

RESEARCH ARTICLE

The Impact of Hospital/Surgeon Volume on Acute Renal Failure and Mortality in Liver Transplantation: A Nationwide Cohort Study

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Abstract

The aim of this study was to assess whether the case volume of surgeons and hospitals affects the rates of postoperative complications and survival after liver transplantation. This population-based retrospective cohort study included 2938 recipients of liver transplantation performed between 1998 and 2012, enrolled from the Taiwan National Health Insurance Research Database. They were divided into two groups, according to the cumulative case volume of their operating surgeons and the case volume of their hospitals. The duration of intensive care unit stay and post-transplantation hospitalization, postoperative complications, and mortality were analyzed. The results showed that, in the low and high case volume surgeons groups, respectively, acute renal failure occurred at the rate of 14.11% and 5.86% ($p < 0.0001$), and the overall mortality rates were 19.61% and 12.44% ($p < 0.0001$). In the low and high case volume hospital groups, respectively, acute renal failure occurred in 11% and 7.11% of the recipients ($p = 0.0004$), and the overall mortality was 18.44% and 12.86% ($p < 0.0001$). These findings suggest that liver transplantation recipients operated on higher case volume surgeons or in higher case volume hospitals have a lower rate of acute renal failure and mortality.

Introduction

Nowadays, liver transplantation is performed to treat for a variety of liver diseases such as acute hepatic failure, cholestatic disease, congenital biliary disease, cirrhosis, liver tumors, and metabolic diseases [1, 2]. The experience of the doctors or the care teams may be an important factor affecting the outcomes of complex surgical procedures. In colorectal cancer surgery, better outcomes were reported for patients treated in high-volume hospitals and by high-volume colorectal specialists [3, 4]. For pancreatic surgery, lower 1-year mortality was observed in higher volume hospitals [5, 6]. Perioperative complications were lower with high-volume surgeons and at high-volume centers after adult spinal deformity revision surgery [7].

Competing Interests: The authors have declared that no competing interests exist.

However, the caseload of medical caregivers or facilities does not always affect outcomes. Hospital volume did not affect the mortality of preterm patent ductus arteriosus and biliary atresia [8, 9]. The survival rate after lung cancer surgery did not correlate with hospital case volume [10, 11]. In laparoscopic partial colectomy, low volume surgeons were observed to have similar outcomes compared to high volume surgeons [12]. It remains unknown whether hospital or surgeon case volume is related to the outcome of liver transplant patients. The goal of this nationwide cohort study was to assess whether case -volume of surgeons and hospitals had an impact on survival after liver transplantation. We therefore followed up the postoperative complication and mortality figures of patients receiving liver transplantation from 1998 to 2012 in Taiwan.

Materials and Methods

Study Population and Database

This was a retrospective cohort study and approved by the National Health Insurance Research Database (NHIRD) research committee (NHIRD-103-103) and the Institutional Review Board of the Chang Gung Medical Foundation.

The data was derived from the Taiwan NHIRD, which is an insurance claim database of Taiwan National Health Insurance launched in 1995 and, by 2014, covered 99.9% of the Taiwanese population. From 1998 onwards, the insurance registration files and original claim files by which patients, medical caregivers, and medical institutions could be identified have been encrypted and then sent to the National Health Research Institutes (NHRI) for setting up the database. The Bureau of National Health Insurance (BNHI) has collected claim data in a de-identified and computerized format and established the NHIRD. No consent was given since the data were analyzed anonymously. Before transferring data to scientists in Taiwan, NHRI encrypt the data again to protect the privacy of patients, medical caregivers, and medical institutions. Further, scientists intending to analyze data from NHRI have to sign a declaration of non-violation of privacy.

Selection of Patients and Variables

The flowchart of patient selection is shown in [Fig 1](#).

Patients with the ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) codes V42.7 (liver replaced by transplant) and 996.82 (complications of transplanted liver) were identified from NHIRD data for the period between July 1998 and December 2012, and a total of 4086 patients were initially included in the study. Of these, 1148 patients were excluded because of not having undergone operation in Taiwan, or because they lacked ICD-9-CM 50.5, 75020A, or 75020B codes [13]. Finally, 2938 patients were included in this cohort study.

Preoperative comorbidity was identified from medical records of inpatient or outpatient departments using ICD-9-CM codes: hypertension (401–405), pulmonary disease (490–496), diabetes mellitus (250, A181), cerebrovascular disease (430–43, A291–A299), coronary heart disease (410–414, A279), liver cirrhosis (571.5, 571.2, 571.6), chronic kidney disease (585), hepatitis B (070.2, 070.3, V02.61, V02.69), and hepatitis C (070.41, 070.44, 070.51, 070.54, 070.7, V02.62).

Defining Surgeon and Hospital Case Volumes

The methods for defining low and high case volume for surgeons and for hospitals are described as below. Surgeons were ranked according to their cumulative number of liver

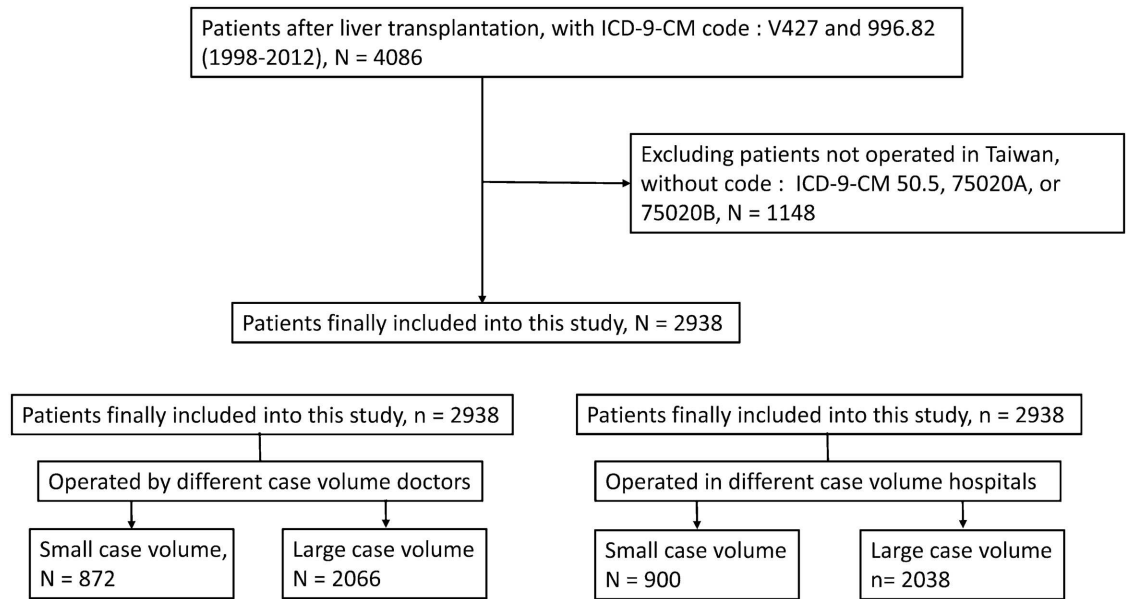


Fig 1. Flowchart of patient selection.

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transplantations performed, and were divided into three groups. The group with the most cases (one-third of all surgeons) was defined as the high case volume surgeons group, and the others (two-thirds) were defined as the low case volume surgeons group [14]. The cutoff number was 100, which meant that surgeons who had performed more than 100 liver transplantation procedures were considered high volume surgeons. Hospitals were ranked according to the cumulative number of liver transplantation cases, and were divided into three groups. The group with the most cases (one-third of all hospitals) was defined as the high case volume hospitals group, and the others (two-thirds) were defined as the low case volume hospitals group [14]. The cutoff number of cumulative liver transplantation procedures for defining case volume in the hospital was 300.

Outcomes

The primary outcome was mortality rates after liver transplantation. Others were the length of intensive care unit (ICU) stay and hospitalization, bacteremia, pneumonia, bleeding, and acute renal failure after liver transplantation. Patients were identified by the postoperative occurrence of the ICD-9-CM code of bacteremia, pneumonia, and bleeding. Acute renal failure after liver transplantation was defined as the patient receiving renal replacement therapy from the end of liver transplantation surgery to discharge from the hospital. Patients were excluded if on renal replacement therapy prior to liver transplantation with ICD-9-CM codes 38.95, 39.27, 39.42, 39.95, 39.43 or 54.98. Recipients with the postoperative ICD-9-CM codes 584, 585, V451 or V56 were regarded as having acute renal failure. Death was defined as the ending of national health insurance or with a death code in the records [13]. The total numbers of renal replacement therapies were calculated.

Statistical Analysis

The SAS statistical software, version 9.3, (SAS institute Inc, Cary, NC) was used to evaluate our data. A p-value less than 0.05 was considered statistically significant. The T test, chi-squared

test, or Fisher’s exact test was used to analyze demographic data, coexisting underlying disease, length of medical inpatient service (such as length of ICU stay and hospitalization), and post-operative complications.

During the post-transplantation period, Kaplan-Meier estimates with the log-rank test were used for comparing survival rates between groups. When analyzing mortality, patients were followed up after liver transplantation until either death or censoring. Mortality risks were evaluated by multivariate logistic regression analysis.

Results

Mortality

This cohort study analyzed 2938 patients. The cumulative mortality rates for all the liver transplantation recipients was 1.1% at 30 days, 2.8% at 3 -months, 7.7% at 1 -year, 14.6% overall.

Volume Effect of Surgeons

Low case volume surgeons were found to have operated on 872 patients, while the other 2066 patients had been operated on by high case volume surgeons. The demographic analysis is shown in Table 1.

Recipients operated on by low case volume surgeons stayed in the ICU for a longer period than those operated on by high case volume surgeons ($p < 0.05$). However, the length of hospital stay after liver transplantation was similar for both groups (Table 2). Postoperatively, the incidence of bacteremia, pneumonia, and bleeding were similar between low and high case volume surgeon groups ($p > 0.05$). More acute renal failure was observed in the low case volume surgeon groups ($p = 0.0004$).

As shown in Table 3, mortality rates were noted at 30 -days, at 3 -months, at 1 -year and overall; recipients in the low case -volume surgeon group had a higher mortality rate than those in the high case -volume surgeon group ($p < 0.0001$).

Table 1. Demography of liver transplantation recipients operated on by low and high case volume surgeons.

	Low case volume surgeons (n = 872)	High case volume surgeons (n = 2066)	P Value
	Mean(SD) / n (%)	Mean(SD) / n (%)	
Age [†]	46.10 (17.23)	46.56 (17.87)	0.5171
Gender			0.5824
Female	252 (28.90)	618 (29.91)	
Male	620 (71.10)	1448 (70.09)	
Pre-operative clinical parameters			
Hypertension	177 (20.30)	423 (20.47)	0.9138
Pulmonary diseases	136 (15.60)	284 (13.75)	0.1906
Diabetes mellitus	169 (19.38)	445 (21.54)	0.1886
Cerebrovascular disease	33 (3.78)	58 (2.81)	0.1626
Coronary heart disease	58 (6.65)	146 (7.07)	0.6857
Liver cirrhosis	739 (84.75)	1745 (84.46)	0.8452
Hepatitis B	434 (49.77)	982 (47.53)	0.2671
Hepatitis C	193 (22.13)	469 (22.70)	0.7364

[†] Values are mean and standard deviation.

SD, standard deviation.

T-test or Chi-square test were used to examine the differences in the demographic characteristics of liver transplant patients between the small and large case volume doctors.

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Table 2. Outcomes of liver transplantation recipients operated on by low and high case volume surgeons.

	Low case volume surgeons (n = 872)		High case volume surgeons(n = 2066)		P Value
	Mean(SD) / n (%)		Mean(SD) / n (%)		
ICU stay, (days) †	17.36 (22.13)		15.45 (14.60)		0.0199*
Hospital stay, (days) †	50.17 (39.53)		47.82 (33.09)		0.1226
Bacteremia	59 (6.77)		106 (5.13)		0.0786
Pneumonia	32 (3.67)		54 (2.61)		0.1208
Postoperative bleeding	44 (5.05)		107 (5.18)		0.8812
Acute Renal Failure	123 (14.11)		121 (5.86)		<0.0001*

† Values are mean and standard deviation.

*P value < 0.05.

ICU stay, intensive care unit stay. SD, standard deviation.

T-test or Chi-square test were used to examine the differences in the outcomes of liver transplant patients between the small and large case volume doctors.

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The unadjusted Kaplan-Meier survival analysis, shown in Fig 2, revealed a one-year survival rate of 87.84% in the low case volume surgeon group and of 94.19% in the high case volume surgeon group. The overall survival was 80.39% in the low case volume surgeon group as compared to 87.56% in the high case volume surgeon group. There is significant association between chronic renal failure before liver transplant and acute renal failure after liver transplant surgery by surgeon groups respectively. The percent of patient with chronic renal failure before surgery and acute renal failure after surgery are 42.9% in high case volume surgeon group and 37.5% in low case volume surgeon group, and without chronic renal failure before surgery and with acute renal failure after surgery are 11.6% in high case volume surgeon group and 20.4% in low case volume surgeon group, high case volume surgeon (Chi-square test p-value < .0001) and low case volume surgeon (Chi-square test p-value = 0.0421) respectively. The average numbers of renal replacement therapies are no different between surgeon groups (p-value = 0.6639).

Volume Effect of Hospitals

The low and high case volume hospital groups comprised 900 and 2038 operated patients, respectively. The demographic information for these two groups is shown in Table 4.

Patients who underwent liver transplantation in low case volume hospitals stayed in the ICU and in hospital for a shorter duration than those in high case volume hospitals (Table 5).

Table 3. Mortality rate of liver transplantation recipients operated on by low and high case volume surgeons.

	Low case volume surgeons (n = 872)		High case volume surgeons (n = 2066)		P Value
	n (%)	Median	n (%)	Median	
Mortality (30-days)	25 (2.87)	17	9 (0.45)	18	<0.0001*
Mortality (3-months)	57 (6.54)	35	25 (1.21)	43	<0.0001*
Mortality (1-year)	106 (12.16)	76.5	120 (5.81)	190.5	<0.0001*
Mortality (Overall)	171 (19.61)	398.5	257 (12.44)	74	<0.0001*

*P value < 0.05.

The Log-rank test were used to examine the differences in the mortality rate of liver transplantation recipients operated by small and large case volume doctors.

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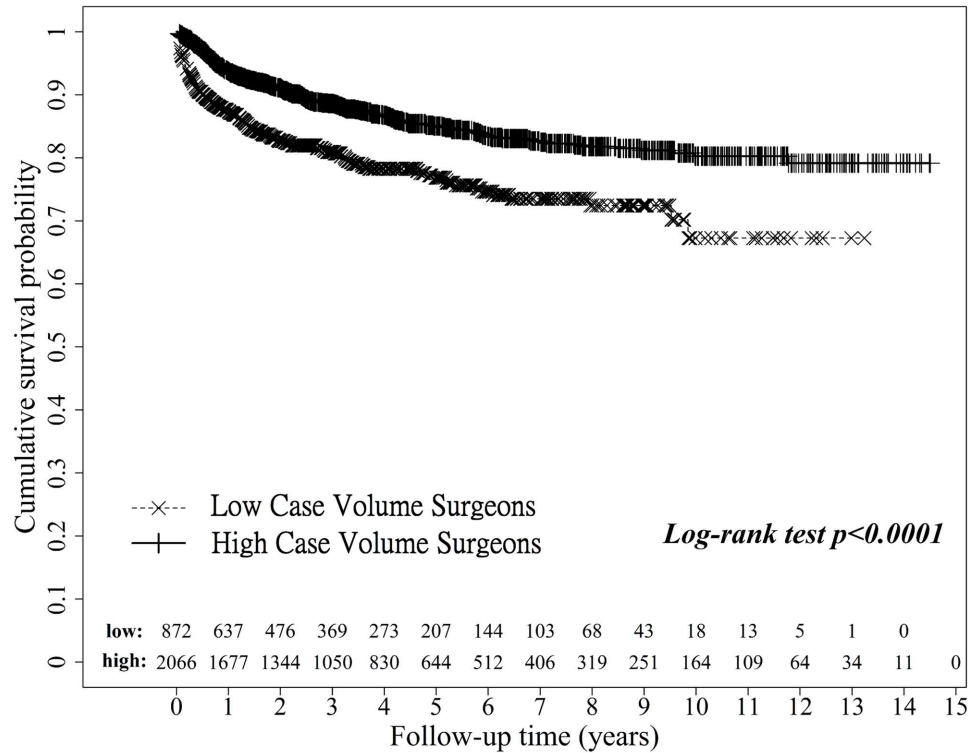


Fig 2. Overall mortality when operated on by high and low case volume surgeons.

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Table 4. Demography of liver transplantation recipients operated on in low and high case volume hospitals.

	Low case volume hospitals (n = 900)	High case volume hospitals (n = 2038)	P Value
	Mean(SD) / n (%)	Mean(SD) / n (%)	
Age [†]	48.86 (14.69)	45.34 (18.75)	<0.0001*
Gender			
Female	224 (24.89)	646 (31.70)	0.0002*
Male	676 (75.11)	1392 (68.30)	
Pre-operative clinical parameters			
Hypertension	222 (24.67)	378 (18.55)	0.0001*
Pulmonary diseases	153 (17.00)	267 (13.10)	0.0054*
Diabetes mellitus	192 (21.33)	422 (20.71)	0.7001
Cerebrovascular disease	35 (3.89)	56 (2.75)	0.0998
Coronary heart disease	72 (8.00)	132 (6.48)	0.1344
Liver cirrhosis	770 (85.56)	1714 (84.10)	0.3150
Hepatitis B	485 (53.89)	931 (45.68)	<0.0001*
Hepatitis C	205 (22.78)	457 (22.42)	0.8324

[†] Values are mean and standard deviation.

*P value < 0.05.

SD, standard deviation.

T-test or Chi-square test were used to examine the differences in the demographic characteristics of liver transplant patients between the small and large case volume hospitals.

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Table 5. Outcomes of liver transplantation recipients operated on in low and high case volume hospitals.

	Low case volume hospitals(n = 900)		High case volume hospitals (n = 2038)		P Value
	Mean(SD) / n (%)		Mean(SD) / n (%)		
ICU stay, (days) †	11.69(13.15)		17.94(18.46)		<0.0001*
Hospital stay, (days) †	38.63 (29.81)		52.89(36.40)		<0.0001*
Bacteremia	49 (5.44)		116 (3.95)		0.7883
Pneumonia	24 (2.67)		62 (3.04)		0.5778
Postoperative bleeding	36 (4.00)		115 (5.64)		0.0630
Acute Renal Failure	99 (11.00)		145 (7.11)		0.0004*

† Values are mean and standard deviation.

*P value < 0.05.

ICU stay, intensive care unit stay. SD, standard deviation.

T-test or Chi-square test were used to examine the differences in the outcomes of liver transplant patients between the small and large case volume hospitals.

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The incidence of bacteremia, pneumonia, and bleeding after liver transplantation was similar between the low and high volume hospital groups. Acute renal failure during the postoperative period occurred more frequently in the low volume hospital group.

As shown in Table 6, the mortality in the low and high volume hospital groups followed up at different times was 2.00% vs. 0.79% at 30 days (p = 0.0045), 4.56% vs. 2.01% at 3 months (p = 0.0001), 10.56% vs. 6.43% at 1 year (p<0.0001), and 18.44% vs. 12.86% overall (p< 0.0001). Thus, higher mortality was observed in low volume hospitals. The unadjusted Kaplan-Meier survival analysis is shown in Fig 3. There is significant association between chronic renal failure before liver transplant and acute renal failure after liver transplant surgery by hospital groups respectively. The percent of patient with chronic renal failure before surgery and acute renal failure after surgery are 36.4% in high case volume hospital and 46.9% in low case volume hospital, and without chronic renal failure before surgery and with acute renal failure after surgery are 12.7% in high case volume hospital and 17.5% in low case volume hospital, high case volume hospital (Fisher exact test p-value = 0.0006) and low case volume hospital (Chi-square test p-value < .0001) respectively. The average numbers of renal replacement therapies are no different between hospital groups (p-value = 0.8912).

Discussion

It was observed that outcomes after transplantation surgery correlated with case volume of the surgeon and the hospital [15, 16]. The mortality at 30 days, at 3 months, at 1 year, and overall,

Table 6. Mortality rate of liver transplantation recipients operated on in low and high case volume hospitals.

	Low case volume hospitals(n = 900)		High case volume hospitals (n = 2038)		P Value
	n (%)	Median	n (%)	Median	
Mortality (30-days)	18 (2.00)	19.5	16 (0.79)	15	0.0045*
Mortality (3-months)	41 (4.56)	35	41 (2.01)	36	0.0001*
Mortality (1-year)	95 (10.56)	108	131 (6.43)	148	<0.0001*
Mortality (Overall)	166 (18.44)	273	262 (12.86)	365.5	<0.0001*

*P value < 0.05.

The Log-rank test were used to examine the differences in the mortality rate of liver transplantation recipients operated by small and large case volume hospitals.

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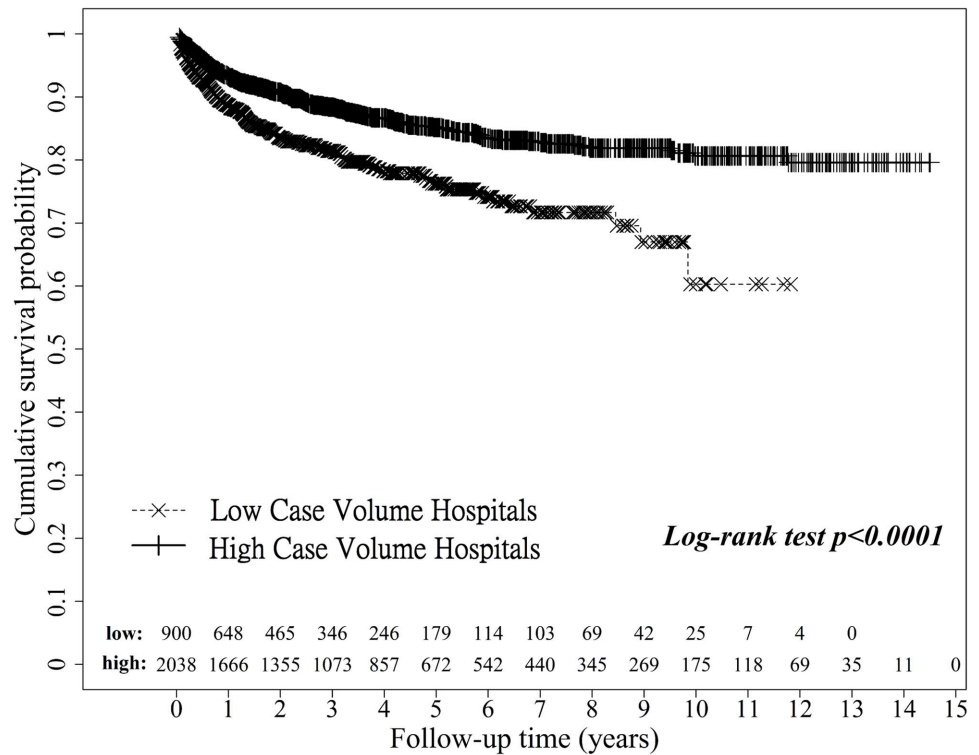


Fig 3. Overall mortality when operated on in high and low case volume hospitals.

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was significantly lower when recipients were operated on by surgeons, or in hospitals, with high case volumes. In addition, the incidence of postoperative acute renal failure was lower if surgery was performed by surgeons, or in hospitals, with high case volumes.

High surgeon case volume has been reported to be a good survival factor in many surgical procedures, such as hepatectomy, colorectal cancer surgery [3, 17, 18]. Liver transplantation is a complex surgical procedure. Previous studies have shown that the steep learning curve for liver transplantation may affect the recipients' outcome [19, 20] and less experienced surgeons had higher short-term postoperative complication rates and lower 1-year survival rates. The 1-year survival rates improved as the surgeons' experience increased, but reached a plateau despite further cumulated experience. Therefore, at this stage, the mortality rate would be related to the surgeons' experience.

High surgical volume of hospitals was also an indicator for a lower complication rate and a factor for better survival in many surgical procedures [5, 15, 21, 22]. High volume hospitals had more experienced healthcare staff and specialized units providing better care. More skilled specialists for perioperative care, as well as more experienced nurses and ICU staff might play an important role [17]. We also found that high case volume hospitals had lower rates of acute renal failure and mortality.

The incidence of postoperative acute renal failure was higher in patients who underwent liver transplantation by low volume surgeons and in low volume hospitals. Patients who encountered acute renal failure after liver transplantation also had increased mortality rates [13, 23]. Consistent with these findings, our study also found that liver transplantation recipients operated on by high case volume surgeons or operated in high case volume hospitals have a lower rate of acute renal failure and mortality. Renal replacement therapy is usually initiated

in the setting of medically refractory hyperkalemia, acidosis, or volume overload or if uremic symptoms developed [24].

This retrospective cohort study has several limitations. First, the NHIRD is an insurance claim database, so clinical data is not collected. The preoperative model for end-stage liver disease (MELD) score, Child-Pugh score, amount of intraoperative blood loss, blood pressure, type and amount of transfusion, urine output, cold and warm ischemia time of the graft, and amount of postoperative blood loss could not be traced and analyzed. Second, the data was from the ICD-9-CM code. Taiwan National Insurance Bureau verifies the code periodically, but coding faults may occur due to human error. Third, our cohort covered a time-span of 14.5 years and, during this period, medical advances could have affected the mortality rates [13]. Finally, this study only reveals the relationship between case volume and mortality after liver transplantation; however, the definite reasons for mortality remain unclear.

Conclusion

Our study suggests that surgeons' and hospitals' case volume are related to patients' mortality after liver transplantation. In this cohort study, patients who underwent liver transplantation by high case volume surgeons or in high case volume hospitals had a better survival rate. Centralization of liver transplantation surgery to high case volume surgeons and hospitals may decrease mortality.

Supporting Information

S1 File. Numbers of liver transplant patients sorted by surgeons.
(XLSX)

S2 File. Numbers of liver transplant patients sorted by hospitals.
(XLSX)

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Author Contributions

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Funding acquisition: H-PY F-CL.

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Writing – review & editing: C-WC F-CL H-PC Y-FT H-PY J-RL.

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