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In Situ Split Liver Transplantation for 2 Adult Recipients: A Single-Center Experience

ABCDEF **Dong-Hwan Jung** Authors' Contribution Division of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea Study Design A Shin Hwang ABCDEFG Data Collection B **Gi-Won Song** BCD Statistical Analysis C Chul-Soo Ahn Data Interpretation D BCD Manuscript Preparation E **Deok-Bog Moon** BCD Literature Search F BCD Ki-Hun Kim Funds Collection G BCD Tae-Yong Ha **Gil-Chun Park** BCD BC Wan-Jun Kim BC Woo-Hyoung Kang BC Seok-Hwan Kim Sung-Gyu Lee ACDE **Corresponding Authors:** Shin Hwang, e-mail: shwang@amc.seoul.kr, Sung-Gyu Lee, e-mail: sglee2@amc.seoul.kr This study was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) fund-Source of support: ed by the Ministry of Science, ICT, and Future Planning (Grant No. 2015R1A2A2A04007141 to Shin Hwang) Split liver transplantation (SLT) for 2 adult patients by in situ splitting is rarely reported. This study analyzed Background: the outcomes of SLT for 2 adult recipients at a single center. Material/Methods: From 2003 to 2014, we performed 16 adult SLTs from 8 deceased donors using in situ splitting technique. We investigated the results of SLT and compared the outcomes of SLT with those of 393 cases of primary whole liver transplantation (WLT). All SLT donors were male. Eight recipients received right liver graft. Seven recipients received left liver graft. **Results:** One recipient received dual-donor liver transplantation with 2 left-liver grafts (1 left liver graft from a living donor). The mean age of the recipients was 49.6±7 years. The Model for End-Stage Liver Disease (MELD) score of the recipients was 21.3±8.6. The mean cold ischemic time was 345.6±311.7 minutes. Graft and patient survival rates were 75.0% and 81.3%, respectively, at both 1 year and 5 years. There were 2 cases of biliary complication and 3 cases of vascular complication, but no incidence of arterial complication or small-for-size graft syndrome. The donor age of the SLT group was younger than that of the WLT group (p<0.001). The MELD score of the SLT group was lower than that of the WLT group (p=0.01). Patient and graft survival rates did not differ significantly between the SLT and WLT groups (p=0.47 and p=0.78, respectively). Conclusions: In situ SLT for 2 adults is a feasible option to expand door pools in selected situations. **MeSH Keywords:** Allografts • Korea • Liver Cirrhosis Abbreviations: BMI - body mass index; CIT - cold ischemic time; CT - computed tomography; DDLT - deceased-donor liver transplantation; GRWR - graft-recipient weight ratio; KONOS - Korean Network for Organ Sharing; LDLT - living-donor liver transplantation; LT - liver transplantation; MELD - Model for End-Stage Liver Disease; SLT – split liver transplantation; UNOS – United Network for Organ Sharing; WLT – whole liver transplantation Full-text PDF: http://www.annalsoftransplantation.com/abstract/index/idArt/902567 **1** 35 2 6 <u>⊥</u> ⊒ 3 3635



Background

The success of liver transplantation (LT) has created challenges in coping with the shortage of organs for patients in need of LT. Split liver transplantation (SLT) was developed in the late 1980s by Pichlmayr et al. as a method to increase donor organs [1], but early SLT experiences resulted in poor outcomes [2]. According to the European Liver Transplant Registry, between 1968 and 2000, SLT represented 3.7% of the total grafts [3]. In the 2000s, the volume of SLTs increased up to 6% [4]. Further understanding of the intrahepatic anatomy, improvement of surgical techniques, and better-established donor and recipient selection criteria for SLT have made SLT more popular. On the contrary, SLT comprised less than 1% of all LTs between 2002 and 2009 in the United States, although it has been estimated that approximately 20% of all deceased donors meet the United Network for Organ Sharing (UNOS) guidelines for SLT [5].

Conventional SLT means dividing the deceased-donor liver into a left lateral section for a pediatric recipient and a right trisection graft for an adult recipient. Most SLTs have been performed as conventional type and have resulted in shortening of the pediatric waiting list for LT [6,7]. Splitting 1 liver into 2 grafts for 2 adult recipients was theoretically more attractive to expand the donor pool for adult patients. SLT for 2 adult recipients (hereinafter, referred to as "two-adult SLT") requires full right-liver and full left-liver grafts. In general, many factors still pose a hurdle to preclude two-adult SLT as a standard procedure, such as preservation injuries from prolonged ischemic time, suboptimal donor conditions before and during organ harvest, donor anatomy not fully assessed using imaging studies, increased technical demands associated with SLT, and urgent procedures performed at night in any donor hospital [8–11]. Adult recipients require sufficient graft volume to satisfy the metabolic demand. A small-sized graft volume for adult recipients can result in increased incidence of primary non-function or small-for-size graft syndrome. So far, few reports exist about the in situ splitting technique for 2 adults with full right-liver and left-liver grafts because of the abovementioned problems.

The surgical procedures for two-adult SLT are similar to those for adult living-donor liver transplantation (LDLT). Therefore, the present study aimed to analyze the results of two-adult SLT performed in a high-volume LDLT center.

Material and Methods

A total of 16 recipients who received SLTs (full right-liver graft in 8, full left-liver graft in 7, and dual full left-liver grafts in 1) using the *in situ* splitting technique at Asan Medical Center from 2003 to 2014 were included in this study. The median follow-up was 113.2 months (mean, 87.3 ± 49.8 ; range 0.7-158.8). The clinical, surgical, and pathologic profiles were recorded in an institutional LT database.

Donor selection

The donor selection criteria of two-adult SLT included age below 50 years, mild steatosis, minimal dose of inotropic support, short hospital stay before operation, and normal or mildly elevated transaminase levels. The Korean Network for Organ Sharing (KONOS) defines a mandatory splitting policy only for combination of adult and child recipients. If the deceased donor candidate fulfills the criteria for SLT, the KONOS selects an appropriate match for adult and child recipient candidates in the waiting list. If no proper candidates are available, the deceased donor is allocated to donating the whole liver graft to an adult recipient candidate. It is possible to consider twoadult SLT only when the whole liver graft appears to be too large for a selected adult recipient candidate. Thus, two-adult SLT is an institutional option to match the graft size as well as to expand the donor graft pool. So far, there is no general rule for two-adult SLT in the KONOS setting.

Recipient selection

One recipient of SLT was allocated to receive the whole liver as the first-priority patient in the waiting list according to the KONOS organ allocation system. We estimated the total graft volume, right- and left-liver volume of the donor liver based on computed tomography (CT), intraoperative ultrasonography, donor body size, and manual palpation of the liver graft by well-experienced surgeons. After exploration of the abdomen in the deceased donors, we explored the whole liver graft through inspection and palpation by an experienced staff surgeon and routinely performed liver biopsy to check the amount of steatosis and the quality of the liver graft.

Most of the first-recipient candidates had small body size; thus, the total liver graft volume of the allocated donors was too large. After reporting the possibility of SLT to the KONOS, we could select the second recipient at our center in case there was no timely available recipient candidate in the waiting list of KONOS.

Most of the secondary recipient candidates were hospitalized at the time of SLT, had a small body size so that the hemi-liver graft had a graft-recipient weight ratio (GRWR) >1%, and had a relatively low Model for End-Stage Liver Disease (MELD) score.

Operative techniques

The surgical techniques for two-adult SLT are described in detail elsewhere [12]. The liver anatomy was evaluated using CT,

Donor No.	Sex	Age (yrs)	Height (cm)	Weight (kg)	BMI (kg/m²)	Total bilirubin (mg/dL)	Maximum AST (U/L)	Maximum ALT (U/L)
1	Male	22	175	60	19.6	0.7	22	17
2	Male	24	167	66	23.7	0.6	62	16
3	Male	27	181	72	22.0	0.8	119	63
4	Male	20	180	80	24.7	0.8	83	53
5	Male	30	184	75.4	22.3	0.8	159	76
6	Male	14	176	64	20.7	0.9	68	61
7	Male	21	178	120	37.9	1.1	25	63
8	Male	48	173	75	25.1	0.9	33	12

 Table 1. Donor profiles for two-adult split liver transplantation.

ALT – alanine transaminase; AST – aspartate transaminase; BMI – body mass index.

ultrasonography, and intraoperative cholangiography. The consistency and color of the liver were evaluated after laparotomy. After liver biopsy and cholecystectomy, intraoperative cholangiography was performed, and the quality and quantity of the bile drained from the common bile duct were observed. The right and left triangular ligament, falciform ligament, and bare area were dissected. Before splitting, the hepatic artery and portal vein were encircled. The right liver was freed from the inferior vena cava through ligation and division of the short hepatic veins. Large inferior right hepatic veins were preserved for reconstruction at the bench operation. *In situ* parenchymal transection was performed with a Cavitron Ultrasonic Surgical Aspirator. The hanging maneuver was used in graft splitting to determine the proper direction and to facilitate hemostasis. Liver grafts were perfused and preserved with Histidine-Tryptophan-Ketoglutarate solution.

All but one of the full right-liver grafts comprised the segment V–VIII, with the right hepatic duct, right hepatic artery, right portal vein, and right hepatic vein. One right liver graft comprised the segment V–III and I, with the common bile duct, celiac axis, main portal vein, and retro-hepatic vena cava. Sizable middle hepatic vein tributaries of the anterior section were reconstructed with interposition of the iliac vein obtained from the same deceased donor. All but one of the full left-liver grafts comprised the segment I–IV, with the common bile duct, celiac axis, main portal vein, and retro-hepatic vena cava. Since one left-liver graft was used as one graft for dual-donor LT, this graft comprised the segment II–IV, with the left hepatic duct, left and middle hepatic artery, left portal vein, and middle and left hepatic vein.

Outcome comparison with whole liver transplantation

During the 12-year study period of two-adult SLT, there were 573 cases of deceased-donor liver transplantation (DDLT) at

our center. To compare the outcomes, we excluded pediatric recipients, SLT recipients using right trisection graft and left lateral section graft. We also excluded cases of re-transplantation using a whole liver graft because of relatively poor outcomes. Doing so, we selected 393 adult recipients who underwent first DDLT using a whole liver graft as a control group, with which we compared the clinical outcome between SLT and whole liver transplantation (WLT).

Statistical analysis

Numerical data are presented as mean \pm standard deviation or median (range). Continuous variables were compared using the Mann-Whitney U test. Survival rates were estimated using the Kaplan-Meier method and compared with the logrank test. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 22 (SPSS Inc., Chicago, IL, USA).

Results

Profiles of the donors for two-adult SLT

The characteristics of the donors are summarized in Table 1. All donors were male. The mean age of the donors was 25.8 ± 9.8 years. The donors, except for one, were aged \leq 30 years. The body mass index (BMI) of donors was 24.5 ± 5.5 kg/m². The BMI of most donors was <25 kg/m². One deceased donor whose death was caused by intracranial hemorrhage after a motor-cycle accident had a BMI of 37.9 kg/m², but he was an athlete with large muscle mass.

All 8 donors were hemodynamically stable during the donation operation. All donation operations were uneventful. Five

Recipient No.	Sex	Age (yrs)	Height (cm)	Weight (kg)	BMI (kg/m²)	GRWR	MELD score	UNOS status	CIT (min)	Primary diagnosis
Right live	r graft recipi	ients								
1-RL	Male	57	165.0	55.2	20.3	2.24	18	2B	144	HBV-LC
2-RL	Male	42	170.9	70.0	24.0	1.36	12	2B	307	HBV-LC
3-RL	Male	53	174.0	57.0	18.8	1.47	40	2A	302	HBV-LC
4-RL	Male	46	176.0	67.8	21.9	1.77	30	2A	172	HBV-LC
5-RL	Female	52	162.0	56.9	21.7	2.11	31	2A	101	ALD
6-RL	Female	51	155.3	51.5	21.4	1.94	21	2A	55	HBV-LC
7-RL	Male	64	165.5	71.6	26.1	1.68	19	2A	334	HBV-LC
8-RL	Female	63	152.0	56.8	24.6	1.58	8	3	386	HBV-LC
Left liver §	graft recipie	nts								
1-LL	Male	37	167.7	56.4	20.0	1.24	23	2A	265	HBV-ALF
2-LL	Female	32	164.3	58.3	21.6	0.99	16	2B	544	Re-LT ¹
3-LL	Male	55	149.0	48.0	21.6	1.15	33	2A	217	HBV-LC
4-LL	Male	51	167.0	59.0	21.2	1.19	19	2B	123	HBV-LC
5-LL	Female	25	157.5	50.1	20.2	1.44	19	2B	120	PSC
6-LL ²	Male	40	173.8	97.1	32.2	1.04	10	3	275	HBV-LC
7-LL	Male	61	160.9	51.4	19.8	1.67	23	2B	354	HBV-LC
8-LL	Female	61	140.5	37.8	19.2	1.72	19	2A	384	lschemia ³

Table 2. Recipient profiles of two-adult split liver transplantation.

¹ The primary disease was Caroli disease and the patient underwent whole liver transplantation. However, she developed graft failure at 12 years post-transplantation. ² The patient underwent dual-graft liver transplantation with combination of a left liver graft from a living donor and a left liver graft from deceased donor splitting. ³ The patient experienced ischemic liver disease after cardiac arrest. ALD – alcoholic liver disease; BMI – body mass index; CIT – cold ischemic time; GRWR – graft-recipient weight ratio; HBV-ALF – hepatitis B virus-associated acute liver failure; HBV-LC – hepatitis B virus-associated liver cirrhosis; LL – left liver graft; MELD – Model for End-Stage Liver Disease; PSC – primary sclerosing cholangitis; re-LT – re-transplantation; RL – right liver graft; UNOS – United Network for Organ Sharing.

cases of donation operations were performed at our center, and the other 3 cases were done at other hospitals.

Profiles of adult recipients who underwent two-adult SLT

The characteristics of the 16 recipients are summarized in Table 2. Their mean age, MELD score, and cold ischemic time (CIT) were 49.6 ± 11.7 years, 21.3 ± 8.6 , and 255.2 ± 131.4 minutes, respectively. Among these 16 recipients, 8 received a right liver graft. Seven recipients received a left liver graft. One recipient received dual-donor liver transplantation with 2 left liver grafts (one left liver graft from a living donor) [13]. Detailed operative techniques are summarized in Table 3.

Outcomes of adult recipients who underwent two-adult SLT

The 1-year and 5-year patient survival rates of all SLTs were 81.3% and 81.3%, respectively. The 1-year and 5-year graft survival rates of all SLTs were the same at 68.8% (Figure 1). The causes of patient death were sepsis (n=2) and graft failure due to heart dysfunction (n=1). One graft failure among the left-liver graft recipients was associated with primary nonfunction due to long CIT; and the other graft failure after left-liver graft implantation was caused by recurrent acute cellular rejection and chronic rejection. These 2 recipients underwent re-transplantation successfully.

The 5-year and 10-year graft survival of the right- and left-liver graft recipients were 87.5% and 50%, respectively (p=0.10).

Graft type	Caval drainage	Bile duct	Portal vein	Artery	Graft type	Caval drainage	Bile duct	Portal vein	Artery
1-RL	Piggyback	RHD, DD	Right PV	Right HA	1-LL	Bicaval	CBD, DD	Main PV	Celiac axis
2-RL	Piggyback	RHD, HJ	Right PV	Right HA	2-LL	Bicaval	CBD, HJ	Main PV	Celiac axis
3-RL	Piggyback	RHD, DD	Right PV	Right HA	3-LL	Bicaval	CBD, DD	Main PV	Celiac axis
4-RL	Piggyback	RHD, DD	Right PV	Right HA	4-LL	Bicaval	CBD, DD	Main PV	Celiac axis
5-RL	Piggyback	RHD, DD	Right PV	Right HA	5-LL	Bicaval	CBD, DD	Main PV	Celiac axis
6-RL	Bicaval	CBD, DD	Main PV	Celiac axis	6-LL	Piggyback	LHD, HJ	Left PV	Left HA
7-RL	Piggyback	RHD, DD	Right PV	Right HA	7-LL	Bicaval	CBD, DD	Main PV	Celiac axis
8-RL	Piggyback	RHD, DD	Right PV	Right HA	8-LL	Bicaval	CBD, DD	Main PV	Celiac axis

 Table 3. Operative techniques for two-adult split liver transplantation.

CBD – common bile duct; DD – duct to duct anastomosis; HA – hepatic artery; HJ – hepaticojejunostomy; LHD – left hepatic duct; LL – left liver graft; PV – portal vein; RHD – right hepatic duct; RL – right liver graft.



Figure 1. Patient survival (A) and graft survival (B) curves of split liver transplantation for 2 adult recipients.

The 5-year and 10-year patient survival of the right- and leftliver graft recipients were 87.5% and 75.0%, respectively (p=0.48) (Figure 2).

Complications of two-adult SLT

There was 1 case of portal vein stenosis requiring portal vein stent in a left-liver graft recipient. There was 1 case of inferior right hepatic vein stenosis and 1 case of right hepatic vein stenosis requiring stenting among the right-liver graft recipients. There were 2 cases of biliary stricture, 1 each in rightand left-liver graft recipients. There was no bile leak in either groups. There was no hepatic arterial complication or small-forsize graft syndrome after SLT. The major complication (grade III or higher according to the Clavien-Dindo classification) rate was 56% (9 of 16). The severities of these complications are summarized in Table 4.

Outcome comparison with WLT

The clinical profiles of recipients who underwent two-adult SLT and WLT are summarized in Table 5. The donor age of the SLT group was younger than that of the WLT group (p<0.001). The MELD score of the SLT group was lower than that of the WLT group (p=0.01).

The 1-year and 5-year patient survival rates in the WLT group were 80.4% and 74.1%, respectively. The 1-year and 5-year graft survival rates in the WLT group were 80.1% and 72.9%, respectively. The patient and graft survival rates did not differ significantly between the SLT and WLT groups (p=0.471 and p=0.781, respectively) (Figure 3).



Figure 2. Comparison of patient survival (A) and graft survival (B) curves of split liver transplantation for 2 adult recipients according to split hemi-liver graft types.

	Table 4. Ma	jor complicat	ions after two-adu	lt split liver tran	splantation a	ccording to the	Clavien-Dindo d	classification.
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Grade	Right liver graft	Left liver graft
П	Liver abscess (n=1)	
Illa	Biliary stricture (n=1) ¹ Hepatic vein stenosis (n=2) ¹	Biliary stricture (n=1) Bleeding requiring embolization (n=1)
IIIb		Portal vein stenosis (n=1) ²
IVa		Primary non-function (n=1)² Chronic rejection (n=1)
IVb		
V	Pneumonia (n=1)	Sepsis (n=1) Heart failure (n=1)

¹ One right liver graft recipient experienced early right hepatic vein stenosis and late biliary stricture. ² One left liver graft recipient showed early portal vein stenosis requiring portal vein stenting and primary non-function requiring re-transplantation.

Discussion

The technique of splitting a deceased-donor liver to be used for 2 adults is a way to increase the number of available liver grafts and to decrease waiting-list mortality. However, this technique remains challenging because it is associated with relatively poor outcomes [10,14], suboptimal graft condition, and technical difficulty [11,15].

Preoperative CT evaluation provides valuable information about the liver anatomy and graft size that might facilitate SLT [12]. However, unstable donor vital signs and concern about worsening of renal function often makes preoperative imaging studies using contrast media unrealistic [11]. Inadequate small graft volume might cause small-for-size syndrome, which is characterized by prolonged cholestasis, synthetic dysfunction, and slow recovery [16]. In this study, all recipients except 1 received a liver graft with GRWR >1%. Considering the inevitable preservation injuries, prolonged CIT, and reperfusion injuries in deceased-donor grafts, we believe that a graft volume with GRWR of at least 1% is necessary for SLT recipients [11,17,18]. Although the routine use of intraoperative ultrasonography and cholangiography can provide information about donor anatomy and graft volume as well as experienced donor surgeons might be able to predict graft weight reliably in the operative field [17], we think that preoperative non-enhanced CT should be considered in the donor candidates for SLT to provide more information about donor anatomy and graft volume, when the vital signs of the donor candidates allow.

Splitting of the donor liver for 2 adults is only recommended in highly selected situations. Proper donor selection is the first step for successful two-adult SLT. The criteria for splitting liver in a deceased donor include young age, low BMI, stable hemodynamic status with minimal inotropic agent, normal liver function, and short period of hospitalization before

	Split liver transplantation (n=16)	Whole liver transplantation (n=393)	p-value
Donor profile			
Sex (Male/Female)	16/0	267/126	0.002
Age (yrs)	24±11.7	42.5±13.9	0.000
BMI (kg/m²)	25.2±5.6	23.2±3.3	0.36
Recipient profile			
Sex (Male/Female)	11/5	266/127	0.58
Age (yrs)	49.6±11.7	49.3±10.8	0.84
BMI (kg/m²)	22.2±3.3	24.0±4.4	0.02
Diagnosis (n)			0.17
HBV-LC	11	222	
Alcoholic liver disease	1	60	
HCV-LC	0	14	
Cryptogenic LC	0	11	
Wilson disease	0	6	
Primary biliary cirrhosis	0	6	
Primary sclerosing cholangitis	1	2	
Autoimmune hepatitis	0	4	
Acute liver failure – toxic	0	29	
Acute liver failure – HBV	1	13	
Acute liver failure – HAV	0	9	
Acute liver failure – others	0	6	
Others	2	11	
CTP score	9.7±2.7	11.0±2.1	0.03
MELD score	21.2±8.5	28.4±10.7	0.01
Pretransplant ventilator	18.8%	33.8%	0.16
Pretransplant dialysis	31.3%	31.0%	0.56
Pretransplant inotropics	25%	19.6%	0.39
Cold ischemic time (min)	309.6±188.5	237.5±128.6	0.11
Posttransplant hospital stay (days)	33.8±18.3	46.8±49.9	0.75

 Table 5. Comparison of clinical profiles of recipients who underwent split liver transplantation and whole liver transplantation.

BMI – body mass index; CTP – Child-Turcotte-Pugh; HAV – hepatitis A virus; HBV – hepatitis B virus; HCV – hepatitis C virus; LC – liver cirrhosis; MELD – model for end-stage liver disease.



Figure 3. Comparison of patient survival (A) and graft survival (B) curves of recipients who underwent split liver transplantation and whole liver transplantation from deceased donors.

donation [10,11,14,15,19,20]. In the present study, the age of donors except 1 was <30 years and the BMI of most donors was <25 kg/m² except in 1 athlete donor. Our relatively good results show the importance of adequate donor selection.

Appropriate recipient selection is also essential to optimize the outcomes of two-adult SLT. SLT has become more difficult with the widespread use of the MELD-based organ allocation system or "sickest first" allocation system because 1 of the 2 partial liver grafts should be engrafted into a high-MELD score recipient or sicker patient. Greater recipient medical risk can increase the split-graft failure. Urgent LT was related to the high mortality rate of the right-liver graft recipients in a United States survey study [21]. Under the "sickest first" MELDbased allocation system, splitting the liver graft that is allocated as the whole graft to urgent recipients with high MELD score gives rise to ethical questions. A large-for-size graft allocated to recipients requiring urgent LT might be suitable for SLT under the MELD-based allocation.

One patient who received a left-liver graft had Caroli disease as her previous primary disease. She had undergone DDLT as the first LT in her childhood. However, she developed graft failure at 12 years post-transplantation. This re-transplantation situation required a long time for dissection because of severe adhesion and massive bleeding, thus the CIT was prolonged to 544 minutes. She suffered from primary non-function and had to undergo a third LT. Minimization of CIT was reported as a major contributing factor for graft loss in SLT [22]. Potential recipients requiring a long operation time for whom a difficult operation is anticipated should not be included as SLT candidates.

Another recipient with a left-liver graft had hepatic failure from ischemic hepatitis. She had undergone mitral valve repair

operation because of mitral valve prolapse. She developed cardiogenic shock after valve operation at postoperative day 1, which caused small bowel ischemia. One day after the valve operation, she underwent small bowel resection and ileostomy. After these 2 operations, she developed hepatic failure. Echocardiography performed before LT showed moderate to severe mitral regurgitation and severe left ventricle dysfunction, with 33% left ventricle ejection fraction. Her MELD score was 19 before LT and the GRWR of this recipient was 1.72. She died because of graft failure associated with heart failure and cardiac congestion at postoperative day 18. Whether her status was appropriate for LT might evoke debates about proper candidates for SLT.

There are 2 methods to split the donor liver: *in situ* and *ex situ* techniques. The *in situ* technique can decrease the CIT by eliminating the graft division procedure in the bench operation, prevent the incidence of bile leak, and facilitate complete hemostasis of the cut surface. However, the *in situ* technique is often time-consuming, requires cooperation with other graftharvesting teams, and may increase blood loss and volume replacement. We performed SLT for 2 adults by using the *in situ* technique. One *ex situ* SLT study using full right- and left-liver graft showed a 33.3% biliary complication rate after LT [9]. The incidence of biliary complication was 12.5% in the present study. This finding is consistent with a meta-analysis of right-liver SLT versus WLT in adult recipients, which showed that biliary complications increased after *ex situ* SLT rather than *in situ* SLT [23].

Surgical techniques for full right- and left-liver grafts in deceased donors are similar to techniques for donor hepatectomy used in LDLT. There are several options to split the deceased-donor liver into full right- and left-liver grafts, according to which the graft includes the segment I, main portal vein,

Publi-				Median	Split Liver Transplantation									Control Group					
Authors	cation year	Nation	Center	follow- up (months)	Total	FRLG	FLLG	Split- ting	OPS	OGS	FRLG- PS	FRLG- GS	FLLG- PS	FLLG- GS	Graft Type	Patient No.	OPS	OGS	p- Value
Humar [19]	2001	USA	Single	9.3	12	6	6	In situ	83.3%	83.3	-	-	-	-	-	-	-	-	-
Azoulay [18]	2001	France	Singe	-	34	17	17	Com- bined	-	-	2 yrs, 74%	2 yrs, 74%	2 yrs, 64%	2 yrs, 43%	WLT	88	2 yrs, 85%	2 yrs, 85%	ND
Zamir [34]	2002	USA	Single	-	6	3	3	In situ	2 deaths	2 deaths	-	-	-	-	-	-	-	-	-
Broering [14]	2005	Germa- ny	Single	27.4	35	16	19	Mix	-	-	87.5%	75%	89.5%	84%	-	-	-	-	-
Giacomoni [15]	2008	Italy	Single	57.37	16	9	7	In situ	5 yrs, 80%	-	-	-	-	-	-	-	-	-	-
Zambelli [10]	2012	Italy	Multi	106.6	43	21	22	In situ	10 yrs, 62.6%	10 yrs, 57.9%	10 yrs, 57.1%	10 yrs, 57.1%	10 yrs, 67.9%	10 yrs, 58.1%	-	-	-	-	-
Lee [17]	2013	Taiwan	Single	-	42	21	21	In situ	5 yrs, 70.1%	-	-	-	-	-	LDLT	282	5 yrs, 70.4%	-	0.49
Aseni [20]	2014	Italy	Multi	-	64	-	-	-	5 yrs, 63.3%	5 yrs, 58.7%	5 yrs, 59.3%	5 yrs, 56.6%	5 yrs, 67.2%	5 yrs, 60.7%	WLT	1199	5 yrs, 83.1%	5 yrs, 80.4%	0.0003
Vagefi [9]	2014	USA	Single	-	18	9	9	Ex situ	-	-	10 yrs, 74%	10 yrs, 74%	10 yrs, 78%	10 yrs, 66%	-	-	-	-	-
Hashimoto [11]	2014	USA	Single	54	25	15	10	In situ	5 yrs, 88.0%	5 yrs, 80.0%	5 yrs, 93.3%	5 yrs, 86.7%	5 yrs, 80.0%	5 yrs, 70.0%	WLT	121	5 yrs, 86.5%	5 yrs, 81.5%	0.81-PS 0.43-GS
Present study		Korea	Singe	113.3	16	8	8	In situ	5 yrs, 81.3%	5 yrs, 68.8%	5 yrs, 78.5%	5 yrs, 87.5%	5 yrs, 75.0%	5 yrs, 50.0%	WLT	393	5 yrs, 74.1%	5 yrs, 72.9%	0.47-PS 0.78-GS

Table 6. Published outcomes of full right-liver and left-liver split liver transplantation for two adult recipients.

FLLG – full left-liver graft; FRLG – full right-liver graft; GS – graft survival; LDLT – living donor liver transplantation; ND – not different; OGS – overall graft survival; OPS – overall patient survival; PS – patient survival; WLT – whole liver transplantation; '–' – not available.

common bile duct, celiac trunk, and middle hepatic vein or retrohepatic vena cava. We think that splitting the liver into the segments V-VIII without the middle hepatic vein as a rightliver graft and the segments I-IV with the middle hepatic vein trunk as a left-liver graft is more suitable for 2 adult recipients. The right-liver graft without middle hepatic vein may cause severe congestion after LT [24]. However, there are several reconstruction methods for middle hepatic vein tributaries to prevent congestion of the anterior section in the LDLT setting [25-27]. The right-liver graft with multiple and complex inferior right hepatic veins drained into the vena cava can also be securely reconstructed in bench operation with the techniques used in LDLT [28,29]. In particular, a deceased donor can provide several major vessels with large diameter suitable for middle hepatic vein reconstruction. The left-liver graft without reconstruction of the caudate veins draining into the retrohepatic vena cava demonstrated congestion and dysfunction after LT [30]. The importance of complete reconstruction of venous drainage of the caudate lobe at the left-liver graft was reported in several LDLT experiences [30-32]. The veins of the caudate lobe were often multiple and relatively small; therefore, we prefer the segments I-IV with the retrohepatic vena cava

for good drainage of the caudate veins. Except for 1 left-liver graft used in dual-graft LDLT, we obtained the segments I-IV with the vena cava as a left-liver graft in two-adult SLT.

Regarding the division of hilar structures in SLT, we prefer a left-liver graft with the celiac trunk, main portal vein, and common bile duct. The right-liver graft has the right hepatic artery, right portal vein, and right hepatic duct. Because the right hepatic artery is generally large and single, and the left liver gets arterial blood supply from the left and middle hepatic arteries, we believe that a left-liver graft with the celiac trunk is better than a right-liver graft with the celiac trunk. The main portal vein and common bile duct may be given to any of the 2 grafts. If intraoperative cholangiography of the deceased donor shows multiple bile duct openings in the right-liver graft, a right-liver graft having the common bile duct is a better option to prevent biliary complication. When the common bile duct is left in the left-liver graft, dissection of the right hepatic artery should be done at the right side of the common bile duct to avoid damage to the surrounding tissues and the arterial flow of the common bile duct [33].

Several studies have reported incidences of major complications of grade III or higher in SLT recipients ranging from 38% to 72% [10,17,20]. Representative complications after two-adult SLT include: biliary complications, including bile leak and biliary stricture; vascular complications, including hepatic artery, portal vein, and hepatic vein thrombus; bleeding requiring intervention or exploratory laparotomy; infection; primary non-function; and small-for-size syndromes [9,14,15,17-21,34]. Among these, biliary and vascular complications were the most common. The major complication rate in the present study was 56%, which is comparable to that in other studies. The biliary complication rate was 12.5% in this study. There were no bile leaks. Two late biliary strictures required endoscopic intervention. Compared with the rates of biliary complications reported in other studies (22-53.5%), the rate of complications in the present study seems to be relatively low. Our high-volume experience in adult LDLT might have contributed to the lower biliary complication rate [35].

The outcomes of full right- and left-liver SLT for 2 adults in the literature are summarized in Table 6, of which most were small-volume studies. The comparison of outcomes of twoadult SLT with those of WLT or LDLT did not yield any differences in several single-center studies [11,17,18]. However, twoadult SLT showed poorer outcomes than WLT in a multicenter study [20]. In the present study, the overall patient and graft survival rates of two-adult SLT were comparable with those of other studies. There was no difference between SLT and WLT in terms of the overall patient and graft survival rates in the present study.

In Korea, the number of adult SLTs is currently small because there are very limiting selection criteria for SLT, although LDLT

References:

- Pichlmayr R, Ringe B, Gubernatis G et al: [Transplantation of a donor liver to 2 recipients (splitting transplantation) a new method in the further development of segmental liver transplantation]. Langenbecks Arch Chir, 1988; 373: 127–30 [in German]
- Broelsch CE, Emond JC, Whitington PF et al: Application of reduced-size liver transplants as split grafts, auxiliary orthotopic grafts, and living related segmental transplants. Ann Surg, 1990; 212: 368–75
- 3. Renz JF, Yersiz H, Reichert PR et al: Split-liver transplantation: A review. Am J Transplant, 2003; 3: 1323–35
- Adam R, McMaster P, O'Grady JG et al: Evolution of liver transplantation in Europe: Report of the European Liver Transplant Registry. Liver Transpl, 2003; 9: 1231–43
- 5. Superina R: To split or not to split: That is the question. Liver Transpl, 2012; 18: 389–90
- 6. Kim JS, Broering DC, Tustas RY et al: Split liver transplantation: Past, present and future. Pediatr Transplant, 2004; 8: 644–48
- 7. Cardillo M, De Fazio N, Pedotti P et al: Split and whole liver transplantation outcomes: A comparative cohort study. Liver Transpl, 2006; 12: 402–10
- Cescon M, Grazi GL, Ravaioli M et al: Conventional split liver transplantation for two adult recipients: A recent experience in a single European center. Transplantation, 2009; 88: 1117–22

is commonly performed. There are no selection criteria for twoadult SLT yet, except for adult and child recipient combination in the KONOS setting. Organ allocation polices to encourage the more widespread application of two-adult SLT are needed. For example, if a whole liver graft for 1 recipient is allocated to a center and two-adult SLT is then attempted, the center has a priority to get all the grafts anyway, independent of the MELD score.

The present study has some limitations. This was a retrospective, single-center study with a small number of patients. Thus, multi-center studies are necessary to collect data regarding rarely-performed procedures. A strong point of this study is that the survival status of all patients was thoroughly followed up for a long period in a high-volume LDLT center.

Conclusions

Preservation injuries, suboptimal donor conditions, incompletely assessed donor anatomy and graft volume before operation, and increased technical demands are innate drawbacks of two-adult SLT. The results of this study demonstrated that the patient and graft survival rates did not differ significantly between the two-adult SLT and WLT groups. Thus, we suggest that *in situ* SLT for 2 adults is a feasible option to expand door pools in selected situations. To acquire favorable results after two-adult SLT, proper donor and recipient selection and experienced surgeons are required.

Conflicts of Interest

None of the authors has any conflict of interest to disclose.

- 9. Vagefi PA, Parekh J, Ascher NL et al: *Ex vivo* split-liver transplantation: The true right/left split. HPB (Oxford), 2014; 16: 267–74
- 10. Zambelli M, Andorno E, De Carlis L et al: Full-right-full-left split liver transplantation: The retrospective analysis of an early multicenter experience including graft sharing. Am J Transplant, 2012; 12: 2198–210
- Hashimoto K, Quintini C, Aucejo FN et al: Split liver transplantation using Hemiliver graft in the MELD era: A single center experience in the United States. Am J Transplant, 2014; 14: 2072–80
- 12. Hwang S, Lee SG, Park KM et al: A case report of split liver transplantation for two adult recipients in Korea. Transplant Proc, 2004; 36: 2736–40
- 13. Lee S, Hwang S, Park K et al: An adult-to-adult living donor liver transplant using dual left lobe grafts. Surgery, 2001; 129: 647–50
- Broering DC, Wilms C, Lenk C et al: Technical refinements and results in full-right full-left splitting of the deceased donor liver. Ann Surg, 2005; 242: 802–12
- Giacomoni A, Lauterio A, Donadon M et al: Should we still offer split-liver transplantation for two adult recipients? A retrospective study of our experience. Liver Transpl, 2008; 14: 999–1006
- Dahm F, Georgiev P, Clavien PA: Small-for-size syndrome after partial liver transplantation: Definition, mechanisms of disease and clinical implications. Am J Transplant, 2005; 5: 2605–10

- 17. Lee WC, Chan KM, Chou HS et al: Feasibility of split liver transplantation for 2 adults in the model of end-stage liver disease era. Ann Surg, 2013; 258: 306–11
- Azoulay D, Castaing D, Adam R et al: Split-liver transplantation for two adult recipients: Feasibility and long-term outcomes. Ann Surg, 2001; 233: 565–74
- Humar A, Ramcharan T, Sielaff TD et al: Split liver transplantation for two adult recipients: An initial experience. Am J Transplant, 2001; 1: 366–72
- Aseni P, De Feo TM, De Carlis L et al: A prospective policy development to increase split-liver transplantation for 2 adult recipients: Results of a 12year multicenter collaborative study. Ann Surg, 2014; 259: 157–65
- Renz JF, Emond JC, Yersiz H et al: Split-liver transplantation in the United States: Outcomes of a national survey. Ann Surg, 2004; 239: 172–81
- 22. Quintini C, Aucejo F, Miller CM: Split liver transplantation: Will it ever yield grafts for two adults? Liver Transpl, 2008; 14: 919–22
- 23. Wan P, Li Q, Zhang J, Xia Q: Right lobe split liver transplantation versus whole liver transplantation in adult recipients: A systematic review and meta-analysis. Liver Transpl, 2015; 21: 928–43
- 24. Lee S, Park K, Hwang S et al: Congestion of right liver graft in living donor liver transplantation. Transplantation, 2001; 71: 812–14
- 25. Gyu Lee S, Min Park K, Hwang S et al: Modified right liver graft from a living donor to prevent congestion. Transplantation, 2002; 74: 54–59
- Hwang S, Jung DH, Ha TY et al: Usability of ringed polytetrafluoroethylene grafts for middle hepatic vein reconstruction during living donor liver transplantation. Liver Transpl, 2012; 18: 955–65

- Hwang S, Lee SG, Ahn CS et al: Cryopreserved iliac artery is indispensable interposition graft material for middle hepatic vein reconstruction of right liver grafts. Liver Transpl, 2005; 11: 644–49
- Hwang S, Lee SG, Park KM et al: Quilt venoplasty using recipient saphenous vein graft for reconstruction of multiple short hepatic veins in right liver grafts. Liver Transpl, 2005; 11: 104–7
- Hwang S, Ha TY, Ahn CS et al: Reconstruction of inferior right hepatic veins in living donor liver transplantation using right liver grafts. Liver Transpl, 2012; 18: 238–47
- Miyagawa S, Hashikura Y, Miwa S et al: Concomitant caudate lobe resection as an option for donor hepatectomy in adult living related liver transplantation. Transplantation, 1998; 66: 661–63
- 31. Takayama T, Makuuchi M, Kubota K et al: Living-related transplantation of left liver plus caudate lobe. J Am Coll Surg, 2000; 190: 635–38
- Hwang S, Lee SG, Ha TY et al: Simplified standardized technique for living donor liver transplantation using left liver graft plus caudate lobe. Liver Transpl, 2004; 10: 1398–405
- Imamura H, Makuuchi M, Sakamoto Y et al: Anatomical keys and pitfalls in living donor liver transplantation. J Hepatobiliary Pancreat Surg, 2000; 7: 380–94
- 34. Zamir G, Olthoff KM, Desai N et al: Toward further expansion of the organ pool for adult liver recipients: Splitting the cadaveric liver into right and left lobes. Transplantation, 2002; 74: 1757–61
- 35. Hwang S, Lee SG, Lee YJ et al: Lessons learned from 1,000 living donor liver transplantations in a single center: How to make living donations safe. Liver Transpl, 2006; 12: 920–27