

# Association between surgical volumes and hospital mortality in patients: a living donor liver transplantation single center experience

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## Research article

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# Abstract

**Background:** Many factors cause hospital mortality (HM) after liver transplantation (LT).

**Methods:** We performed a retrospective research in single center from October 2005 to June 2019. The study included 466 living donor LT patients. They were divided into a no-HM group (n=436, 93.56%) and an HM group (n=30, 6.44%). Logistic regression analysis of factors affecting clinical features and surgical volume of HM. We regrouped patients into met the surgical volume periods based cutoffs of LTs, and analyze the clinical features.

**Results:** Multivariate analysis revealed that donor age (OR= 1.049, 95% CI: 1.011– 1.090, p=0.013), blood loss (OR=1.000, 95% CI: 1.000–1.000, p=0.004), and annual surgical volumes being < 30 LTs (OR=2.521, 95% CI: 1.004–6.332, p=0.049) were significant risk factors. A comparison of years based on surgical volume found that when the annual surgical volumes were at least 30 there was significantly higher recipient age (p=0.022), donor age (p=0.024), and ABO-incompatible operations (p<0.001) and also significantly blood loss (p<0.001), operative time (p<0.001), intensive care unit days (p<0.001), length of stay (p=0.013), re-operative (p<0.001), and HM (p=0.029) compared to when the annual surgical volumes were less than 30.

**Conclusions:** Donor age, blood loss and an annual surgical volume < 30 LTs were significant pre- and peri-operative risk factors. Hospital mortality and annual surgical volume were associated with statistically significant differences; surgical volume may impact quality of care and transplant outcomes.

## Introduction

Liver transplantation (LT) is a major and difficult abdominal operation, and it involves multiple teams administering such things as anesthesia, color Doppler techniques, and critical care. Living donor liver transplantation (LDLT) was associated with a high rate of surgical complications after transplantation, and the hospital mortality rate after LDLT has ranged from 3.6% to 18.9% [1-3]. Factors related to in-hospital death include infection, a high model for end-stage liver disease (MELD) score, the recipient being of advanced age, and vascular complications such as hepatic artery thrombosis and portal vein thrombosis [3-4]. However, centers with higher surgical volumes (based on annual liver transplantations) had better techniques and multiple team organization compared to centers with lower surgery volumes; higher in-hospital mortality was associated with lower surgical volume centers [1, 5]. In this paper, we therefore mainly analyzed hospital mortality in living donor liver transplant patients and tried to pinpoint the factors that influence postoperative prognosis in order to provide a reference for liver transplant teams.

## Methods

We performed a retrospective research in Changhua Christian Hospital from October 2005 to June 2019. Living liver grafts were from the family of the donor, and none of the donors were prisoners who were

executed. The study was approved by the Institutional Review Board of Changhua Christian Hospital (CCH 191244). The donors were selected based on general physical condition, blood tests, liver volumetry measured by a computed tomography scan, clinical psychological evaluation, and social assessment. A final total number of 466 living donor liver transplant patients were included in this study, and 3 of the patients underwent combined liver and kidney transplantation.

For right lobe grafts (n=462), there was venous reconstruction of the middle hepatic vein using an artificial vascular graft (Gore-Tex graft) or cryopreserved vein grafts of V5 or V8 that were anastomosed to the recipient's right hepatic vein or inferior vena cava (IVC). For left lobe grafts (n=4), there was venous reconstruction of the hepatic vein using either an artificial vascular graft (goretex graft) of V4a and V4b that was anastomosed to the recipient's IVC or a cryopreserved vein graft patch of V4a and the left hepatic vein (venoplasty) that was anastomosed to the recipient's IVC. The right or left portal vein of the graft and the recipient's portal vein were anastomosed with 5-0 prolene with 0.5 cm growth factor. In all patients the right hepatic artery was reconstructed using microvascular surgery techniques. Intraoperative Doppler ultrasonography was performed immediately after the vascular reconstruction to assess the anastomotic patency. Biliary anastomosis was from the intrahepatic duct to the common hepatic duct with interrupted 6-0 prolene suture.

The patients were divided into two groups: the no hospital mortality group (n=436, 93.56%) and the hospital mortality group (n=30, 6.44%). Logistic regression analysis of factors affecting clinical features and surgical volume of hospital mortality in liver transplantation patients. We regrouped patients into met the surgical volume periods based cutoffs of liver transplantations, and analyze and comparisons of the demographic data and clinical features.

## Definitions

Renal failure (acute or chronic) was defined as the presence of a median glomerular filtration rate  $<30$  mL/min/1.73 m<sup>2</sup> for at least 3 to 6 months or the need for long-term dialysis [6]. Re-operative was defined as the presence of a hemorrhage, vascular thrombosis (portal vein or hepatic artery thrombosis), abdomen abscess, or biliary complication that required another abdominal surgery. Biliary complication was defined as the presence of bile leakage or biliary stenosis. Hepatic artery complication was defined as the presence of thrombosis, dissection, stenosis, or steal blood flow with the need for thrombectomy, percutaneous transluminal angioplasty with stenting, or transarterial embolization for steal blood flow from the splenic artery. Portal vein complication was defined as the presence of thrombosis and stenosis with the need for thrombectomy and percutaneous transluminal angioplasty with stenting. Delayed graft function was defined as the presence of at least 1 of the following parameters 7 days after liver transplantation: a serum bilirubin level  $\geq 10$  mg/dL, an international normalized ratio (INR)  $\geq 1.6$  or an alanine aminotransferase (ALT) level  $> 2000$  IU/L [7]. Cardiovascular complication was defined as the presence of acute coronary syndrome, acute myocardial infarction or ruptured aortic mycotic aneurysms. Cerebrovascular complication was defined as the presence of subarachnoid hemorrhage, intracerebral hemorrhage, or central pontine myelinolysis. Pulmonary complication was defined as the presence of a

lower respiratory tract infection, pneumonia or adult respiratory distress syndrome. Infection complication was defined as the presence of a bloodstream infection, intra-abdominal infection, or urinary tract infection. We distinguished pairs of surgical volume periods based on cutoffs of 20, 30, and 50 yearly liver transplantations (Figure 1).

### **Antimicrobial Prophylaxis**

Prophylaxis was administered intravenously from the day of transplantation. Piperacillin/tazobactam (Tazocin) as well as selective bowel decontamination (neomycin and nystatin administered orally) were used. Routine prophylactic antiviral therapy was not performed.

### **Immunosuppression**

All patients received calcineurin-inhibitor based initial immunosuppression. The majority also received and were maintained on cyclosporine or tacrolimus in combination with mycophenolate and methylprednisolone. The target levels after the first post-transplant year were as follows: 70–150 ng/mL for cyclosporine and 5–10 ng/mL for tacrolimus. Methylprednisolone was administered intravenously in four divided doses daily; the dosage was tapered from 200mg/day to 20mg/day over 6 days.

We had a program for ABO-incompatible patients. First, we administered a preoperative anti-CD20 antibody (rituximab, 375 mg/m<sup>2</sup>) treatment with preoperative plasma exchange to lower the anti-AB antigen titer (1:32); second, we administered a postoperative anti-CD20 antibody (rituximab, 187.5mg/m<sup>2</sup>) treatment on post-liver transplantation day 1. Mycophenolate mofetil was given in doses of 0.5~1.5g/day, and tacrolimus was kept at a trough level of 7-10ng/dL. When the isoagglutinin titer was above 64, a plasma exchange was performed to lower the isoagglutinin titer to less than or equal to 64.

### **Statistical Analysis**

The pre- and peri-operative periods had correlated clinical factors, including age, gender, MELD score, total bilirubin, creatinine, prothrombin time, INR, graft-recipient weight ratio (GRWR), blood loss, operative time, renal failure (acute or chronic), pre-LT in the intensive care unit, ABO-incompatible liver transplantation and surgical volume. All data were recorded on a computerized database. The patients were classified into two subgroups based on their hospital mortality status, and there were distinguished risk factors of liver transplantation. There were comparisons of pre-, peri-, and post-operative characteristics between the high and low surgical volume periods. The clinical post-operative factors included blood loss, operative time, intensive care unit days, length of stay, dialysis, re-operative, biliary complication, hepatic artery complication, portal vein complication, delayed graft function, cardiovascular complication, cerebrovascular complication, pulmonary complication, hemorrhage and infection. Pearson's chi-squared test and the independent t-test were used to examine the differences between the two subgroups in terms of demographic factors and the clinical characteristics of the LDLT patients. Values for the continuous variables are presented as mean ± standard deviation (SD) in this study. Categorical variables were compared using the chi-squared test or Fisher exact test where appropriate.

Significant variables in the univariate analyses were evaluated with multivariate logistic regression to identify the most important risk factors. A p value less than 0.05 was considered to be statistically significant. The statistical analysis was performed with SPSS (Statistical Package for Social Science, version 20.0).

## Results

A total of 466 liver transplant patients were included in this study; they had a hospital mortality rate of 6.88%. The patients were divided into two groups: the no hospital mortality group (n=436, 93.56%) and the hospital mortality group (n=30, 6.44%). A comparison between the two groups found statistically significant differences in terms of senior donor age (p=0.019), high MELD score (p<0.001), blood loss (p=0.014), annual surgical volume <30 liver transplantations (p=0.029), and pre-LT in the intensive care unit (<0.001) (Table 1). For annual surgical volumes of more than 20, 30, and 50 living donor liver transplantations, the hospital mortality rates were 6.3%, 5.4%, and 5.1%, respectively. The 30 surgeries per year cutoff yielded statistically significant differences, unlike the other two cutoffs.

Multivariate analysis revealed that donor age (OR= 1.049, 95% CI: 1.011– 1.090, p=0.013), blood loss (OR=1.000, 95% CI: 1.000–1.000, p=0.004) and annual surgical volume <30 liver transplantations (OR=3.244, 95% CI: 1.352–7.785, p=0.008) were significant risk factors from the pre- and peri-operative periods (Table 2). The most common cause of hospital death was infection (n=13, 43.3%), and other causes often coincided with infection: hemorrhage with/without infection (n=4, 13.3%), cerebrovascular with/without infection (n=3, 10.0%), cardiovascular with/without infection (n=6, 20.0%), and delayed graft function with infection (n=4, 13.3%) (Table 3). Most causes of patient death were major post-LT complications, which developed into septic shock and led to mortality.

The high surgical volume period (annual surgical volume  $\geq$ 30 liver transplantations) had significantly higher recipient age (p=0.022), donor age (p=0.024), and ABO-incompatible rate (p<0.001) and significantly lower blood loss (p<0.001), operative time (p<0.001), intensive care unit days (p<0.001), length of stay (p=0.013), re-operative cases (p<0.001), and hospital mortality rate (p=0.029) compared to the low surgical volume period (annual surgical volume <30 liver transplantations).

## Discussion

A comparison by multivariate analysis between the hospital mortality group and the no hospital mortality group found high donor age, high blood loss and annual surgery volume <30 liver transplantations to be statistically significant risk factors. Annual LDLT volume was less than 10 cases in the first 5 years of our transplantation center (Figure 1). It was a little surprising that the outcome for the period with <20 annual cases and the outcome for the period with  $\geq$  20 annual cases were not statistically different. When the case volumes were small, we were more cautious in that selected recipients had lower MELD scores, the GRWR was kept above 0.8% and safety donor graft (normal vessel or biliary tract anatomy). The first 15-20 LDLT cases are associated with a significant surgery learning curve [8, 9]. Annual surgery volume grew

to 20-30 cases in the 6<sup>th</sup> and 7<sup>th</sup> years; there were more urgent patients with acute liver failure conditions, including some recipients with rapid development of hepatic dysfunction associated with encephalopathy or renal failure. By putting the recipient in a positive pressure isolation room with 2 beds in the intensive care unit, the nosocomial infection risk was reduced. Over the period with 30 to 50 annual cases, we used soft power of critical care training and continuing education of the staffs. An important point is that multidisciplinary characteristics such as integration and organization management add to the operative learning curve (multiple anastomoses of vessel or biliary tract anatomy). The training of the multidisciplinary staffs covered color Doppler techniques, anesthesia, critical care, rejection identification and infection treatment. We have a combined intensivist in infectious diseases and critical care, and we established a specialized liver transplantation ward. Thus, we had put infrastructure in place to ensure favorable outcomes. Operative time, blood loss, re-operative, intensive care unit days, length of stay and hospital mortality decreased significantly after annual surgical volume reached 30 cases. After improving soft power and care quality, our physical selection criteria became less strict in regard to senior recipients, donor age, the GRWR lower bound (range 0.55-0.8), ABO-incompatible liver transplantation, and multiple hepatic duct or portal vein anastomoses, which were not limiting factors or difficult techniques. However, neither portal vein complications nor delayed graft function conditions led to a significantly higher mortality rate. In addition, the hospital mortality rate when the annual surgical volume was less than 20 liver transplantations was 10.5%, and it decreased to 5.4% and 5.1% when annual surgical volume was  $\geq 30$  and  $\geq 50$  liver transplantations, respectively.

Liver transplantation patients commonly acquire nosocomial infections, which can cause morbidity and mortality [10-12]. High MELD scores, large volume of blood loss, post-transplant hemodialysis, ABO incompatibility, and older donor age were independent risk factors for postoperative bacteremia [13-15]. However, high MELD scores, restrictive lung patterns and surgical complexity were risk factors with major impacts [16, 17]. Postoperative pulmonary complications with or without infections may cause mechanical ventilation time to be prolonged. Prolonged mechanical ventilation increases postoperative mortality since it frequently results in infection that can lead to bacterial pneumonia or nosocomial pneumonia and the development of septic shock.

The complications with the highest mortality rates were cerebrovascular problems, including subarachnoid and intracerebral hemorrhages [18, 19]. Common early postoperative complications following LDLT include thrombosis in reconstructed major blood vessels (portal vein or hepatic artery reconstructed with an artificial vascular graft or cryopreserved vein grafts) [20]. In the absence of ongoing bleeding after operation, our center considered maintaining an INR between 1.5 and 2, a platelet count  $>50000/\mu\text{L}$  and a fibrinogen level  $>100\text{ mg/dL}$  as satisfactory. Hypertension occurs usually in the initial treatment when the systolic blood pressure is greater than 160mmHg or the diastolic blood pressure is greater than 100mm Hg. In the general population, intracranial hemorrhage may occur in association with coagulopathy, acute hypertension or chronic hypertension. An intracranial or subarachnoid hemorrhage after liver transplantation that requires immediate craniotomy and removal of a hematoma may be

combined with nosocomial infections and result in high mortality. Postoperatively, blood pressure and fibrinogen levels can be monitored closely to help prevent post-transplant intracranial hemorrhages [18].

In our center's policy, when old age, cardiomegaly, history of coronary artery disease (CAD), or massive ascites is a trait in an alcoholic cirrhosis patient, the patient undergoes regular electrocardiograms and echocardiographies for pre-operative cardiovascular assessment of LT. If the patient is an LT candidate, then dobutamine stress myocardial perfusion scanning is performed for detection of CAD. Active coronary artery disease is a relative contraindication to liver transplantation and at a minimum should be treated as aggressively as possible preoperatively (stenting, angioplasty). For high cardiopulmonary risk patients, we evaluated their hemodynamic measurements by pulmonary artery catheter. Cardiac dysfunction and moderate to severe portopulmonary hypertension (mean pulmonary arterial pressure  $\geq$  35 mmHg and elevated pulmonary vascular resistance) were diagnosed and were considered contraindications of liver transplantation [21]. Cardiovascular complications occurred in 8 patients after LDLT. Two patients survived. One survivor had arrhythmia with atrial fibrillation, paroxysmal supraventricular tachycardia, ventricular tachycardia and ventricular fibrillation in the first week after liver transplantation. The recurrent arrhythmia was poorly controlled by anti-arrhythmia treatment and defibrillation. Careful laboratory monitoring and supplementation were warranted; electrolytes were provided to maintain a normal level. Echocardiography showed moderate mitral regurgitation and tricuspid regurgitation. Still, anti-arrhythmia treatment did not prevent the arise of severe bradycardia with atrioventricular block. The discontinuation of antiarrhythmic drug therapy showed no significant improvement, and a cardiologist suggested inserting temporary pacemakers. The other surviving patient's electrocardiogram presented ST elevation and increased levels of myocardial enzymes. Percutaneous coronary intervention was done to exclude an obvious problem.

The other 6 cases with cardiovascular complications resulted in hospital mortality. One case involved the rupture of an aortic mycotic aneurysm after transplantation. This patient had a diagnosis of abdominal mycotic aneurysms and infection by salmonella species in pre-transplantation image evaluation. Treatments of patients with mycotic aneurysms caused by salmonella should include antibiotic therapy and surgery [22]. This patient had a high MELD score and massive ascites; a cardiovascular surgeon recommended antibiotic therapy and endovascular stent repair after liver transplantation. On the 12<sup>th</sup> day after liver transplantation, a rupture of an aortic mycotic aneurysm resulted in emergency surgery; the cause of death was hemorrhage. Surgery as an early stage prevention of aneurysm rupture may decrease morbidity or mortality [22]. In three cases, cardiac arrest occurred within 2-5 minutes after reperfusion in intraoperative status. They experienced high-quality cardiopulmonary resuscitation, but their hemodynamic conditions remained unstable. They were then placed on extra-corporeal membrane oxygenation (ECMO). The 2<sup>nd</sup> case had hyperkalemia combined with acidosis due to a massive intraoperative blood transfusion and renal failure history. In the 3<sup>rd</sup> and 4<sup>th</sup> cases, CAD and pulmonary embolism diagnoses were ruled out by percutaneous coronary intervention. Cardiac death within 5 minutes after graft reperfusion may result from many possible causes, including hyperkalemia, acidosis, pulmonary embolism, hypothermia, arrhythmia, cardiac tamponade, acute heart failure, and myocardial

infarction [23, 24]. We finally reached the diagnoses of acute coronary syndrome. The patients' conditions were hemodynamically stable, and their ECMOs were successfully removed after a few days. However, they suffered from cardiac arrest in the ICU. In the 5<sup>th</sup> case, we diagnosed acute coronary syndrome by percutaneous coronary intervention, and the 6<sup>th</sup> case showed mild pulmonary hypertension by echocardiography. Both cases developed septic shock. CAD was the leading cause of early mortality, and it was followed by infection [25]. Cardiovascular complications are the main cause of non-graft-related mortality after LT.

Delayed graft function occurred in 10 cases after LDLT. Successful liver function recovery occurred in 2 cases. Six cases resulted in additional liver transplantations (2 case deaths from severe sepsis), and 2 cases resulted in death while waiting for graft liver. An analysis revealed that causes of delayed graft function are high MELD score ( $\geq 35$ ) combined with low GRWR (range 0.67 ~ 0.69), hepatic steatosis (moderate) in the donor graft and senior donor age (59 and 65 years). Due to this family no any candidates, we only selected the donors. The donor's age and moderate and severe steatosis were already established risk factors for delayed graft function or primary graft dysfunction or non-function [26-30]. Donor age ( $\geq 50$  years) was an independent risk factor to affect regeneration after transplant [26]. Effective graft regeneration may be associated with stem cells or progenitor cells in an elderly donor's liver [9]. The best survival results in our study were observed when the MELD score was below 15. Those with low MELD scores (n=2, MELD 7 and 13) could better tolerate an initial graft dysfunction than the recipients with medium or higher MELD scores who were not achieving successful transplantations due to hepatic steatosis (moderate), senior donor age, or a small-sized graft (GRWR<0.7) succumbing to delayed graft function or graft failure. Values above this limit constitute important factors associated with post-transplant hospital mortality [28-30]. This should also be taken into account when deciding whether to transplant.

Many studies have analyzed the association between transplantation volume in centers and hospital mortality [1, 5]. Our study analyzed the association between surgeon volume (LT cases) and hospital mortality. The early phase of a surgeon's LDLT practice involves frustration and numerous hardships. Massive blood loss, long operative time, prolonged mechanical ventilation, and post-operative complications lead to sepsis and early hospital mortality. Our center is a non-metropolitan hospital; decisive transplant leadership and team staff centripetal force were absolutely essential. Transplant leadership made decisions on valid multidisciplinary integration and organization management. We found a statistically significant association between hospital mortality and surgical volume. This study has some limitations. This study excluded deceased donor liver transplants. Our center only performed 4 to 8 deceased donor liver transplants per year due to a shortage of available organs in Taiwan, and initial development was lower liver graft. An LDLT department needs multidisciplinary integration and organization management. In sharing the development experience of our center, we believe all emerging centers must have access to mentoring while developing an LDLT program.

## Conclusions

The many causes of hospital death were infection, hemorrhage, cerebrovascular complications, cardiovascular complications and delayed graft function. Donor age, blood loss and a surgical volume <30 yearly liver transplantations were significant risk factors from the pre- and peri-operative periods. A comparison showed that annual surgical volumes  $\geq 30$  liver transplantations had significantly higher recipient age, donor age, and ABO-incompatible liver transplantations and significantly lower blood loss, operative time, intensive care unit days, length of stay, re-operative, and hospital mortality than annual surgical volumes <30 liver transplants. During the annual surgical volume  $\geq 30$  period, we practiced more soft power; this may impact quality of care and therefore transplant outcomes.

## Abbreviations

LT: liver transplantation; LDLT: living donor liver transplantation; MELD: model for end-stage liver disease; IVC: inferior vena cava; INR: international normalized ratio; ALT: alanine aminotransferase; GRWR: graft-recipient weight ratio; CAD: coronary artery disease; ECMO: extra-corporeal membrane oxygenation.

## Declarations

### Author`s Contributions

Chia-En Hsieh, Ya-Lan Hsu, Yao-Li Chen, Li-Chueh Weng designed the study, wrote the manuscript and helped to acquire and interpret the data. Ping-Yi Lin, Yu-Ju Hung, Yi-Chun Lai helped with the data management and interpretation. Yu-Ju Hung, Yi-Chun Lai acquired the data. Kuo-Hua Lin, Ping-Yi Lin, Li-Chueh Weng developed the analytical method and analyzed the samples. Chia-En Hsieh, Ya-Lan Hsu helped to interpret the data and to write the manuscript. Chia-En Hsieh, Kuo-Hua Lin, Yao-Li Chen, Li-Chueh Weng helped critical review. All authors read and approved the final manuscript.

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### Availability of data and materials:

Ethical restrictions prohibit the authors from making the data publicly available in order to protect confidentiality and privacy of patient. Interested researchers can submit data access requests to the Changhua Christian Hospital Institutional Data Access.

### Ethics approval and Conflict of Interest information:

The study was approved by the Institutional Review Board of the Changhua Christian Hospital (No. CCH 191244).

### Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no conflicts of interest.

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## Tables

Table 1. Comparisons of demographic data and pre- and peri-operative clinical features based on hospital mortality in liver transplantation patients

Demographic and clinical features	No hospital mortality (n=436)	Hospital mortality (n=30)	p
	Mean±SD (range)	Mean±SD (range)	
Recipient age (years)	54.09±8.40 (11-73)	52.43±11.66 (21-73)	0.451
Donor age (years)	31.17±9.18 (18.0-65.00)	35.27±9.28 (20.0-56.00)	0.019
MELD score	17.24±9.18 (3.0-40.0)	23.33±9.32 (9.0-37.0)	<0.001
Total bilirubin (mg/dL)	6.72±9.55 (0.19-47.69)	8.75±10.33 (0.32-38.68)	0.264
Creatinine ( mg/dL)	1.20±1.07 (0.32-8.96)	1.55±1.10 (0.40-4.90)	0.084
INR	1.53±0.637 (0.87-4.76)	1.69±0.62 (0.95-3.64)	0.193
GRWR	1.10±0.30 (0.55-2.28)	1.13±0.33 (0.68-2.04)	0.604
Blood loss (ml)	3472.29±3646.63 (300.0-39450.0)	7003.00±7371.99 (200.0-40000.0)	0.014
Operative time (min)	408.86±93.68 (215.00-855.00)	434.33±105.65 (280.00-660.00)	0.154
	(%)	(%)	
Gender			0.867
(Male)	340 (78.0)	23 (76.7)	
(Female)	96 (22.0)	7 (23.3)	
Pre-LT renal failure			0.230
(Yes)	23 (5.3)	3 (10.0)	
(No)	413 (94.7)	27 (90.0)	
Pre-LT in intensive care unit			<0.001
(Yes)	27 (6.2)	7 (23.3)	
(No)	409 (93.8)	23 (76.7)	
ABO incompatible			1.000
(Yes)	52 (11.9)	3 (10.0)	
(No)	384 (88.1)	27 (90.0)	
Liver transplant cases / year			
(<20 /year)	17 (3.9)	2 (6.7)	0.350
(≥20 /year)	419 (96.1)	28 (93.3)	

(<30 /year)	65 (14.9)	9 (30.0)	0.029
(≥30 /year)	371 (85.1)	21 (70.0)	
(<50 /year)	137 (31.4)	14 (46.7)	0.084
(≥50 /year)	299 (68.6)	16 (53.3)	

Note: model for end-stage liver disease (MELD) score, international normalized ratio (INR), graft-recipient weight ratio (GRWR), liver transplantation (LT)

Table 2. Logistic regression analysis of factors affecting clinical features of hospital mortality in liver transplantation patients

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Recipient age (years)	0.979	0.941-1.020	0.979	-	-	-
Donor age (years)	1.044	1.007-1.082	0.020	1.049	1.011-1.090	0.013
MELD score	1.065	1.026-1.105	0.001	1.039	0.992-1.088	0.107
Total bilirubin (mg/dL)	1.019	0.986-1.054	0.267	-	-	-
Creatinine (mg/dL)	1.224	0.964-1.554	0.098	-	-	-
INR	1.377	0.847-2.239	0.197	-	-	-
GRWR	1.370	0.418-4.492	0.603	-	-	-
Blood loss (ml)	1.000	1.000-1.000	<0.001	1.000	1.000-1.000	0.004
Operative time (min)	1.003	0.999-1.006	0.155	-	-	-
<20 LT cases/year	1.761	0.387-8.004	0.464	-	-	-
<30 LT cases/year	2.446	1.073-5.577	0.033	2.521	1.004-6.332	0.049
<50 LT cases /year	1.910	0.906-4.024	0.089	-	-	-
Male	0.928	0.386-2.227	0.867	-	-	-
Pre-LT renal failure	1.995	0.563-7.066	0.284	-	-	-
Pre-LT in ICU	4.610	1.817-11.701	<0.001	2.503	0.764-8.195	0.130
ABO incompatible	0.821	0.240-2.800	0.752	-	-	-

Note: model for end-stage liver disease (MELD) score, international normalized ratio (INR), graft-recipient weight ratio (GRWR), liver transplantation (LT), intensive care unit (ICU)

Table 3. Causes of hospital mortality in liver transplantation patients

Cause of hospital mortality	N=30 (%)
Infection	13 (43.3)
Hemorrhage with / without infection	4 (13.3)
Cerebrovascular with / without infection	3 (10.0)
Cardiovascular with / without infection	6 (20.0)
Delayed graft function with infection	4 (13.3)

Table 4. Comparisons of demographic data and clinical features of surgical volume periods in liver transplantation patients

Demographic and clinical features	annual surgical volumes <30 (n=74)	annual surgical volumes ≥30 (n=392)	p
	Mean±SD (range)	Mean±SD (range)	
Recipient age (years)	51.88±9.33 (11-70)	54.38±8.46 (18-73)	0.022
Donor age (years)	29.22±8.13 (18.0-54.00)	31.86±9.37 (18.0-65.00)	0.024
MELD score	17.32±8.95 (6.0-40.0)	17.70±9.37 (3.0-40.0)	0.753
Total bilirubin (mg/dL)	6.01±9.10 (0.19-47.69)	7.01±9.70 (0.32-37.94)	0.408
Creatinine ( mg/dL)	1.13±0.81 (0.38-4.90)	1.14±1.11 (0.32-8.96)	0.440
INR	1.57±0.71 (0.92-4.59)	1.53±0.62 (0.87-4.76)	0.651
GRWR	1.15±0.31 (0.65-2.16)	1.09±0.30 (0.55-2.28)	0.099
Blood loss (ml)	6143.92±5202.98 (200.0-23000.0)	3238.16±3649.88 (200.0-40000.0)	<0.001
Operative time (min)	474.51±91.78 (290.00-730.00)	398.41±90.24 (215.00-885.00)	<0.001
APACHE II score	17.55±7.00 (5.00-29.00)	18.51±7.24 (3.00-37.00)	0.294
Intensive care unit (days)	15.23±10.03(4.0-58.00)	9.65±9.62 (1.00-114.00)	<0.001
Length of stay (days)	35.55±17.38 (14.00-119.00)	29.99±17.38 (3.00-159.00)	0.013
	(%)	(%)	
Gender			0.085
(Male)	52 (70.3)	311 (79.3)	
(Female)	22 (29.7)	81 (20.7)	
Pre-LT renal failure			0.782
(Yes)	3 (4.1)	23 (5.9)	
(No)	71 (95.9)	369 (94.1)	
Pre-LT in intensive care unit			0.332
(Yes)	3 (4.1)	31 (7.9)	
(No)	71 (95.9)	361 (92.1)	
ABO incompatible			<0.001
(Yes)	0 (0.0)	55 (14.0)	
(No)	74 (100.0)	337 (86.0)	

Dialysis			0.067
(Yes)	13 (17.6)	40 (10.2)	
(No)	61 (82.4)	352 (89.8)	
Re-operative			<0.001
(Yes)	29 (39.2)	72 (18.4)	
(No)	45 (60.8)	320 (81.6)	
Biliary complication			0.163
(Yes)	12 (16.2)	41 (10.5)	
(No)	62 (83.8)	351 (89.5)	
Hepatic artery complication			0.741
(Yes)	3 (4.1)	14 (3.6)	
(No)	71 (95.9)	378 (96.4)	
Portal vein complication			0.367
(Yes)	0 (0.0)	8(2.0)	
(No)	74 (100.0)	384 (98.0)	
Delayed graft function			0.376
(Yes)	0 (0.0)	10 (2.6)	
(No)	74 (100.0)	382 (97.4)	
Cardiovascular complication			0.158
(Yes)	3 (4.1)	6 (1.5)	
(No)	71 (95.9)	386 (98.5)	
Cerebrovascular complication			1.000
(Yes)	1 (1.4)	6 (1.5)	
(No)	73 (98.6)	386 (98.5)	
Pulmonary complication			0.175
(Yes)	12 (16.2)	42 (10.7)	
(No)	62 (83.8)	350 (89.3)	
Hemorrhage			0.094

(Yes)	13 (17.6)	42 (10.7)
(No)	61 (82.4)	350 (85.2)
Infection		0.204
(Yes)	28 (37.8)	119 (30.4)
(No)	46 (62.2)	273 (69.6)
Hospital mortality		0.029
(Yes)	9 (12.2)	21 (5.4)
(No)	65 (87.8)	371 (94.6)

Note: model for end-stage liver disease (MELD) score, international normalized ratio (INR), graft-recipient weight ratio (GRWR), liver transplantation (LT)

## Figures

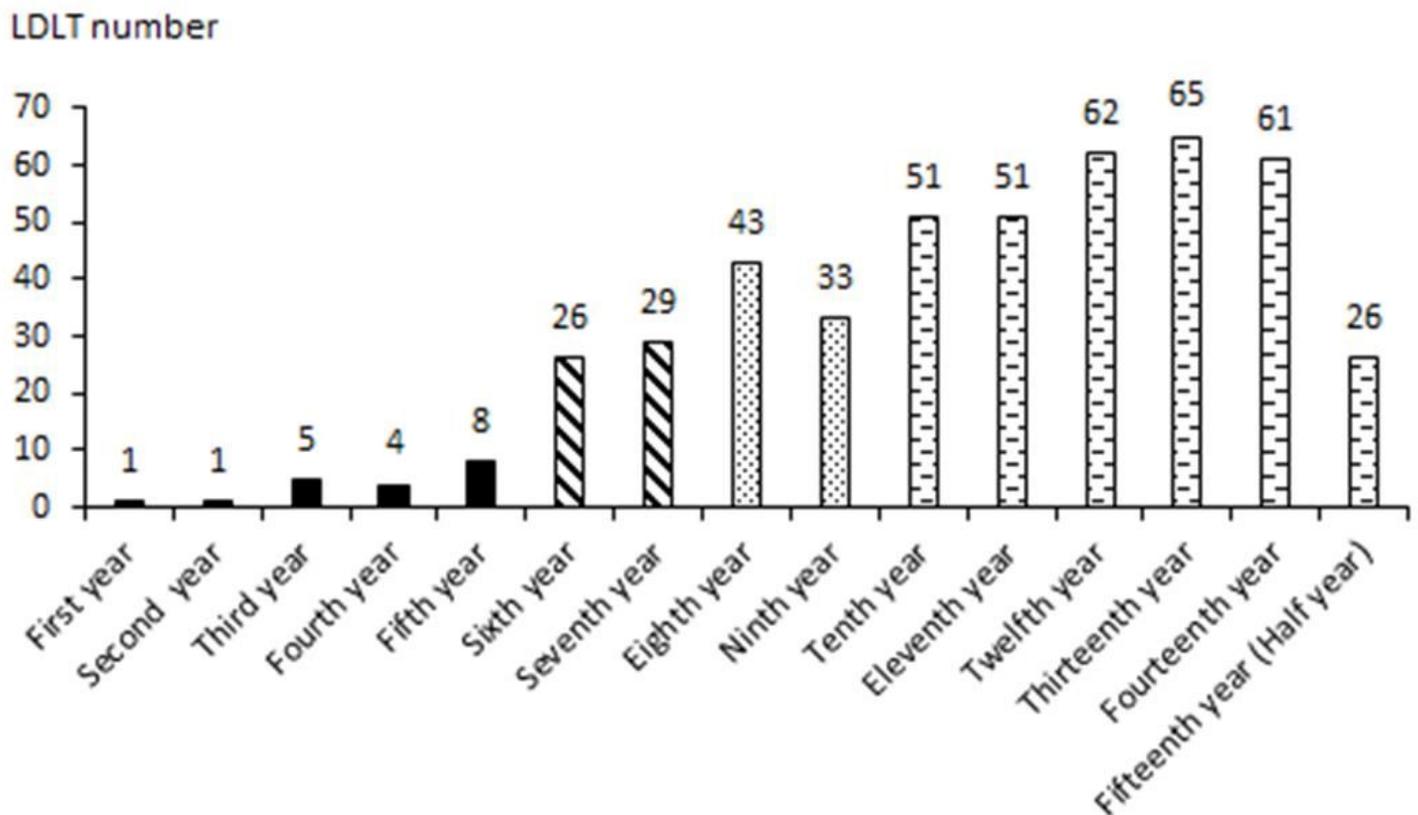


Figure 1

Liver donor liver transplantations in our center. Legend: Annual LDLT volume was less than 10 cases in the first 5 years of our transplantation center (total 19 transplantation cases). It grew to 20-30 cases in

the 6th and 7th years, over 30 cases after 8 years, and over 50 cases after 10 years.