, 23 of class B, and 12 of class C. The model for end-stage liver disease (MELD) scores were: ≤18 in 44 cases; 19–24 in one case; 25–30 in four cases; and ≥30 in two cases (Table 2).

The absolute contraindication of LDLT for HCC was gross vascular invasion or distant metastasis detectable at

the time of pretransplant evaluation. Of the 36 HCC patients, six patients were beyond Milan criteria [4]. Of these six recipients, only one had HCC exceeding the UCSF criteria [5].

Salvage transplantation was performed in eight patients with HCC and one patient with intra-hepatic cholangiocarcinoma after previous partial hepatectomy. The liver resection consisted of right hepatectomy in two patients, left hepatectomy in two, left lateral sectionectomy in two, central bisectionectomy in one, right anterior sectionectomy in one, and wedge resection in one. Pretransplant nonsurgical treatments were used in 33 patients and included transarterial chemoembolization (TACE) in 29 patients, radiofrequency ablation (RFA) in one, and radiation therapy in five.

Immunosuppression was based on tacrolimus and steroids. Acute rejection episodes were confirmed by biopsies and treated with steroid boluses. Mycophenolate mofetil was added for 20 patients who required reduction of tacrolimus dose because of adverse effects.

The patients transplanted for HBV or HCV cirrhosis were managed with antiviral prophylaxis protocol using combined lamivudine and intravenous hepatitis B immune globulin therapy or ribavirin, respectively. All recipients were followed monthly for a year after transplant and thereafter every 2 months.

Operative strategy

In principle, a graft to recipient body weight ratio (GRWR) of 0.8% was chosen as the minimum cut-off value for the recipients. However, if patients were young and in good condition, graft quality was good, and the drainage of the anterior segment was secured, a GRWR more than 0.6 was selected carefully.

The middle hepatic vein (MHV) was included in the graft when the estimated remaining liver volume was greater than 35% of the whole liver without fatty change and when the GRWR was less than 0.8%, in which case venoplasty of the right hepatic vein (RHV) and MHV was performed to form a large triangular orifice [6]. Any inferior RHV larger than 5 mm in diameter was preserved for subsequent anastomosis to the recipient inferior vena cava (IVC). To prevent the congestion of the anterior section, expanded polytetrafluoroethylene (ePTFE) grafts were used to drain any MHV branch over 5 mm in diameter [7]. The minimal anhepatic technique was devised and used in group 3 to reduce splanchnic congestion and to minimize anhepatic period so that the native liver function could last longer, especially in patients with HCC or fulminant hepatitis who lacked adequate portosystemic collaterals in the splanchnic area [8].

Donor right hepatectomy

Donor right hepatectomy was previously described elsewhere [9]. The liver was exposed through a J-shaped abdominal incision. After cholecystectomy, the right hepatic artery and portal vein were dissected. The right liver was fully mobilized, and the RHV and inferior RHV, if present, were isolated. Following the demarcation line revealed on the liver surface by temporary occlusion of the right hepatic artery and portal vein, the parenchymal transection was performed with the ultrasonic dissection device using hanging maneuver, without any vascular inflow occlusion [10]. The bile duct was cut just 1 mm to the right side of the confluence under direct visualization after the liver parenchymal transection to reduce injury to the remaining bile duct and bile contamination. The stump was oversewn with a 6–0 monofilament, nonabsorbable suture. The right hepatic artery was ligated proximally, bulldog-clamped distally, and transected. A vascular clamp was applied to the right portal vein. The RHV and inferior RHV, if present, were clamped and divided. Then, the right portal vein was cut distally to the clamp. The graft was extracted through the incision. The stumps of the RHV and right portal vein were oversewn with a 4–0 and a 6–0 monofilament, nonabsorbable suture, respectively. The fibrin glue was applied to the cut surface of the liver. The falciform ligament was reconstructed. A closed suction drain was placed near the cut surface. The abdominal incision was closed layer by layer.

Bench work

The liver grafts were flushed with University of Wisconsin solution in the first seven cases, and thereafter with histidine–tryptophan–ketoglutarate solution at 4 °C. A total of 48 tributaries of the MHV over 5 mm in diameter in 36 recipients were reconstructed by interposing an ePTFE graft in each vessel.

Recipient operation

All 51 LDLTs were performed without venovenous bypass. The operation was commenced with dissection of the porta hepatis after cholecystectomy. The left hepatic artery and the artery to segment IV were divided as high up as possible to secure the length of the vessels. The right anterior and posterior hepatic arteries were then divided as high up as possible at the right side of the common bile duct, without touching the connective tissue between the right hepatic artery and the common bile duct. The bile duct with the right hepatic artery was dissected off from the portal vein and was slinged with a tape. The portal vein trunk was dissected above its bifurcation. The hilar structure of the bile

duct was dissected off from the portal vein. The bile duct was then transected sharply right on the hilar plate as high as possible, confirming that the left and the right hepatic ducts were patent. After complete mobilization of liver from perihepatic ligaments and the IVC, the right and left portal veins were clamped and divided. The middle and left hepatic veins were stapled, and the RHV was clamped and divided so that the diseased liver could be removed. In 43 patients, after total hepatectomy, the graft implantation was started with the RHV or the common orifice of RHV and MHV, or ePTFE graft draining the anterior section formed on the bench work anastomosed end-to-side to the IVC and any inferior RHV over 5 mm in diameter, if present, was directly anastomosed to the IVC. In the other eight patients in group 3, the minimal anhepatic technique was used in the graft implantation [8]. The right portal vein of the graft was anastomosed to the right or main portal vein of the recipient, considering size discrepancy and redundancy. Of the 51 liver grafts, five had two portal veins, and separate anastomoses were performed in two of these. In the remaining three grafts, the two neighboring portal veins were sutured together and anastomosed end-to-end to the main portal vein. After reperfusion, hepatic artery anastomosis was performed using surgical microscopy between the right hepatic artery of the graft and the right or left hepatic artery of the recipient in all cases except one, in which the right gastroepiploic artery was used because of insufficient flow of the hepatic artery. Biliary reconstruction was performed by a duct-to-duct anastomosis in all cases. Of the 51 liver grafts, 11 had two bile ducts, and separate anastomoses were performed in three of these. In the remaining eight grafts, the two neighboring ducts were sutured together and anastomosed end-to-end to the common bile duct. Three closed-suction drains were placed in the abdominal cavity before closure.

Statistical analysis

For this study, we retrospectively compared the outcomes of the first 17 patients (group 1) with those of the middle 17 (group 2) and the last 17 cases (group 3). Categorical and continuous variables were compared using Fisher's exact test and the Mann–Whitney *U*-test, respectively. A *P*-value <0.05 was considered statistically significant.

Results

The donor operation was aborted in two other donors not included in this study, because of severe fatty change of more than 60% confirmed by intra-operative biopsy in one and intra-abdominal metastasis detected late during the recipient operation in the other. There was no hospital mortality in donors and recipients. In a mean follow-up of 34 months (range: 12–48 months), there was a case of late mortality in a donor and a recipient each, but otherwise there was no graft loss or re-transplant.

Donor

The mean donor residual left liver volume measured by CT was 33.5% (range: 25–42%). The mean graft weight was 682.9 g (range: 420–1005 g). The fatty change by routine intra-operative liver biopsy was less than 30% in all cases. The MHV was preserved in all except three donors. The blood type of the recipient was identical in 43 cases and compatible in eight cases.

The operative time became significantly shorter in group 2 than that in group 1, and in group 3 than that in group 2. Postoperative complications occurred in nine donors (17.6%), and the incidence was not significantly different among the three groups. Four donors (7.8%) underwent re-operation because of bleeding immediately after operation, and three of these underwent blood transfusion (Table 1). The bleeding points were the dissected wall of the common bile duct in two patients and the abdominal wall punctured for drain insertion in two. Otherwise, no transfusion was required. Transient bile leak in one donor ceased with conservative treatment after 20 days. Asymptomatic bile collection in another donor detected at the follow-up CT 1 month after discharge resolved with percutaneous catheter drainage. Two donors had wound infections and in one of the two, the abdominal drain tube was sutured together with the fascial layer of the abdominal wall so that the drain was removed with a minor bedside procedure under local anesthesia 7 days after the operation. Iatrogenic pneumothorax occurred in a donor during the intra-operative central vein catheterization, and this was treated with a chest tube.

The donor liver functions showed transient liver enzyme elevation, hyperbilirubinemia, and prolonged prothrombin time in the immediate postoperative period, but in all cases these indices normalized by the end of the first week.

The mean hospital stay was 10.6 days (range: 7–20 days) and was not significantly different among the three groups. All donors fully recovered and returned to their previous occupation within 2 months after operation without any long-term complications including psychological impairment. The only case of late donor mortality that occurred was from a traffic accident 2 years after the operation.

Recipient

The demographics and disease indications for LDLT were comparable among the three groups. The Child-Pugh

Table 1. Demographics and perioperative outcome of donors.

	Group 1 (*n* = 17)	Group 2 (*n* = 17)	Group 3 (*n* = 17)	Total (*n* = 51)	*P*-value
Gender (male:female)	10:7	13:4	9:8	32:19	0.350
Age (years; mean ± SD)	31.0 ± 9.13	29.1 ± 9.02	31.2 ± 10.14	30.4 ± 9.30	0.770
Operation time (min)					
Mean ± SD	325.7 ± 9.16	300.8 ± 8.39	271.4 ± 10.19	299.3 ± 6.11	0.001
Median	317	297	267	298	
Range	251–414	230–382	211–362	211–414	
Postoperative complications					
Bleeding	1	1	2	4	0.528
Biliary leakage	1	1	0	2	0.610
Pneumothorax	0	1	0	1	0.375
Wound infection	0	1	1	2	0.610
Re-operation	1	1	2	4	0.528
Postoperative hospital stay (days; mean ± SD)	11.4 ± 5.33	9.4 ± 1.50	11.1 ± 4.37	10.6 ± 4.08	0.319

Table 2. Demographics, perioperative status, and perioperative outcome of recipients.

	Group 1 (*n* = 17)	Group 2 (*n* = 17)	Group 3 (*n* = 17)	Total (*n* = 51)	*P*-value
Gender (male:female)	13:4	16:1	14:3	43:8	0.369
Age (years; mean ± SD)	52.6 ± 6.12	52.7 ± 5.52	50.4 ± 7.98	51.9 ± 6.86	0.557
Body weight (kg; mean ± SD)	64.9 ± 11.97	68.2 ± 9.78	65.42 ± 9.33	66.2 ± 10.32	0.613
Original liver disease					
Viral hepatitis/cirrhosis	15	15	15	45	0.811
Others	2	2	2	6	
Accompanying HCC	11	14	11	36	0.443
MELD score (mean ± SD)	17.7 ± 9.45	11.4 ± 4.06	10.9 ± 4.31	13.4 ± 7.04	0.005
≤18	12	16	16	44	
19–24	0	1	0	1	
25–30	3	0	1	4	
≥30	2	0	0	2	
Child-Pugh score (mean ± SD)	9.4 ± 2.18	6.9 ± 2.02	7.5 ± 2.24	7.9 ± 2.34	0.005
A (5–6)	2	8	6	16	
B (7–9)	8	7	8	23	
C (≥10)	7	2	3	12	
Operative time (min)					
Mean ± SD	607.9 ± 17.00	682.8 ± 40.09	602.6 ± 31.19	631.1 ± 18.24	0.133
Median	610	680	605	611	
Range	451–737	471–1107	329–904	329–1107	
Postoperative complications					
Bleeding	3	3	4	10	0.207
Biliary stricture/leakage	4	9	5	18	0.172
Vascular problem	2	0	1	3	0.360
Adhesive ileus	0	1	0	1	0.375
Re-operation	3	4	5	12	0.411
Postoperative hospital stay (days; mean ± SD)	21.9 ± 5.67	27.8 ± 7.04	27.1 ± 7.80	25.6 ± 6.50	0.640
Acute rejection	1	3	2	6	0.583

score and MELD score were significantly higher in group 1 than that in groups 2 and 3 (Table 2).

The mean GRWR was 1.06% (range: 0.63–1.92%). Three patients of GRWR less than 0.8 were successfully transplanted without small-for-size graft syndrome. The mean ratio of graft volume to estimated standard liver volume of the recipient was 38% (range: 30–60%). The mean cold ischemic time of the graft was 96.4 min (range: 8–242 min) and was not significantly different among the three groups. The mean warm ischemic time of the graft was 53.6 min (range: 25–136 min) and was significantly shorter in groups 1 and 3 than that in group 2, but showed no significant difference between groups 1 and 3 (Table 3).

Table 3. Data of right liver grafts.

	Group 1 (n = 17)	Group 2 (n = 17)	Group 3 (n = 17)	Total (n = 51)	P-value
Graft weight (g; mean ± SD)	674.2 ± 86.81	757.0 ± 156.23	617.5 ± 78.04	682.9 ± 124.58	0.003
GRWR* (%; mean ± SD)	1.09 ± 0.370	1.12 ± 0.200	0.96 ± 0.170	1.06 ± 0.253	0.158
Cold ischemic time (min)					
Mean ± SD	91.5 ± 31.88	89.2 ± 12.11	98.6 ± 8.97	96.4 ± 11.67	0.533
Median	89	88	105	91	
Range	44–167	8–242	32–176	8–242	
Warm ischemic time (min)					
Mean ± SD	44.4 ± 2.10	67.8 ± 6.52	48.7 ± 4.16	53.6 ± 2.99	0.002
Median	45	59	45	48	
Range	32–59	35–136	25–92	25–136	

*Graft to recipient body weight ratio.

The mean operative time was 631.1 min (range: 329–1107 min) and was shorter in groups 1 and 3 than that in group 2, but was not statistically significant among the three groups. The mean postoperative intensive care unit stay was 6.4 days (range: 3–12 days), and the mean postoperative hospital stay was 25.6 days (range: 14–93 days), which was not significantly different among the three groups.

The postoperative surgical complications occurred in 32 patients (62.7%), and the incidence was not significantly different among the three groups. Twelve recipients (23.5%) suffered re-laparotomy because of bleeding (10), splenorenal shunt (one), and adhesive ileus (one) (Table 2). The bleeding points were the dissected ligaments around the liver in 5, diffuse oozing in two, and stab wounds of the abdominal wall for drain insertion in three.

There were three vascular complications. One case of hepatic vein stenosis was treated with percutaneous transluminal angioplasty and intra-luminal stent placement. One case of anastomotic pseudoaneurysm of the hepatic artery detected by routine follow-up CT before discharge was successfully treated with endovascular embolization. One case with pre-operative spontaneous splenorenal shunt had no portal flow on the Doppler ultrasonography and CT angiography on the next day after transplantation. The patient immediately underwent re-laparotomy and the portal flow recovered fully with ligation of the left renal vein [11], and the patient was discharged with normal liver functions 16 days after LDLT and has been doing well for 13 months after LDLT. Of the 36 ePTFE grafts (6–8 mm in internal diameter) used to drain 48 MHV branches, the 1-month and 3-month patency rates of the ePTFE grafts were 72.2% (26/36) and 44.4% (16/36) when the patency of the ePTFE graft was checked with dynamic CT scans.

Biliary complications were encountered in 18 patients (35.3%) who were successfully managed with radiologic or endoscopic interventions and, though not significantly different among the three groups, the incidence was higher in group 2 than that in groups 1 and 3. Six recipients (11.8%) experienced an episode of acute rejection within 6 months of surgery and were treated with steroid boluses.

There were two cases of recurrence among the 36 recipients with HCC, and both of them were beyond the Milan criteria [4]. One patient expired 23 months after LDLT as a result of metastases to the brain, lung, and liver detected 11 months after LDLT, although the patient underwent mass excisions for brain and lung lesions and TACE for the liver lesions. The other patient who had undergone RFA 5 months before LDLT developed seeding along the needle track at the right lower chest wall 19 months after LDLT. Wide excision including an adjacent rib was performed, and he has now no evidence of disease 12 months after resection.

One patient who had previously undergone liver resection for intra-hepatic cholangiocarcinoma suffered from multiple bone metastases a year after LDLT. He is still alive 35 months after LDLT, with partial remission after chemoradiotherapy.

In eight recipients treated with the minimal anhepatic technique [8], hemodynamic stability with a urine output of 0.5–1 ml/kg/h or greater was maintained without any vasopressor or diuretic, and no blood transfusion was required during LDLT. All eight patients were extubated following the transplant procedure.

Discussion

All cases were adult right liver LDLT, reflecting a cancer center population mainly with HCC in a region with shortage of organs from cadaveric donors. The overall results of this study seem good in view of no hospital mortality and well-managed complications in both donors and recipients. To our knowledge, there is no published series with more than 50 consecutive cases without hospital mortality of adult right liver LDLT performed at a

single center with no previous experience in organ transplantation. At a mean follow-up of 34 months, there was only one case of late mortality from recurrence of HCC in a recipient. Although not related to the surgery, there was also a case of late donor mortality resulting from a motor vehicle accident.

Good LDLT outcome is a function of three variables: pre-operative patient selection, postoperative management, and surgical technique. The first two could be enhanced by referring to the most recent literature on LDLT, whereas the last is the most decisive factor and furthermore requires a significant learning curve. Instituting adult right liver LDLT, which requires a higher technical complexity and proficiency in a hospital, is highly likely to result in serious complications, including mortality. There is an international consensus that this procedure should be restricted to centers with substantial experience in deceased donor liver transplantations as well as in hepatobiliary surgery, because donor and recipient complication rates are liable to be high because of inexperience. It was reported that data from nine centers showed significant improvements in graft and recipient outcomes after 20 cases [12].

The challenge for our newly established cancer center, which lacked any transplantation experience, was to perform LDLT as a treatment for HCC as safely as veteran centers. We thought that having preliminary assistance from an experienced liver transplantation team would most easily enable us to surmount the steep learning curve and to become as proficient in LDLT as other experienced teams. The outcomes of our initial 17 cases resulted from two factors: thorough preparation from the full support of our center and supervision by an outside expert liver transplantation team. For our independent 34 cases, we had three ways of dealing with difficult situations and reaching a good outcome: communication with the outside expert team at any time in need, even during operation; continuous updating of the technique and knowledge of LDLT based on review of an extensive core of the latest reference materials; and our efforts for better operation. The first let us to use the right gastroepiploic artery as a hepatic artery alternative in a recipient, when the native hepatic artery could not be used for reconstruction because of insufficient flow. The second led us to use the artificial ePTFE grafts to drain the graft MHV territory in a situation where we had no tissue bank, and gave an idea of recovering portal flow with renal vein ligation in a patient with no portal flow because of splenorenal shunt detected the next day after LDLT. The third made us to devise the minimal anhepatic technique to minimize the seemingly inevitable anhepatic period for LDLT using right liver graft to address the two main problems of the anhepatic period: splanchnic congestion and no liver function [8], and eight patients in this study showed good outcomes.

The overall operative outcomes were comparable among the three groups. The operative time for donor hepatectomy shortened as experience accumulated from group 1 to group 2 and then from group 2 to group 3. The warm ischemic time during which anastomoses of hepatic vein and portal vein were performed to reperfuse the graft was longer in group 2 than that in group 1, but was not significantly different between groups 1 and 3. These outcomes reflect the increased proficiency not only in hepatic and portal venous anastomoses but also in hepatic artery anastomosis under the operating microscope, the most important and technically exacting part of the implantation. The whole procedure for LDLT took less than 6 h in the later cases in the series.

Although the good overall outcomes and absence of perioperative mortality in our fledgling LDLT program are encouraging, there were unexpected events that could have discouraged our LDLT program from going on. In the mean time, our team had to stand the psychological strain in performing the big surgery we had never done before. In the fourth case, the hepatic artery anastomosis had to be performed again because of rupture of the anastomosis by excessively forceful retraction of the hepatoduodenal ligament to secure the operative field. There were five cases of re-laparotomy for abdominal wall bleeding related to drain tube insertion, a complication which we had never experienced in more than 700 liver resections before. Till then, we had blindly pierced the abdominal wall with a cutting end connected to a closed-suction drain. After these events, a hole was made carefully in the abdominal wall with the tip of an electric coagulator, and there were no more instances of such abdominal wall bleeding. In our series, there were two cases of aborted donor hepatectomy, which is estimated to occur in 1–5% of cases [13]. The first case was severe fatty change found by routine intra-operative biopsy in a patient with normal liver function and mild fatty change on pre-operative CT scan. This could have been detected by pre-operative biopsy. In the second case, intra-abdominal metastasis in a recurrent HCC patient who had undergone previous partial hepatectomy was not detected by the pre-operative imaging studies, but was found late during the operation. This reminds us that despite negative pre-operative imaging findings in LDLT for HCC, the donor operation should be started only after confirming the absence of intra-abdominal metastasis, with full exploration in the recipient. These lessons are so characteristic of this report, reflecting the initial experience of a fledgling new center, which we believe will be an example to other centers that consider starting LDLT.

Group 1 had a significantly higher MELD score than that of groups 2 and 3, but the three groups showed similar outcomes. It may be expected that to reach a better outcome LDLT be performed initially with stable patients with lower MELD scores, especially in a newly established institution. However, we did not hesitate to start a LDLT program with the patients with higher MELD scores in group 1, because LDLT was a realistic hope of new life for such patients in a country with scarce supply of cadaveric organs, and we believed that thorough preparation and initial help of an experienced liver transplantation team could result in a good outcome. In the setting of LDLT and on the condition that donor autonomy and safety should be secured, it would be extremely difficult, ethically and practically, to deny liver transplantation to patients with advanced but potentially curable liver disease.

The LDLT procedure has the potential of donor morbidity and even mortality. The reported morbidity after donor hepatectomy has ranged widely between 0% and 100%, with a median of 16% [14], which is not much different from the 17.6% in our study. The donor mortality definitely related to donor surgery is estimated to be about 0.15% [15]. The donor complication rate is higher for right liver than that for left liver donation [16]. In this study, four donors (7.8%) underwent re-operation because of immediate postoperative bleeding, which might be considered significantly worrisome. But, thanks to proper steps taken timely, for all donors, their normal life was ultimately restored with a sense of well-being and, particularly, psychic balance.

In conclusion, thorough preparation and the assistance of an experienced liver transplantation team at the beginning can facilitate a more rapid learning curve and bring about a good outcome even in a small, newly established institution. We hope our experience can assist any institution considering the establishment of LDLT as a treatment for HCC or end-stage liver disease.

Authorship

SHK: designed this study and wrote the article. SHK and SJP: performed this study. SHK and SYC: collected the data. KWL, SSH, SL, JWP, and CMK: contributed important advice to this study.

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