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ORIGINAL ARTICLE

Splenic devascularization can replace splenectomy during adult living donor liver transplantation – a historical cohort study

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SUMMARY

Simultaneous splenectomy (SSPX) in adult living donor liver transplantation (ALDLT) has definitely beneficial roles such as portal flow modulation in small-for-size graft and correction of hypersplenism-related pancytopenia, and so on, but disastrous complications after SSPX often occur. For the first time, we devised unique and innovative splenic devascularization (SDV) procedure to alleviated untoward effects of SSPX but to maintain its benefits for the indicated patients. From April 2013 to December 2014, 520 recipients underwent ALDLT, and the SSPX and SDV were simultaneously performed in 62 (11.9%) and 61 (11.7%) patients, respectively. The most common indication was hypersplenism-related pancytopenia (n = 101), small-for-size graft (n = 14), hepatitis C virus (HCV) (n = 7), and splenic artery aneurysm (n = 1). Postoperative small-for-size graft syndrome (SFSS) was absent in both SSPX and SDV, and preoperative pancytopenia was improved in both groups since postoperative 1 week, although SSPX was more substantial than SDV. Preoperative splenic volume (706.2 ± 282.9 ml) after SDV significantly decreased to 425.5 ± 204.4 ml on 1 month, respectively. In contrast to SDV, SSPX resulted in longer operation time and higher incidence of postoperative complications including mortality. In conclusion, SDV can replace SSPX during ALDLT without hampering its beneficial roles seriously, but get rid of splenectomy-related lethal complication.

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Key words
adult, living donor liver transplantation, splenectomy, splenic devascularization

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Introduction

The presence of liver cirrhosis and subsequent portal hypertension in the recipients results in splenomegaly, which may lead to adverse effects such as pancytopenia and large portosystemic collaterals [1]. Deceased donor liver transplantation (DDLT) using whole liver graft can promptly resolves portal hypertension, and splenomegaly rarely cause a problem. Living donor liver transplantation (LDLT) with partial liver graft, however, often requires simultaneous splenectomy (SSPX) to correct severe cytopenia in early post-LDLT period [2] and to protect small-for-size graft from portal hyperperfusion injury [3].

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In Western countries, SSPX in DDLT is mostly contraindicated based on historical reports of post-SPX sepsis and other complications [4–7]. In adult-to-adult living donor liver transplantation (ALDLT), however, SSPX is definitely attractive and beneficial intraoperative procedure when indicated. We had also performed SSPX infrequently since November 2008. The preliminary outcomes of SSPX seemed to be satisfactory, and we routinely adopted SSPX since April 2013. Both beneficial and harmful effects were observed during that period. The chance of adverse events was not low and some of them such as hemorrhage from splenectomy bed, pancreatic fistula and/or abscess, portal venous thrombosis, and septic complications were so disastrous that might overshadow the benefits of SSPX.

As a result, we abandoned SSPX from August 2013 and alternatively adopted a unique and innovative procedure so-called "splenic devascularization (SDV)," which was developed at our institution for the first time in the world. In view of beneficial and harmful effects of SSPX, this study to evaluate roles of the innovative SDV in ALDLT by reviewing our ALDLT series during the study period.

Materials and methods

We retrospectively analyzed our prospective database for the ALDLTs undergone SSPX or SDV on chronic liver disease patients at our institution from April 2013 to December 2014, and compared SDV with SSPX using a historical cohort. All patients were followed up regularly by the same team of surgeons. No patients were lost to follow-up. The last census date for this study was December 30, 2016. This study was approved by the Institutional Review Board of our institution. All living donors were voluntary and altruistic.

Patients

During the study period, total 520 ALDLTs were performed at our institution. Of these, 123 adult recipients required SSPX in 62 patients and SDV in 61 patients during ALDLT according to the same indications. Fifteen patients who underwent splenic artery ligation only were excluded because the splenic artery ligation only did not correspond to the purpose of this study. In view of beneficial and harmful effects of SSPX, we reviewed the patients who underwent simultaneous SD or SSPX to focus on the clinical outcomes. Patient characteristics, intraoperative parameters, and postoperative outcomes were compared between the two groups.

Indication for SSPX and SDV

During the study period, the indications for SSPX and SDV in ALDLT at our institution were same and as follows: first, to improve the cytopenia early after ALDLT for patients with a low platelet count ($<30 \times 10^3/mm^3$) or a low leukocyte count ($<1.5 \times 10^3/mm^3$), and to decrease the incidence of postoperative hemorrhagic or infectious complications, respectively; second, to reduce excessive shear-stress injury to the implanted partial liver graft by decreasing portal hyperperfusion for patients with moderate-to-severe portal hypertension who received small-size-graft (graft to recipient weight ratio (GRWR) <0.8–1.0%); third, to improve the tolerance and adherence to pegylated interferon (IFN) and ribavirin therapy for HCV by preventing postoperative thrombocytopenia; and finally, for concomitant splenic arterial aneurysm. Currently, usage of IFN-free direct antiviral therapy for HCV eradication, which has been proved to be safe and effective,[8] eliminated the need for SSPX because of HCV. We did not perform SSPX for ABO-incompatible recipient during study period because introduction of rituximab alleviated the requirement for SSPX.

Surgical procedure of SSPX and SDV

On SSPX, basically we performed two times manual ties at the remaining sites and then division of vascular structures with scissors initially by two surgeons. In early period, we did not used vessel sealing system or endostapling devices followed by reinforcing sutures, but infrequent severe complications after SSPX could not be avoidable. Then, as a trial to avoid post-SSPX complications, we had adopted following various methods by four competent surgeons; manual division after individual dissection of splenic arteries and veins, or after encircling of intra-splenic pedicles without individual dissection of splenic vessels, or even vessel sealing system and endo-stapling division with reinforcing sutures. However, there was no secure method to get rid of the post-SSPX complications.

In August 2013, we initiated SDV during LDLT to decrease the splenic venous outflow effectively by maximal reduction in arterial supplies to the spleen and also to augment the area of aseptic splenic infarction, and subsequently to reduce the untoward effects of SSPX such as bleeding from the splenectomy bed, pancreatic injury-related fistula and/or abscess, splenic vein to portal vein thrombosis. SDV is an aggressive form of splenic artery ligation with more profound reduction in

Transplant International 2019; 32: 535–545

hypersplenism effects. We perform not only ligation of splenic artery but also ligation of right gastroepiploic artery and division of gastrosplenic ligament including short gastric arteries (Fig. 1). As a result, remnant arterial supply to the spleen is maintained only by intrapancreatic collaterals from the superior mesenteric artery (Fig. 2). Considering its characteristics of SDV procedure, SSPX inherently must be superior option in view of its beneficial effects in ALDLT. However, we have performed SDV not only to achieve the comparable benefits but also to reduce the harmful effects of SSPX.

Perioperative management

We did not routinely perform the vaccination against pneumococci and any other encapsulated bacteria, either during pretransplant period or during post-transplant follow-up. For the recipients having large portosystemic shunt, possible route of postoperative portal flow steal, we performed surgical interruption and additionally secured by intraoperative cine-portogram [9]. Multi-detector computed tomography was performed every week during postoperative in-hospital stay, and postoperative 1, 3, 6 months. To prevent thrombosis in the recipients, we have routinely used antiplatelet agents including aspirin from postoperative day (POD) 8 if there was no evidence of postoperative hemorrhage. In the recipients who underwent SSPX, anticoagulation using warfarin was added to maintain prothrombin time and international normalized ratio (PT(INR)) 1.5–2.0 after recovery of graft function, but the anticoagulation was not administered for recipients undergone SDV.

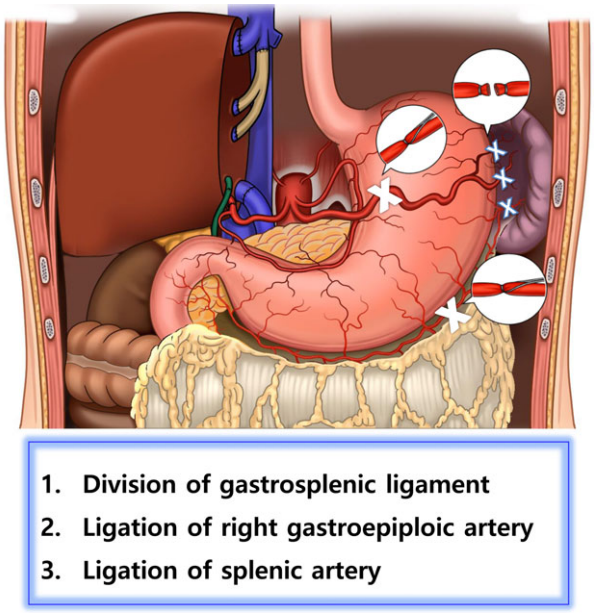


Figure 1 Splenic devascularization is depicted as a following schema. We should divide gastrosplenic ligament and ligate right gastroepiploic artery and splenic artery. Intrapnacreatic collateral from superior mesenteric artery is the only remnant arterial supply to the spleen.

Assessment of clinical outcomes

Postoperative liver function was assessed by postoperative total bilirubin, prothrombin time, ascites amount on POD 7, and also assessed by the time of abdominal drain removal and of total bilirubin decrease under 2 mg/dl. We applied the definition of small-for-size syndrome in accordance with previous reports [10] but modified the time point from POD 14 to 7 because of the absence of small-for-size syndrome (SFSS) in our series on POD 14. Briefly, it was defined as having both prolonged cholestasis (total bilirubin > 10 mg/dl) and refractory ascites (daily amount of ascites > 1 l) at POD 7.

Postoperative complication was defined as Clavien-Dindo classification grade ≥ III requiring surgical, endoscopic or radiological intervention including complications-directly related to the treatment and others [11]. The splenic and portal vein thrombosis is specific complication after SSPX and SDV, and was separately classified to clarify the pros and cons between SSPX and

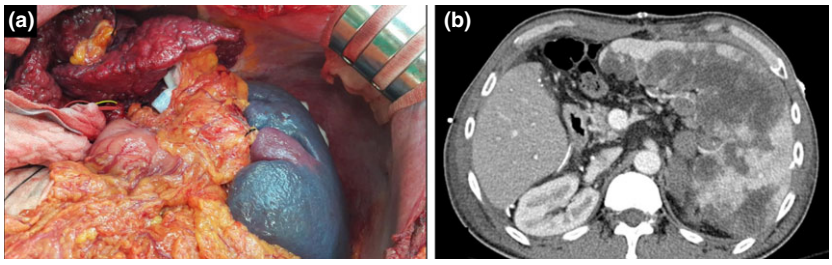


Figure 2 Effective case of splenic devascularization showed darkly discolored and shrunken spleen intraoperatively (a) and massive perfusion defect of the spleen on CT of postoperative day 7 (b).

SDV. Duration of hospital stay and in-hospital mortality was compared between them.

On the basis of CT scan in the recipients, we measured volume of preoperative liver and spleen in both SSPX and SDV group, also splenic volume in the SDV group at POD 7 and postoperative 1, 3, and 6 months.

Statistically analyses

During the study period, all demographic data and radiologic and laboratory data were entered into a computerized database and retrospectively reviewed. Statistical analysis was performed using the IBM SPSS Statistics program (IBM Corp, New York, NY, USA). All values are expressed as the means ± the standard deviation. Categorical and continuous data were compared between groups using the chi-square test, Fisher's exact test, Student's *t*-test. A *P* value of <0.005 was considered statistically significant.

Results

Patient characteristics

Follow-up period of the population was 28.8 ± 7.7 months (range, 1–36.7 months). Preoperative Model for End-Stage Liver Disease (MELD) score was 14.4 ± 7.5 points (range, 6–46 points) and the platelet count was 58.8 ± 33.8, $\times 10^3/mm^3$. As for primary reason of SSPX or SDV in the recipients, splenomegaly and related cytopenia was the most common (n = 101, 82.1%), and followed by low GRWR (n = 14, 11.4%), HCV cirrhosis (n = 7, 5.7%), and splenic artery aneurysm (n = 1, 0.8%).

Between SSPX and SDV groups, there were no significant differences among the variables. Only the operative time, however, showed significant difference between SSPX (845.7 ± 137.8 min) and SDV (794.8 ± 118.9 min) (P = 0.03) (Table 1).

Table 1. Patients characteristics.

Variables	Total	Splenectomy (N = 62)	Splenic devascularization (N = 61)	*P*-value
Sex, male/female	92/31	48/14	44/17	0.54
Age, year	52.6 ± 8.6	51.3 ± 8.7	53.7 ± 8.4	0.16
Primary disease				
hepatitis B virus	85 (69.1)	41 (66.1)	44 (72.1)	0.40
Alcoholic	16 (13.0)	11 (17.7)	5 (8.2)	
Hepatitis C virus (HCV)	10 (8.1)	6 (9.7)	4 (6.6)	
Others*	12 (9.8)	4 (6.5)	8 (13.1)	
Model for End-Stage Liver Disease score	14.4 ± 7.5	15.0 ± 8.3	13.9 ± 6.7	0.43
PreOP components of blood cell, $\times 10^3/mm^3$				
Hemoglobin	10.7 ± 2.1	10.9 ± 2.2	10.6 ± 2.1	0.43
Platelet	58.8 ± 33.8	62.2 ± 41.2	55.3 ± 23.9	0.26
WBC	3.3 ± 2.2	3.4 ± 2.4	3.1 ± 1.9	0.42
Treatment reasons				
Splenomegaly	101 (82.1)	49 (79.0)	52 (85.2)	0.09
Low graft to recipient weight ratio (GRWR)	14 (11.4)	8 (12.9)	6 (9.8%)	
HCV	6 (4.9)	4 (6.5)	3 (4.9)	
SA aneurysm	1 (0.8)	1 (1.6)	–	
Graft type, right/left/dual	110/5/8	56/2/4	54/3/4	0.83
Graft volume, gm	741.7 ± 151.8	732.8 ± 153.6	750.8 ± 150.8	0.51
GRWR%	1.12 ± 0.22	1.10 ± 0.03	1.15 ± 0.22	0.24
Treatment time				
Prehilar dissection	31 (25.2)	16 (25.8)	15 (24.6)	0.89
Posthilar dissection	92 (74.8)	46 (74.2)	46 (75.4)	
Operation time, min		845.7 ± 137.8	794.8 ± 118.9	0.03
IntraOP red blood cell, units	8.3 ± 10.7	8.3 ± 10.0	8.2 ± 11.5	0.96

*Including cryptogenic, autoimmune hepatitis, Wilson's disease, secondary biliary cirrhosis, and primary biliary cirrhosis.

Transplant International 2019; 32: 535–545

Changes in splenic volume after SDV

Preoperative liver volume was 1023.2 ± 283.3 ml (range, 503–1580 ml) and the splenic volume was 709 ± 280.2 ml (range, 215–1253 ml). There was no difference in the preoperative splenic volume between SSPX and SDV group, and their volume were 712.3 ± 279.3 ml (range, 243–1253 ml) and 706.2 ± 282.9 ml (range, 215–1230 ml), respectively. After SDV, the splenic volume was significantly decreased until 1 month after ALDLT; 509.6 ± 236.3 ml at POD 7 ($P < 0.001$) and 425.5 ± 204.4 ml on postoperative 1 month ($P = 0.002$) (Fig. 3).

Changes in components of blood cell (CBC)

Chronologic changes in CBC profiles between SSPX and SDV groups are shown in Fig. 4. The platelet count significantly increased in both group at POD 7, but it increased more rapidly in the SSPX group than SDV group during postoperative 1 month, leading to a significant difference in the platelet count between groups. The highest difference in the platelet count achieved by SSPX or SDV at 1 month after LDLT was maintained until 6 months. The platelet counts at postoperative 6 months were 296.4 ± 121.7 × 10^3/mm^3 in the SPX group and 127.9 ± 121.7 × 10^3/mm^3 in the SDV group ($P < 0.001$).

The leukocyte count significantly increased to the peak level in both group at POD7 after LDLT, but it was more remarkable in the SSPX group than SDV group and leading to a significant difference between groups until 6 months. The leukocyte counts at postoperative 6 months were 6.7 ± 3.4 × 10^3/mm^3 in the SSPX group and 3.7 ± 1.6 × 10^3/mm^3 in the SDV group ($P < 0.001$).

The hemoglobin level, however, significantly decreased in both group at POD 7 after LDLT and then increased significantly until 1 month in SSPX group ($P < 0.001$) and until 3 months in SDV group ($P < 0.001$), respectively. At the time of 6 months after LDLT, the hemoglobin level reached a plateau in both group.

Clinical outcomes

The prothrombin time (INR) on POD 7 prolonged more in SDV group (INR, 1.2 ± 0.2) than SPX group (INR, 1.1 ± 0.1) ($P < 0.001$). However, postoperative total bilirubin level and amount of ascites did not show any differences between SSPX and SDV group.

The SFSS occurred in two patients, and one patient in SSPX and one patient in SDV group, respectively.

The number of postoperative complication including Clavien-Dindo classification III, IV, and V ($n = 20$) was significantly higher in the SSPX group ($n = 15$) than in the SDV group ($n = 5$) ($P = 0.026$), and the procedure-related complications ($n = 8$) was also more common after SSPX than after SDV ($P = 0.032$). Among 12 procedure-unrelated complications, the most common complications was postoperative hemorrhage ($n = 10$). The incidence of postoperative thrombosis in the splanchnic venous system after ALDLT ($n = 16$) was significantly higher in the SSPX

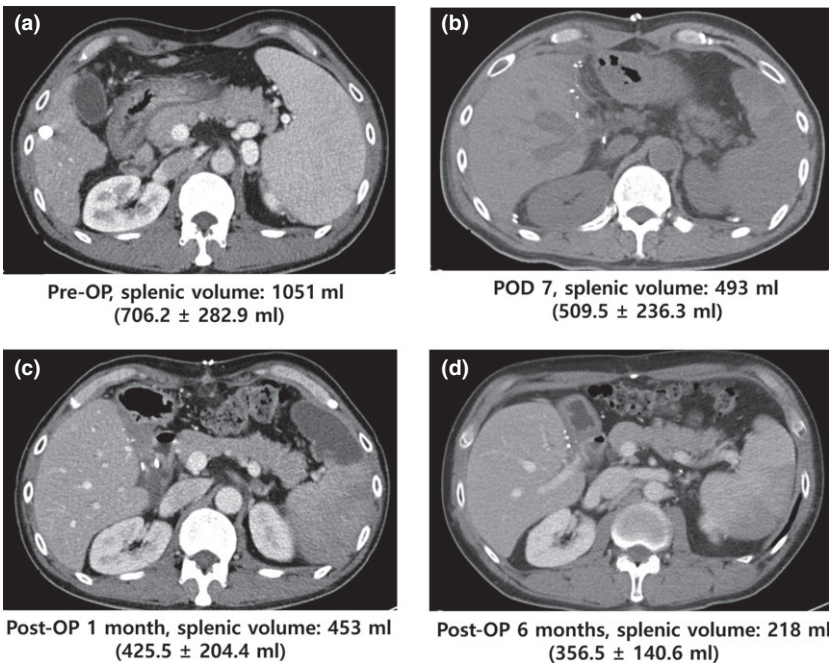
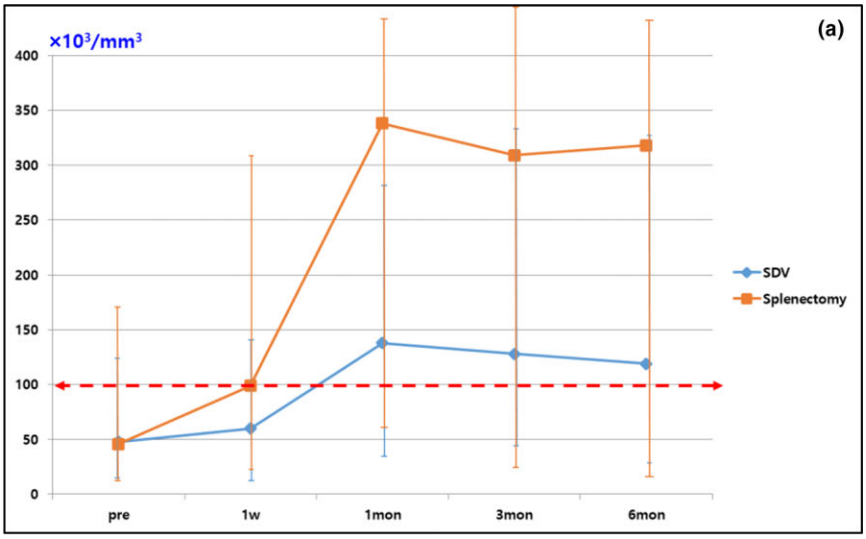
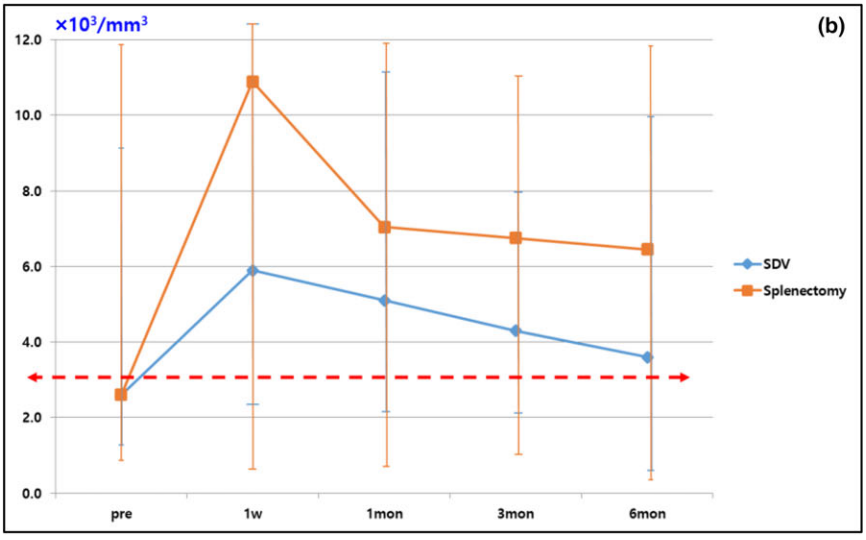


Figure 3 Chronologic changes of the splenic volume after splenic devascularization (SDV). Typical CT images on preoperative (a), postoperative day 7 (b), 1 month (c), and 6 months (d) revealed serial decline of splenic volume from 1051, 493, 453 to 218 ml in the recipient, and the its mean value and standard deviation in all SDV patients are given in brackets.





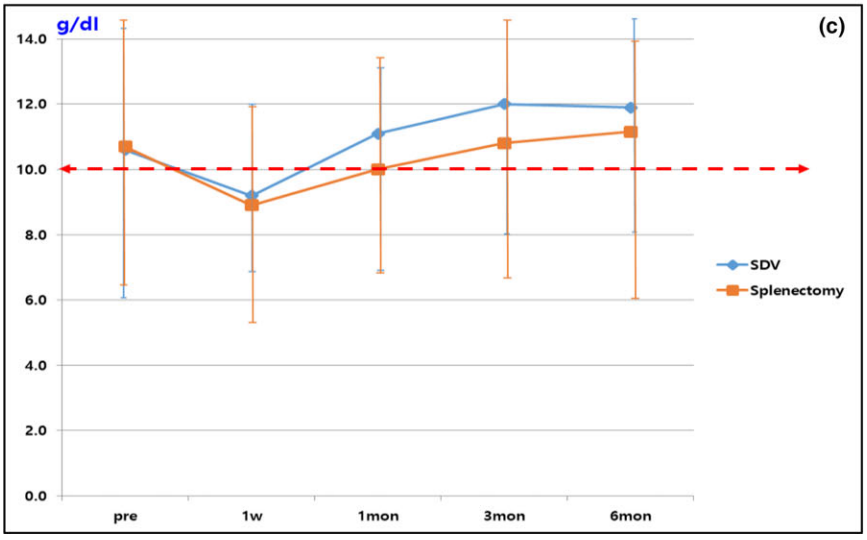


Figure 4 Chronologic changes in the (a) platelet count, (b) leukocyte count, (c) hemoglobin level, stratified by simultaneous splenectomy (SSPX) and splenic devascularization (SDV).

Transplant International 2019; 32: 535–545

group (n = 14) and in the SDV group (n = 2) (0.002), and all the patients were successfully treated with anticoagulation alone. When pancreatic fistula developed after SSPX, the pronloged hospital stay required. However, other complications after SSPX such as postoperative bleeding from surgical bed or thrombosis of splanchnic venous system did not lengthen the hospital stay significantly when compared to SDV. As a result, there was no statistically difference in hospital stay between SSPX and SDV group. In-hospital mortality occurred only in SSPX group but there was no significance between them (Table 2).

Although there was no statistical difference (P = 0.069), the 1- and 3-year overall survival rates were 88.7% and 82.5%, respectively, in SSPX group, and 98.4% and 95.1%, respectively, in SDV group.

Summary of the procedure-specific complications

The eight patients having procedure-related complications required aggressive managements postoperatively, and there were seven SSPX-related complications and only one SDV-related complication. SDV-related complication was simple hemorrhage from the splenic flexure and retrogastric wall and was controlled easily with laparotomy. However, SSPX-related complications were more serious hemorrhage and pancreatic fistula. As a result, only two patients were successfully managed with simple laparotomy, but the others required more than one additional managements including drainage, embolization, and even re-transplantation in Case number 4 having graft damage because of postoperative hemorrhage-related hypovolemic shock. Three patients led to lethal status because of SSPX-related complications, and one of them barely survived through the 315 in-hospital days (Table 3).

Discussion

SSPX during LT was known to increase mortality and morbidity rates because of the septic complications [4–7], but it is still attractive and beneficial intraoperative procedure in ALDLT, particularly, for the cirrhotic recipient with severe cytopenia related to hypersplenism and small-for-size graft. The Kyoto and Kyushu group in Japan have been advocated SSPX for recipients with portal pressure ≥15 mmHg after reperfusion to prevent small-for-size syndrome and also contributes to a rapid increase in the platelet count in LDLT recipient [3,12–14]. In addition, there were no significant differences between SSPX and non-SSPX group regarding the incidence of postoperative hemorrhage, post-transplant bacteremia, and infection-related mortality rates. On the other hand, Tokyo group in Japan did not recommend SSPX any more in LDLT because SSPX was an independent predictor for both postoperative hemorrhage and lethal infectious complication [15].

Based on infrequently performed preliminary experiences of SSPX at our institution, SSPX during ALDLT was a feasible procedure despite a little longer operation time, and the outcomes including beneficial effects and

Table 2. Postoperative outcome.

Variables	Total (N = 123)	Splenectomy (N = 62)	Splenic devascularization (N = 61)	P-value
T. Bil on postoperative day (POD) 7 (mg/dl)	3.4 ± 3.1	2.9 ± 2.5	3.8 ± 3.5	0.12
PT on POD 7 (INR)	1.15 ± 0.16	1.1 ± 0.1	1.2 ± 0.2	<0.001
Ascites on POD 7 (ml/day)	585.6 ± 365.3	546.0 ± 368.5	625.9 ± 360.5	0.23
SFSG syndrome*, number	2	1	1	1.00
Removal of Abd. drain, days	18.9 ± 8.2	18.8 ± 9.3	18.9 ± 6.9	0.91
Less than T.Bil 2 mg/dl, days	14.2 ± 22.1	11.8 ± 23.6	16.7 ± 20.5	0.20
PostOP complication, number†	20 (16.3)	15 (24.2)	5 (8.2)	0.026
Treatment-related complication., number	8 (6.5)	7 (11.3)	1 (1.6)	0.032
PostOP thrombosis‡	16 (13.0)	14 (22.6)	2 (3.3)	0.002
Hospital stay, days	31.5 ± 33.9	34.9 ± 43.1	28.1 ± 20.5	0.30
In-hospital mortality, number	2 (1.6)	2 (3.2)	–	0.50

*Small-for-size graft syndrome, Tbil 10 mg/dl and Ascites 1 l/day on the postOP day 7.

†Clavien-Dindo classification grade III, IV, V. Treatment-unrelated complications are mostly bleeding-related complication except two cases including evisceration, jejunal perforation.

‡Distal SVT (n = 13), intrahepatic PV branch (n = 2), MPV partial thrombus (n = 1), Operation (n = 0).

Table 3. Procedure-specific complications.

No.	Model for End-Stage Liver Disease	Treatment	Complication	Postoperative day	Site	Management	Outcome
1	11	Simultaneous splenectomy (SSPX)	Bleeding	D1	Splenectomy bed	Laparotomy	Alive
2	26	SSPX	Pancreatic fistula	D1	Pancreas tail	Pigtail drain	Dead (related sepsis)
			Aneurysm rupture	D43	Hepatic artery	Laparotomy & HA ligation	
3	19	SSPX	Bleeding	D2	Pancreas tail	Laparotomy	Alive
4	32	SSPX	Bleeding	D1	Splenic artery	Laparotomy	Dead (related sepsis)
			Graft failure	D3 D16	Short gastric artery	Re-laparotomy Re-LT using split DDLT	
5	9	SSPX	Pancreatic fistula	D1	Pancreas tail	Pigtail drain	Alive
			Bleeding	D44	Splenic artery	SPA embolization	
6	19	SSPX	Bleeding	D9	Hilum, Pancreas tail	Laparotomy	Alive (Near mortality, 315 Hosp. day)
			Pancreatic fistula	D10	Pancreas tail	Keep drainage	
			Bleeding	D26, 27	Pancreas tail	Re-lapa. → SPA embol.	
			Bleeding	D33, 34	Duodenum	GDA → RGEpi. A embol.	
7	16	SSPX	Bleeding	D7	Splenic artery	SPA embolization	Alive
			Pancreatic pseudocyst	D68	Splenectomy bed	Endoscop. internal drain	
8	19	Splenic devascularization	Bleeding	D7	Splenic flexure & retrogastric wall	Laparotomy	Alive

complications seemed to be similar to the reports of the Kyoto and Kyushu groups. Since we performed SSPX in ALDLT as a routine procedure when indicated, we had often encountered adverse events including hemorrhage from splenectomy bed, pancreatic fistula and/or abscess, portal venous thrombosis, and septic complications. Some of the complications after SSPX were too disastrous to apply strictly to the indicated recipients, which was corresponding to the results of Tokyo group based on the largest series of LDLTs with SSPX over a long observation period[15]. In ALDLT, however, considering the benefit of SSPX to the indicated recipient, we could not abandon the management strategy for small-for-size graft and splenomegaly-related cytopenia. Hence, for the first time in the world we devised SDV to avoid occasional occurrence of lethal complication after SSPX since August 2013, and have performed SDV to the indicated recipients during ALDLT as an alternative management of SSPX.

So far as known, ligation or embolization of splenic artery in the cirrhotic recipient could be an alternative management of SSPX [16–19]. Ligation of proximal or mid-splenic artery might be a minimally invasive procedure to improve the SFSS and severe cytopenia, but the treatment effect is less reliable because arterial supply to the spleen still remains through gastrosplenic ligament and intrapnacreatic collaterals after ligation of proximal or mid-splenic artery. On the contrary, pre or postoperative embolization of distal splenic artery may be more effective method for avoidance of SFSS and correction of cytopenia, but it has a substantial risk of splenic infarction and/or abscess, portal vein thrombosis, pancreatitis, and postembolization syndrome [20]. SDV leaving remnant arterial supply to the spleen via intrapancreatic collateral from superior mesenteric artery is a unique and innovative procedure, developed at our institution in August 2013, to enhance the effects of splenic artery ligation and also to mitigate the untoward effects of SSPX or splenic artery embolization.

In terms of simplicity of procedure, SDV is much more simple than SSPX and the operation time is significantly shorter. Usually SDV takes around 20–30 min

Transplant International 2019; 32: 535–545

but SSPX itself takes a little longer. However, the completion process such as bleeding control around the splenectomy bed and pancreas tail consumes additional time. As a result, SSPX has taken about 50 min.

SSPX might be an effective procedure to reduce portal hyperperfusion, particularly for small-for-size grafts, when considering the recent reports of the association between SSPX and portal venous pressure/flow [3,12,14]. In this study, the incidence of SFSS on POD 7 was low (1.6%) and did not differ significantly between the SSPX and SDV groups, and the patients finally recovered well. As a result of our efforts to comply with the institutional strategy giving enough graft volume to the recipient around 1.0% [21], the reason of SSPX or SDV because of low GRWR comprised just 10.6% and the incidence of small-for-size syndrome was lower than that reported in previous series [3,12,22]. Only the prothrombin time (INR) on POD 7 in SSPX group was significantly shorter than SDV group. The other variables including total bilirubin level and amount of ascites drainage on POD 7, and the decreasing time until <2 mg/dl total bilirubin level, seemed to be favorable in SSPX group but were not statistically significant. The results might partially be attributed to the following beneficial effects of SSPX for the graft function.

It is well-known fact that ligation of splenic artery in LDLT can correct cytopenia more effectively than the nonligation group during post-transplant period [18]. In the aspect of cytopenia correction including platelet, leukocyte, and hemoglobin, SSPX was definitely superior to the SDV. However, its effect of SDV belonged to acceptable range in absolute terms, and additional negative clinical impact related to cytopenia was absent such as postoperative hemorrhage and infection. Based on follow-up CT imaging after SDV (Fig. 3), SDV can not only preserve immunologic function of spleen but also effectively correct excessive mechanical filtration related to huge splenomegaly. Hence, we can infer the SDV has definitely lower risk of portal vein thrombosis and septic complication in contrast to the SSPX because normally functioning spleen is still maintained after the SDV. Although our mid-term results did not show any reappearance of splenomegaly like as preoperative state, reappearance of splenomegaly after SDV might be possible in the long-term perspectives by augmentation of remaining intra-pancreatic arterial supply through superior mesenteric artery particularly when portal hypertension develops again because of slowly deteriorating liver graft.

According to the recent reports from Japan in regards to SSPX in LDLT,[12,15] Tokyo group and Kyoto group suggested conflicting results for the outcomes. In this study, we did not compare between SSPX and non-SSPX in LDLT and could not suggest correctly corresponding answer for the SSPX. However, we may assume the answer indirectly because SDV in LDLT at our institution rarely had procedure-related complications requiring treatment except one patient. Clavien-Dindo classification grade 3 and more complications occurred significantly more in SSPX group than in SDV group, and most of them were related to postoperative hemorrhage. The sites of postoperative hemorrhage after SSPX were evenly distributed between SSPX-related and SSPX-unrelated area. The increased risk of postoperative hemorrhage after SSPX was not localized at SSPX site and this finding is similar to the report of Tokyo group. The incidence of postoperative thrombosis including splenic and portal vein after SSPX was 22.6% (14/62), which is the highest value among the three LDLT centers. It may be related to the reason for the SSPX unlike the other reports [3,12,23] that splenomegaly-related cytopenia comprising 74.2% was the most common cause of the SSPX and the portal flow decreased the most effectively compared to other indications. However, all the patients having postoperative splenic or portal vein thrombosis during study period were successfully managed without surgical thrombectomy under the medication of antiplatelet and anticoagulation agents. Postoperative thrombosis in the portal system after SDV was quite rare but occurred when the recipient had huge splenomegaly. As a result, routine anticoagulation after SDV was not necessary but required when patient had splenic vein thrombosis on the follow-up CT scan. For ALDLT recipient who underwent SSPX, however, life-long anticoagulation is recommended at our institution because we experienced total portomesenteric thrombosis on 1 month after cessation of anticoagulation at time of post-ALDLT 34 months (Fig. 5).

Even though there were statistically no difference in in-hospital mortality and overall survival rate between SSPX group and SDV group, the SSPX group had significantly higher chance of procedure-related major complications requiring treatment and also had more serious complication than SDV group. SSPX-specific pancreatic complication such as fistula, abscess, and pseudocyst often resulted in massive bleeding from arterial pseudoaneurysm and required treatments at least once including laparotomy, embolization, and drainage. Two in-hospital mortality cases and the other one near-mortality case resulted from postoperative complications after SSPX, and the infectious complications causing mortality was actually secondary sequelae of SSPX complications. The Kyoto and Kyushu group describes that vessel sealing systems and endo-stapling devices during SSPX has been proved to be safer and associated

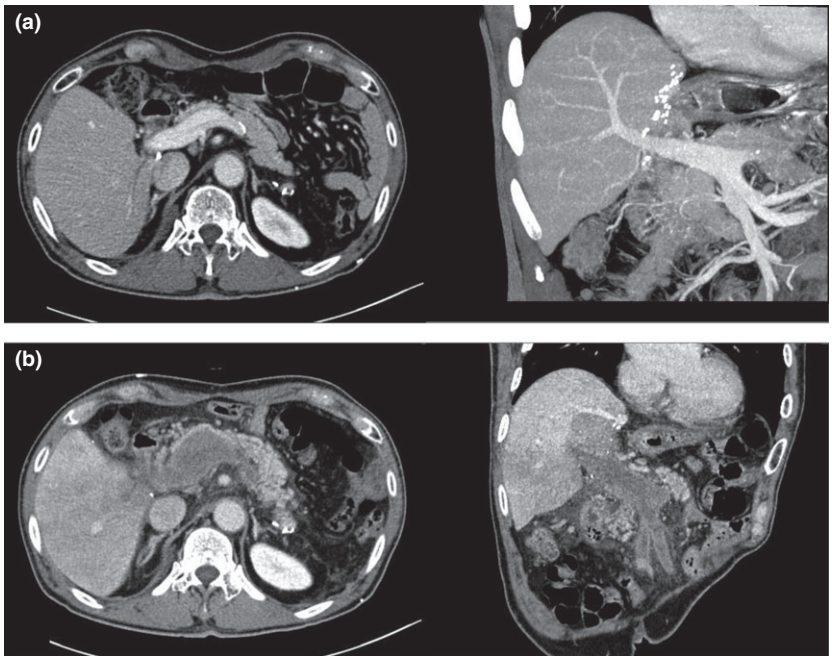


Figure 5 Total portomesenteric venous thrombosis on 1 month after cessation of anticoagulation in the simultaneous splenectomy patient. Post-LDLT 24 months CT scan (a) revealed patent portal venous system, but post-LDLT 34 months CT scan (b) showed total thrombosis in the splanchnic venous system.

with less chance of bleeding [12,24], and it might be possible explanation for their outcomes of SSPX in LDLT. We had performed SSPX with described various methods by four competent surgeons but any method of SSPX did not give us superior outcome in the procedure-related complication. The fact – postoperative hemorrhage from the SSPX-unrelated sites also occurred commonly – indirectly implies that procedure-related complication after SSPX is simply not the technical problem but related to complicated nonsurgical problems. Among SSPX recipients, many patients had severe splenomegaly extending to the retro-pancreatic side with some adhesion to the pancreas parenchyma. In addition, patients with recurrent spontaneous bacterial peritonitis or high MELD score indicating severe portal hypertension seemed to have higher chance of procedure complications. In our opinion, those findings are prone to injure the pancreas parenchyma unavoidably at the time of SSPX, and resulted in higher incidence of pancreas leakage and bleeding from the pancreatic side, and subsequently it led to disastrous complications in contrast to SDV group.

When we compared to the SSPX, the SDV is not superior procedure but acceptable option to improve cytopenia postoperatively. There was no difference of clinical outcome between SSPX group and SDV group to manage the small-for-size graft in ALDLT. However, the one of the greatest benefits of SDV was free from the procedure-related lethal complications.

Regrettably, this study has several limitations, as it is a retrospective study with a relatively small number of patients, medium-term follow-up and observation from a single center. So, a large multicenter study with long-term follow-up is necessary to evaluate the role of SDV to replace the SSPX in LDLT. When we perform procedures in LDLT using partial liver graft, we put the safety first because LDLT is basically complication-prone operation having many weakness. Efficacy and feasibility of the procedure are also important to perform some procedures in LDLT. Hence, we cautiously suggest following conclusion that the SDV can replace the role of SSPX in ALDLT considering the outcomes of this study.

Authorship

SGL, DBM, GCP, GWS, TYH, SH: Study conception and design. DBM, CSA, KHK, DHJ, GWS, GCP, HDC, YGJ, SMH: Acquisition of data. DBM, SGL, DHJ, SH, KHK, HDC, YKJ, SMH, YIY: Analysis and interpretation of data. DBM, SGL, TYH, DHJ, CSA, KHK, SMH, YIY: Drafting of manuscript. DBM, SGL, TYH, GCP, GWS, SH, YKJ: Critical revision. SGL, DBM, SH, CSA, GWS, DHJ, YIY: Final approval of the version to be published.

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