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Adult split liver transplantation

A PRISMA-compliant Chinese single-center retrospective case-control study

Lingxiang Kong, MD, Tao Lv, MD, Jian Yang, MD, Li Jiang, MD, Jiayin Yang, MD*

Abstract

Although pediatric split liver transplantation (SLT) has been proven safe and the waitlist mortality rate has been successfully reduced, the safety of adult SLT has not been confirmed.

Using 1:2 matching, 47 recipients who underwent adult SLT were matched to 94 of 743 recipients who underwent adult whole graft liver transplantation (WGLT). Eventually, 141 recipients were included in the case-control study. Subgroup analysis of 43 recipients in the SLT group was performed based on the presence of the middle hepatic vein (MHV) in the grafts.

No significant differences in 5-year survival (80.8% vs 81.6%, $P = .465$) were observed between the adult SLT and WGLT groups. However, compared to recipients in the WGLT group, those in the SLT group had more Clavien–Dindo grade III-V complications, longer hospitalization duration, and higher mortality within 45 days. Furthermore, on multivariate analysis, 45-day postoperative mortality in recipients in the SLT group was mainly affected by hyperbilirubinemia within postoperative day (POD) 7–14, surgery time, and intraoperative blood loss. Subgroup analysis showed no significant differences in hyperbilirubinemia within POD 7–14, complications, and survival rate between $SLT^{MHV(+)}$ and $SLT^{MHV\ [-]}$.

Adult SLT is safe and effective based on long-term survival rates; however, a reduction in the incidence of short-term complications is required. Non-obstructive hyperbilirubinemia within POD 7 to 14 is an independent predictor of short-term mortality after SLT.

Abbreviations: HCC = hepatocellular carcinoma, LT = liver transplantation, MHV = middle hepatic vein, POD = postoperative day, SLT = split liver transplantation, WGLT = graft liver transplantation.

Keywords: donation after brain death, liver transplantation, split liver transplantation

1. Introduction

Since the first successful split liver transplantation (LT; SLT) in 1988,[1] this technique has theoretically doubled the donor pool and alleviated the shortage of donor livers. The significant value of this technique has attracted close attention from research centers worldwide. However, in the 20 years following the first successful SLT, many centers have found a high rate of graft mortality, high rates of complications, and low long-term survival. Most researchers believe that split livers should be considered marginal donor livers.[2] As LT has become a necessary treatment for congenital biliary atresia and some congenital metabolic diseases in children, the demand for donor livers in children has increased dramatically. The ethical problem regarding the conversion of an excellent organ into 2 marginal quality grafts exists, although many families have no alternative to living donor liver transplantation. The proportion of living donor livers for pediatric living donor liver transplantation in our center in China is about 75%, whereas that in other Asian countries, such as Korea, ranges between 66.6% to 80%.[3,4] To meet the growing demand for pediatric recipients, solving the safety problem of SLT has become the research focus of many transplantation centers. Presently, SLT has been confirmed by many centers to be safe in pediatric recipients and to reduce waitlist mortality rates.[5] Although negative evaluations of SLT in children are rarely reported, many centers for adult SLT have inconsistent views on its safety.[6] Because of its safety is questionable, many countries have not yet enacted SLT legislation, and a children-first allocation scheme still remains unresolved. This article discusses the experience of adult SLT in a single center.

2. Methods

2.1. Ethical approval and graft source

In this study, the grafts for LT were obtained from dead donors according to a new organ acquisition and distribution policy

Editor: Wen-Wei Sung.

This study was supported by grants from 1.3.5 project for disciplines of excellence, West China Hospital, Sichuan University. (No. ZY2017308) and Major National Science and Technology Special Projects (No. 2017ZX10203205-005-002 and 2017ZX10203205-001-004).

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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How to cite this article: Kong L, Lv T, Yang J, Jiang L, Yang J. Adult split liver transplantation: a PRISMA-compliant Chinese single-center retrospective case-control study. Medicine 2020;99:51(e23750).

Received: 10 March 2020 / Received in final form: 13 November 2020 / Accepted: 17 November 2020

http://dx.doi.org/10.1097/MD.0000000000023750

established in China after 2012[7] or brain death donation (DBD) before 2012. No prisoners were included as donors. The protocol was approved by the Ethics Committee of the West China Hospital of Sichuan University West China Hospital. Written informed consent was obtained from all recipients prior to surgery, and all donations were voluntary and altruistic and in accordance with the ethical guidelines of the Declaration of Helsinki.

2.2. Recipients

From September 2007 to October 2019, only recipients 18 years of age or older were included. The indications for LT in this study were end-stage liver diseases and malignant liver tumors.[8] The exclusion criteria in this study were multiple organ transplantation (ie, combined liver-kidney transplantation), domino LT, double donor LT, and re-transplantation. The mean follow-up for the post matched groups was 774 days. Using 1:2 propensity score matching, 47 recipients who underwent adult SLT were matched to 94 out of a total of 743 recipients who underwent adult graft liver transplantation (WGLT). Eventually, 141 recipients were included in the case-control study. Subgroup analysis of 43 recipients in the SLT group was performed based on the presence of the middle hepatic vein (MHV) in the grafts. Every LT, whether for SLT or WLT recipients, was performed *in vivo*; on the contrary, donor liver acquisition was performed *in vivo* via an in-situ splitting surgery. Follow-up was routinely performed in the outpatient clinic. Measurements of alpha-fetoprotein and hepatitis B virus DNA and abdominal ultrasonography were performed every 3 months; a computer tomography scan was performed every 6 months. All hepatitis B virus DNA-positive patients were treated with antiviral therapy before and after surgery. When intrahepatic recurrence was difficult to ascertain, magnetic resonance imaging or contrast-enhanced ultrasonography were performed. Tumor recurrence was based mainly on radiographic evidence and/or alpha-fetoprotein level. Patients who showed tumor recurrence after surgery were treated with the following alternatives: resection, radiofrequency ablation, salvage LT, transcatheter arterial chemoembolization, or sorafenib. Recipients were monitored until August 2019 or until death, and their medical records were retrospectively reviewed. The causes and proportions of death in DBD liver grafts were as follows: severe head injury caused by trauma event (32.6%), hypertension-related intracranial hemorrhage (36.2%), rupture of intracranial aneurysm (7.1%), intracranial infection (5.7%), hypoxic ischemic encephalopathy caused by respiratory diseases (9.9%), and hypoxic ischemic encephalopathy caused by severe trauma (8.5%). Every 1 SLT case in our study means that we used 1 hemi-liver graft for 1 adult liver transplantation, instead of 1 whole liver were split into 2 hemi-livers.

2.3. Definitions

The Clavien–Dindo complication classification[9] system was used for post-operative complication grading, and grade III–IV complications were defined as severe complications. Early allograft dysfunction was defined as the presence of 1 or more of the following postoperative laboratory findings: bilirubin ≥10 mg/dL on day 7, international normalized ratio ≥1.6 on day 7, and alanine or aspartate aminotransferases >2000 IU/L within the first 7 days.[10] Primary nonfunction was defined as non-recoverable graft function needing urgent liver replacement during the first 7 days after LT.[11]

Table 1

Baseline demographic and disease features characteristics.

Variables	After matching 1:2*		
	SLT (n = 47)	WGLT (n = 94)	*P*
Age^{Donor} (yr)	30.77 ± 10.31	29.79 ± 11.46	.622
$Male^{Donor}$ (%)	37 (78.7%)	78 (83%)	.539
Age (yr)	50.74 ± 11.42	51.67 ± 9.67	.615
Male (%)	35 (74.5%)	76 (80.9%)	.383
BMI (kg/m^2)	21.37 ± 3.73	21.71 ± 2.70	.577
CRE ≥133 (μmol/L)	5 (10.6%)	3 (3.2%)	.157
ALB (g/L)	35.37 ± 7.83	35.68 ± 8.01	.831
TB ≥170 (μmol/L)	14 (29.8%)	23 (24.5%)	.499
INR	1.43 ± 0.48	1.5 ± 0.60	.478
MELD ≥25	11 (23.4%)	16 (17%)	.364
Child-Pugh	9.47 ± 2.16	9.21 ± 2.54	.555
PLT<100 (10^9/L)	33 (70.2%)	63 (67%)	.702
WBC (10^9/L)	5.06 ± 2.54	4.75 ± 1.89	.457
HGB (g/L)	110.28 ± 28.98	112.21 ± 27.09	.697
HBsAg positive (%)	30 (63.8%)	66 (70.2%)	.443
Tumor (%)	27 (57.4%)	58 (61.7%)	.626
Single tumor (%)	14 (29.8%)	27 (28.7%)	.896
AFP >400 ng/mL (%)	16 (34%)	33 (35.1%)	.900
Tumor size >3 cm (%)	17 (36.2%)	35 (37.2%)	.902
Tumor differentiation grade III (%)	11 (23.4%)	26 (27.7%)	.588

AFP = Alpha-fetoprotein, ALB = albumin, BMI = Body mass index, CRE = Creatinine, HBsAg = Hepatitis B surface antigen, HGB = Hemoglobin, INR = international normalized ratio, MELD = model end-stage liver disease, PLT = platelet, TB = total bilirubin, WBC = white blood cell.

* 47 adult SLT and 731 adult WGLT were matched in a 1:2 ratio.

2.4. Statistical analysis

The R (version 3.6.2) was used for survival curve analysis. Overall, patient survival was estimated using the Kaplan–Meier method, and differences between groups were determined using log-rank test. To minimize the influence of other confounders on outcomes, a propensity score analysis was used to match the 2 cohorts using nearest neighbor matching and based on the variables listed in Table 1. Categorical data are presented as number (percent) and compared using the Pearson chi-Square and Fisher exact test. On the contrary, continuous variables are expressed as mean value ± SD and analyzed using t-test and repeated measure analysis of variance. Overall, survival was estimated using the Kaplan–Meier method, and differences between 2 groups were determined using log-rank test. $P < .05$ was considered statistically significant.

3. Results

3.1. Baseline demographic characteristics, disease features, and surgical characteristics between SLT and WGLT

Baseline demographic characteristics and disease features in the experimental (SLT) and control (WGLT) groups in the post-matched samples are summarized in Table 1. The perioperative course of the post-matched samples is summarized in Table 2. The organs were preserved in 4°C perfusate, in which a thermometer was equipped to monitor the temperature. Compared with the traditional in vitro perfusion LT, the time period from the ogan's blood supply stops to its surface temperature drops to 4 °C is greatly shortened. Because the difference of warm ischemia time between in situ perfusion and in vitro perfusion lies in this part of time. For an accurate comparison, we defined this part of time as partial warm ischemia time. Given that adult recipients in the SLT

Table 2

Perioperative course and postoperative outcome.

Variables	SLT (n = 47)	WGLT (n = 94)	P
GRWR	1.21 ± 0.24	2.01 ± 0.73	<.001
Partial warm ischemia time* (min)	3.74 ± 1.46	4.18 ± 2.01	.146
Cold ischemia time (min)	155.66 ± 52.7	160.07 ± 51.02	.633
Intraoperative blood loss (mL)	1129.79 ± 764.62	732.45 ± 546.87	.002
Blood transfusion (mL)	462.71 ± 313.89	380.59 ± 323.29	.153
Operation time (hours)	9.38 ± 1.88	7.49 ± 0.58	<.001
Postoperative hospital stays (days)	13.85 ± 5.24	10.94 ± 3.14	.002
Postoperative infection (%)	10 (21.3%)	18 (19.1%)	.765
Hyperbilirubinemia** (POD1-7, %)	24 (51.1%)	27 (28.7%)	.009
Hyperbilirubinemia (POD7-14, %)	17 (36.2%)	13 (13.8%)	.002
Vascular complication (%)	3 (6.4%)	3 (3.2%)	.658
Biliary complication (%)	9 (19.1%)	16 (17%)	.755
Intra-abdominal bleeding (%)	8 (17%)	6 (6.4%)	.091
Acute rejection (%)	8 (17%)	14 (14.9%)	.743
AKI*** (%)	9 (19.1%)	8 (8.5%)	.067
EAD (%)	3 (6.4%)	5 (5.3%)	.898
PNF (%)	1 (2.1%)	2 (2.1%)	.536
Clavien–Dindo ≥ Grade 3 (%)	12 (25.5%)	11 (11.7%)	.036
30-d patient mortality	7 (14.9%)	4 (4.3%)	.059
45-day patient mortality	8 (17%)	6 (6.4%)	.091
1-yr patient survival	80.8%	88.2%	.197
5-yr patient survival	80.8%	81.6%	.465
1-yr graft survival	78.6%	88.2%	.117
5-yr graft survival	78.6%	77.1%	.328

GRWR = graft recepient weight ratio, EAD = early allograft dysfunction, PNF = primary nonfunction.
* Partial warm ischemia time: the time period from the organ's blood supply stops to its surface temperature drops to 4°C
** Postoperative hyperbilirubinemia is defined as total bilirubin value greater than 82.6 μmol/L according to the peak value in the first week after donation.
*** AKI = acute renal injury, defined as a consistent decrease in the absolute serum creatinine to less than 133 μmol/L, confirmed on 2 separate blood investigations at least 72 hours apart.

group received the split graft and those in the WGLT group received the whole graft, statistically significant differences were observed between the SLT and WGLT groups (1.21 ± 0.24 vs 2.01 ± 0.73, $P < .001$) regarding the graft–recipient weight ratio (GRWR). In addition, recipients in the SLT group showed higher intraoperative blood loss (1129.79 ± 764.62 vs 732.45 ± 546.87 mL, $P = .002$) and longer surgery time (9.38 ± 1.88 vs. 7.49 ± 0.58 hours, $P < .001$) than those in the WGLT group. Of the 141 recipients included in the case-control study, there were 27 and 58 Hepatocellular carcinoma (HCC) recipients in the SLT group and WGLT group, respectively. Of these HCC recipients, 21 met the Milan criteria[12] in the SLT group and 39 met the Milan criteria in the WGLT group [21 (44.7%) vs 39 (41.5%), $P = .118$]. The 1-year survival rate of HCC recipients in the SLT group compared to those in the WGLT group was 85.0% vs 86.0%, $P = .878$; 5-year survival rate was 85.0% vs 74.5%, $P = .614$; 1-year tumor-free survival rate was 85.0% vs 84.2%, $P = .968$; and 5-year tumor-free survival rate was 74.4% vs 68.1%, $P = .591$.

3.2. Postoperative course and survival between SLT and WGLT

None of the liver recipients died during surgery. In the postoperative recovery stage, recipients in the SLT group showed a higher rate of Clavien-Dindo grade III-V complications (25.5% vs 11.7%, $P = .036$), higher incidence of postoperative hyperbilirubinemia (POD1–7 51.1% vs. 28.7%, $P = .009$; POD7-14 36.2% vs 13.8%, $P = .002$), and longer length of hospital stay (13.85 ± 5.24 vs 10.94 ± 3.14 days, $P = .002$) than those in the WGLT group. The incidence of AKI and intra-abdominal bleeding was higher in recipients in the SLT group than those in the WGLT group, although no significant difference was observed ($P < .1$). In terms of graft survival, no significant differences were observed between recipients in the SLT and WGLT groups with regards to the incidence of early allograft dysfunction and primary nonfunction. Regarding survival rate, the 30-day and 45-day mortality rates of recipients in the SLT group were higher than those in the WGLT group (14.9% vs. 4.3%, $P = .059$; 17% vs 6.4%, $P = .091$, respectively); however, no significant differences were observed in the 1-year and 5-year long-term survival rates (Fig. 1A).

3.3. Surgical characteristics, postoperative course, and survival of $SLT^{MHV(+)}$ and $SLT^{MHV[-]}$

The subgroups of SLT were analyzed according to MHV. Adult SLT [extended right lobe (n = 17), full left split (n = 10), and full right split grafts (n = 20)] were classified into 2 subgroups: $SLT^{MHV(+)}$ (n = 27) and $SLT^{MHV[-]}$ (n = 20) based on the inclusion of the middle hepatic vein (MHV). No significant difference was observed in baseline demographic characteristics, disease features, and perioperative course between recipients in the $SLT^{MHV(+)}$ and $SLT^{MHV[-]}$ subgroups [Supplemental Digital Content (table S2, http://links.lww.com/MD/F405)]. The recovery of TB in recipients in the $SLT^{MHV[-]}$ group was significantly slower than that of recipients in the $SLT^{MHV(+)}$ group within POD3. However, the levels of aspartate aminotransferase and alanine aminotransferase were similar between the $SLT^{MHV[-]}$ and $SLT^{MHV(+)}$ groups (Fig. 2). In addition, no significant difference was observed between the $SLT^{MHV[-]}$ and $SLT^{MHV(+)}$ groups in terms of graft and overall survival (Fig. 1B). Furthermore, we made a detailed classification and comparison of complications between groups (Table 3). However, no significant difference in Clavien-Dindo grade III-V complications was observed between the groups (25.9% vs 25.0%, $P = .943$).

3.4. Univariate and multivariate analyses for 45-day postoperative SLT mortality

A high incidence of postoperative bilirubinemia was observed in recipients in the SLT group; therefore, univariate and multivariate analyses were performed for postoperative bilirubinemia. The results of the univariate analysis are shown in [Supplemental Digital Content (table S1, http://links.lww.com/MD/F404)]. Multivariate analysis revealed that only hyperbilirubinemia (POD7-14), surgery time ≥10 hours, and intraoperative blood loss ≥2000 mL were independently related to 45-day postoperative SLT mortality (Table 4).

4. Discussion

Recipients in the SLT group showed slow postoperative recovery and a high incidence of serious complications independent of MHV inclusion in the split graft. However, once recipients passed the period of high incidence of postoperative complications and successfully recovered, long-term survival outcomes were not significantly different from those of recipients in the WGLT group. SLT with MHV can reduce hyperbilirubinemia in the early postoperative stage; however, we did not observe that SLT with MHV significantly reduces complications, accelerates discharge time, or increases survival rates of grafts or recipients.

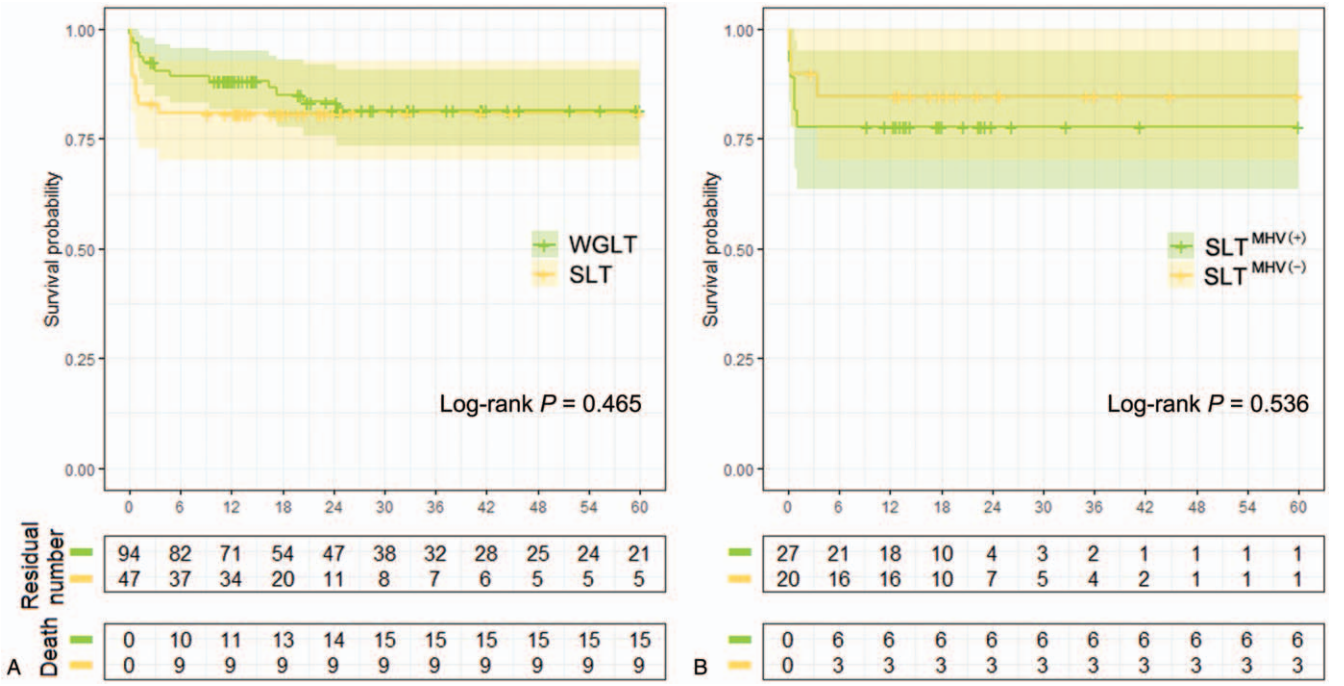

Figure 1. Five-year graft survival rates.

Reducing bleeding and surgery time by improving surgery skills may reduce short-term postoperative mortality in SLT. In addition, hyperbilirubinemia within POD 7-14 differed from hyperbilirubinemia within POD7 and can predict short-term mortality in SLT. In our study, SLT refers to the surgery using a split liver on a transplant recipient, rather than SLT is for 1 donor, 2 recipients.

4.1. Adult SLT is safe and effective based on long-term survival rates

SLT is different from WGLT, and the most important technical problem is the method of splitting. Inadequate graft volume might cause small-for-size syndrome, which mainly manifests as blood from the portal vein flowing into the small liver as a shunt

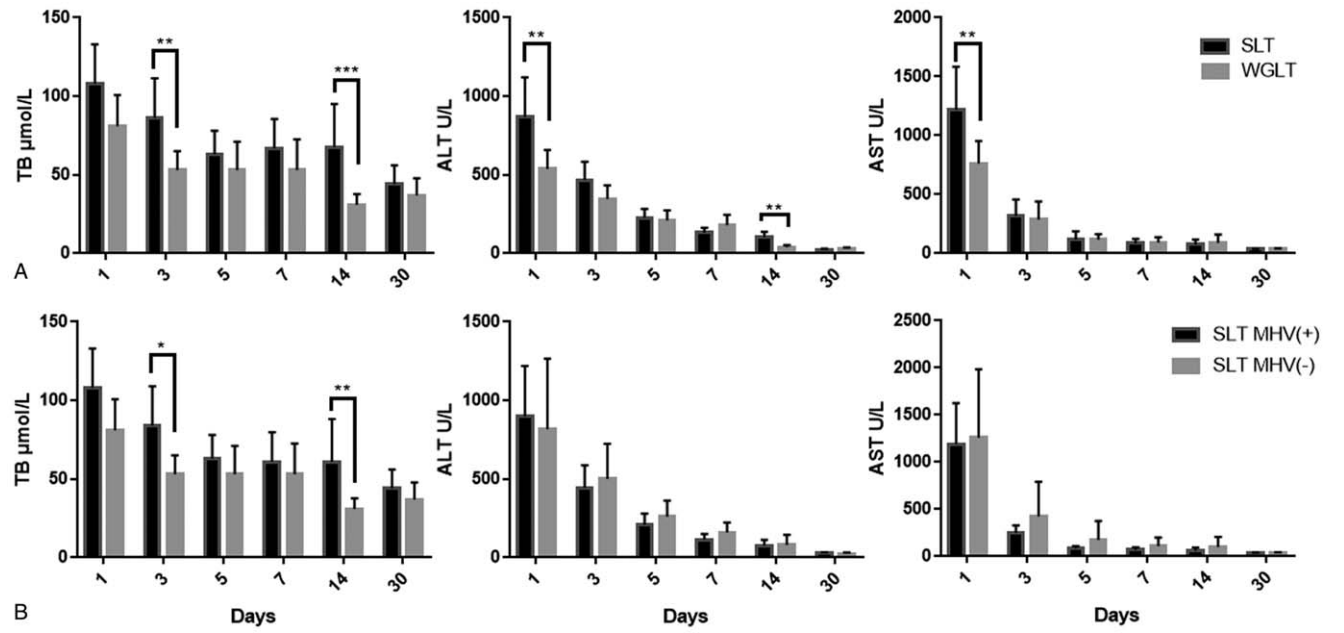

Figure 2. Comparison of TB, AST and ALT levels after surgery. (A) SLT and WGLT; (B) $SLT^{MHV(+)}$ and $SLT^{MHV\ [-]}$. AST = aspartate aminotransferase.

Table 3

Classification of postoperative complications.

Grades	Complications*	$SLT^{MHV\ (+)}$ (n = 27)	$SLT^{MHV\ [-]}$ (n = 20)
1	Transient bile leak treated/ Slight stenosis	4	5
	Mild pleural effusion	3	1
	Atelectasis	2	1
	Intra-abdominal bleeding	5	3
2	Bleeding requires blood transfusion	3	2
	Pneumonia managed with antibiotics	2	1
	Fever (>38 °C) managed with antibiotics	5	3
	Wound infection	1	1
	Hepatic artery embolism	1	2
3a	Bile leakage/strictures	2	1
	Pleural effusion	0	0
3b	Intra-abdominal bleeding	1	1
	Portal vein thrombosis	0	0
	Hepatic artery embolism	1	1
4a	Single organ dysfunction	1	2
4b	Multiple organ dysfunction	2	0
5	PNF	0	1
	Hepatic artery embolism	1	0
	Abdominal hemorrhage	1	0
	Multiple organ failure	2	0

PNF = primary nonfunction.

* Each patient may have more than 1 complication, and the low level of complication includes the high level with regard to the same complication.

and causing rapid swelling of the liver.[13] Considering inevitable preservation injuries, prolonged ischemia time, and reperfusion injuries, most transplant centers believe that a graft volume with ≥ 1% GRWR is necessary for SLT recipients.[14] S4 splitting is the main split method: extended right lobe (containing the MHV)/left lateral lobe split and full-left (containing the MHV)/full-right split. The average weights of adult Asian males and females are 66.2 kg and 57.3 kg, respectively. With the aforementioned methods of splitting, the GRWR for adult recipients is usually guaranteed to be >1.0. The full-left/full-right splitting mode may result in the congestion of residual S4 and a decrease in the effective liver volume. However, using the in-situ perfusion technique, the warm ischemia time during SLT was significantly shortened. In addition, using the in-situ splitting technique processes the cross-section of the liver without blocking the blood flow of the donor liver; thus, the bile duct and vascular tissue can be better recognized, thereby reducing the occurrence of hemorrhage and bile fistula. Concurrently, cold ischemia time was equally significantly reduced. The decrease in ischemia time can reduce the degree of liver injury and consequently reduce the effect of liver parenchyma loss caused by SLT. To some extent, it is equivalent to expanding the GRWR. Presently, in contrast to the fixed 5-year long-term survival rate (about 80%)

Table 4

Independent variables in the multivariate analysis for 45-day postoperative mortality in SLT recipient.

Variables	Logistic regression		
	B	*P*	95%CI
Hyperbilirubinemia (POD7-14)	3.019	.022	1.537 to 272.396
Operation time ≥10 h	3.206	.029	1.391 to 437.691
Intraoperative blood loss ≥ 2000 mL	3.165	.016	1.799 to 312.194

CI = confidence interval, POD = postoperative day.

of WLT,[15,16] the long-term survival rate of different SLT central receptors shows significant differences (63% - 90.8%).[17–20] The 5-year survival rate of SLT in our center was 80.8%. Furthermore, no significant difference was observed between WLT and SLT, a finding consistent with most central research results.[21] Based on the incidence of small liver syndrome, graft function, and graft survival rate, the data from our center reveals that in-situ S4 segment splitting and in-situ rapid organ acquisition are feasible.

4.2. Slow recovery and high incidence of serious complications concentrated within 45-day after surgery in SLT

Even if the long-term survival rate of recipients with SLT is acceptable with continuous technical improvement, it was observed that recipients who underwent SLT had a higher risk of intraoperative bleeding, longer postoperative hospital duration, and more grade III-V complications than those who underwent WGLT. The results of multicenter studies show that unlike WGLT, SLT is usually accompanied by resection of the bile ducts and blood vessels, which increases the incidence of postoperative bile leakage and bleeding.[22,23] In addition, bile leakage and bleeding may similarly respond to the bare cut surface and SLT-specific S4 vascular deprivation, which increase the risk of parenchymal necrosis of S4. Based on our experience, as long as the surgery is carefully performed and ligation is performed in a stepwise manner, bile leakage and bleeding after surgery are often transient. By prolonging the indwelling time of an abdominal drainage tube, recipients with S4-related complications can completely recover. However, arterial and venous embolisms are different from transient biliary leakage and often require resurgery. In this study, vascular complications, abdominal hemorrhage, and renal failure were the major causes of grade III-V complications and high 45-day mortality among recipients in the SLT group. Presently, there is no consensus on whether there is a difference in the short-term survival rate between SLT and WGLT.[21,22,24] Based on the survival curve, the data showed that WGLT and SLT showed the maximum difference in survival rate 30-45 days after surgery; however, the difference was not significant 6 months after the operation. Previous studies revealed that it usually takes at least 6 months for the donor liver to grow to 80% of the total liver volume.[25–30] In these 6 months, there may be a close balance between residual liver function after SLT and recipient requirements. Breaking this balance will significantly affect recipient prognosis. Specifically, during this time, because it takes a while for the split liver to recover its primary function, relatively weak liver function will be accompanied by coagulation disorder, further increasing the risk of bleeding. Massive hemorrhage and massive blood transfusion will subsequently aggravate the impairment in renal function. Therefore, improving the surgical techniques of transplantation and anastomosis, early detection of complications, timely treatment, and helping recipients survive past the first 6 months after surgery are important to improve the survival rate in SLT.

4.3. Hyperbilirubinemia within POD 7-14 is an independent risk factor for 45-day mortality

Currently, most predictors of short-term mortality are from WGLT or all kinds of LT;[31–37] however, the selection of SLT as an independent object of observation is extremely rare.[2,38,39]

The risk factors for 45-day mortality were analyzed. Bleeding, surgery time, and hyperbilirubinemia within POD 7-14 were independent risk factors for high mortality. These factors are different from those reported by other LT centers with regard to short-term postoperative mortality. The explanation is that not only were SLT recipients selected as research participants, but the donor selection process was also considered. At present, there is no full legislation on SLT in China. The appropriateness of splitting a donor liver depends on the transplant hospital. Therefore, both donors and recipients are usually strictly chosen by doctors. For example, recipients with a high MELD score will not be selected as SLT recipients. Furthermore, a donor liver with abnormal pathological changes or potential diseases, such as high liver steatosis and viral hepatitis, will not be employed. Strict implementation of in-situ perfusion and in-situ split significantly reduces ischemia time. Therefore, most preoperative and intraoperative risk factors were not significant because they were avoided.

4.4. Hyperbilirubinemia and SLT reserved MHV

Complications and mortality were the focus of previous SLT studies, while few studies have considered liver function, such as non-obstructive hyperbilirubinemia, a postoperative complication that can lead to severe consequences and even death.[40] Abnormal liver function, such as hyperbilirubinemia, can lead to subsequent complications including postoperative biliary tract complications and acute rejection. Similarly, even vascular complications and bleeding can increase bilirubin levels. Eventually, the length of stay will increase and medical expenses will equally increase. Compared with WGLT, SLT usually has a higher bilirubin level within 7 days owing to liver resection; however, the level is not always high. The data show that this increase can often be reduced to the same level as WGLT on the 5th day after surgery, and this transient increase after surgery has no significant impact on short-term mortality. However, it was observed that the bilirubin levels of some recipients remained high 7 days after SLT or gradually increased after early decline. The risk of short-term postoperative death in SLT recipients will be significantly increased. The TB level of liver transplant recipients without MHV was higher and the retention of MHV could accelerate recipient recovery.[41] In subgroup analysis, $SLT^{MHV\ [-]}$ showed a higher level of TB on POD3 than $SLT^{MHV\ (+)}$. However, no difference was observed in subsequent periods. No significant differences were observed in the hospital stay duration, grade III complications, and overall survival rate. In addition, there was no significant difference in the incidence of primary nonfunction and early allograft dysfunction. Consequently, although the split with the MHV might be helpful to relieve early hyperbilirubinemia, whenever the MVH was included, SLT recovery was slow after surgery. Thus, bleeding and surgery time are closely related to surgery techniques; this means that short-term postoperative SLT mortality may be reduced by improving surgical skills. Besides, for SLT recipients with hyperbilirubinemia within POD 7-14, prolonging the length of stay, early detection and treatment of related complications may reduce short-term mortality.

4.5. Limitations

Although we adopted propensity score matching and controlled for possible bias due to the various LT surgeries, the retrospective nature of the study should be acknowledged as a study limitation. In addition, data from a single center was used, which further limited the scope of the study. Therefore, multicenter studies must be conducted to verify the generalizability of the results to populations from other centers. Furthermore, the small sample size should be acknowledged as a limitation because only 47 recipients were undergoing SLT. Further studies with larger sample sizes are warranted to confirm our findings so that appropriate clinical decision making can be achieved.

5. Conclusions

Adult SLT is safe and effective based on long-term survival rates. However, the incidence of complications in SLT recipients is high and recovery is slow. The key to improving the survival rate of recipients with SLT is to help them safely pass through the high-incidence period of postoperative complications. Non-obstructive hyperbilirubinemia within POD 7-14 is an independent predictor of short-term mortality during SLT, and increased bilirubin within POD 7-14 may prolong hospital stay, lead to subsequence complications, and increase medical expenses.

Author contribution

LK and JY2 designed the study; LJ, JY1, TL, LK performed the research and collected the data; LK analyzed and interpreted the data; LK wrote the first draft of the manuscript; All authors edited the manuscript and approved the final draft; The acquisition of funding is from J Y2.

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Formal analysis: Lingxiang Kong, jiayin yang.
Funding acquisition: jiayin yang.
Investigation: Lingxiang Kong, Tao Lv, Jian Yang, Li Jiang, jiayin yang.
Methodology: Lingxiang Kong, Tao Lv, Jian Yang, Li Jiang, jiayin yang.
Project administration: Lingxiang Kong, Li Jiang.
Resources: Lingxiang Kong, Tao Lv, Jian Yang, Li Jiang.
Software: Lingxiang Kong.
Supervision: Lingxiang Kong, Tao Lv, Jian Yang, jiayin yang.
Validation: Lingxiang Kong, Tao Lv, Jian Yang, Li Jiang, jiayin yang.
Visualization: Lingxiang Kong, Tao Lv, Jian Yang, Li Jiang, jiayin yang.
Writing – original draft: Lingxiang Kong, jiayin yang.
Writing – review & editing: Lingxiang Kong, Tao Lv, Jian Yang, Li Jiang, jiayin yang.

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