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A Novel Predictor of Posttransplant Portal Hypertension in Adult-To-Adult Living Donor Liver Transplantation: Increased Estimated Spleen/Graft Volume Ratio

Kazuyuki Gyoten, MD,¹ Shugo Mizuno, MD,¹ Hiroyuki Kato, MD,¹ Yasuhiro Murata, MD,¹ Akihiro Tanemura, MD,¹ Yoshinori Azumi, MD,¹ Naohisa Kuriyama, MD,¹ Masashi Kishiwada, MD,¹ Masanobu Usui, MD,¹ Hiroyuki Sakurai, MD,¹ and Shuji Isaji, MD¹

Background. In adult living donor liver transplantation (ALDLT), graft-to-recipient weight ratio of less than 0.8 is incomplete for predicting portal hypertension (>20 mm Hg) after reperfusion. We aimed to identify preoperative factors contributing to portal venous pressure (PVP) after reperfusion and to predict portal hypertension, focusing on spleen volume-to-graft volume ratio (SVGVR). **Methods.** In 73 recipients with ALDLT between 2002 and 2013, first we analyzed survival according to PVP of 20 mm Hg as the threshold, evaluating the efficacy of splenectomy. Second, we evaluated various preoperative factors contributing to portal hypertension after reperfusion. **Results.** All of the recipients with PVP greater than 20 mm Hg ($n = 19$) underwent PVP modulation by splenectomy, and their overall survival was favorable compared with 54 recipients who did not need splenectomy (PVP ≤ 20 mm Hg). Graft-to-recipient weight ratio had no correlation with PVP. Multivariate analysis revealed that estimated graft and spleen volume were significant factors contributing to PVP after reperfusion ($P < 0.0001$ and $P < 0.0001$, respectively). Furthermore, estimated SVGVR showed a significant negative correlation to PVP after reperfusion ($R = 0.652$), and the best cutoff value for portal hypertension was 0.95. **Conclusions.** In ALDLT, preoperative assessment of SVGVR is a good predictor of portal hypertension after reperfusion can be used to indicate the need for splenectomy before reperfusion.

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In adult-to-adult living donor liver transplantation (ALDLT), the elevation of portal venous pressure (PVP) after reperfusion causes critical problems, especially in small-for-size grafts, usually defined as graft-to-recipient weight ratio (GRWR) less than 0.8, causing severe critical manifestation defined as small-for-size syndrome (SFSS): persistent hyperbilirunemia, coagulopathy, massive intractable ascites, sepsis, gastrointestinal portal hypertensive bleeding, and renal dysfunction.^{1–3} The regulation of PVP by splenectomy, portocaval shunting,

and splenic arterial ligation is the key to preventing SFSS, and the appropriate threshold of PVP after ALDLT is thought to be between 15 and 20 mm Hg.^{1,3,4}

Portal venous pressure consists of 3 factors: outflow, intrahepatic vascular resistance, and hemodynamic status. Outflow is affected by the construction of the hepatic vein.^{5,6} Intrahepatic vascular resistance is related to the size and quality of the graft.^{7,8} Hemodynamic status is related to the development of collateral vessels and spleen volume.^{8,9} Although GRWR is generally used as an index for selection of graft in ALDLT, GRWR reflects just graft size. Ogura et al¹ reported that a GRWR of 0.8 or less did not show a statistical difference in respect of the elevation of PVP and the proportion of deceased recipients. At our institution, some recipients had that PVP exceeding 20 mm Hg after reperfusion even when an adequate graft with GRWR of 0.8 or more was used. These findings indicate that not only graft size but also hemodynamic status, especially spleen volume, should be considered in evaluating PVP after reperfusion. Recently, Cheng et al¹⁰ revealed that the spleen volume was significantly associated with excessive portal venous flow measured by intraoperative Doppler ultrasonography just after reperfusion, emphasizing the graft-to-recipient spleen size ratio as a novel predictor of portal hyperperfusion syndrome in ALDLT.

If posttransplant portal hypertension can be predicted preoperatively using suitable indicators such as the ratio

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¹ Department of Hepatobiliary Pancreatic and Transplant Surgery, Mie University School of Medicine, Tsu, Mie, Japan.

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Correspondence: Shugo Mizuno, MD, Department of Hepatobiliary-Pancreatic and Transplant Surgery, Mie University School of Medicine, 2-174 Edobashi, Tsu, Mie, 514-0001, Japan. (mizunos@clin.medic.mie-u.ac.jp).

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of graft-to-spleen size, we can decide on splenectomy before reperfusion to prevent severe shear stress of the liver graft due to transient portal hypertension after reperfusion. There are few ALDLT studies on posttransplant PVP or portal flow focusing on the relationship between graft size and spleen volume; that is, the ratio of graft to spleen size in ALDLT. The aims of our study were to evaluate the significance of posttransplant PVP on recipient survival and to identify the significant factors which predict portal hypertension after reperfusion in ALDLT.

MATERIALS AND METHODS

Adult living donor liver transplantation was performed in 112 consecutive recipients at Mie University Hospital from March 2002 to March 2013. We reviewed precise records on PVP in 75 recipients (Figure 1).

In study 1, we evaluated the efficacy of splenectomy for portal hypertension of more than 20 mm Hg in 73 recipients after excluding 2 recipients who underwent splenectomy for ABO incompatibility and thrombocytopenia and further analyzed recipient survival according to PVP after reperfusion. There were 42 men and 31 women. The mean age was 54.3 years (20-70). The mean Child-Pugh score was 9.7 (5-15). The mean model for end-stage liver disease (MELD) score was 18.1 (6-44). Graft type consisted of left lobe grafts in 27 recipients, right lobe grafts in 45 and posterior graft in 1. Right lobe grafts without middle hepatic vein were selected in 30 recipients, on whom the reconstruction of V5, V8, or both was performed in 5, 11, and 8 recipients, respectively. Right lobe grafts with MHV were selected in 15 recipients.

Of these 73 recipients, the 55 on whom preoperative computed tomography (CT) volumetry of the spleen could be performed comprised study 2. We evaluated various preoperative factors contributing to PVP after reperfusion, such as the Child-Pugh score, MELD score, estimated graft volume, estimated GRWR, %graft volume/standard liver volume, estimated spleen volume and spontaneous shunt, and further investigated factors to predict PVP of more than 20 mm Hg after reperfusion.

All procedures and studies were carried out according to the ethical guidelines outlined by the Institution Review Board (2934).

Donor Selection

According to the ethical guidelines of the Japan Society for Transplantation, donor candidates are basically limited to blood relatives within the sixth degree, or relatives through marriage within the third degree, if they manifest a strong desire to donate part of their liver of their own freewill. When an unrelated person becomes a donor candidate, the transplant center requires approval by the ethics committee of Japan Society for Transplantation. Our clinical criteria for living donors were as follows: healthy individuals between 18 and 62 years of age, no significant medical history, no abnormalities in blood examinations or cardiopulmonary function tests, and no history of viral hepatitis. Preoperative estimation of the graft and remnant liver volume was performed using 3-dimensional reconstructed images from multidetector CT of the liver, aiming to obtain 0.8 or more GRWR, and 35% or more remnant liver volume.^{11,12} When the estimated remnant liver was more than 35% of the total liver volume of the donor liver and GRWR was less than 0.8, a right liver graft including MHV harvesting was considered.

Procedure of LDLT

All LDLT procedures for both donors and recipients were performed according to our previously reported methods.^{12,13} The right hepatic vein or common trunk of the left and middle hepatic veins were anastomosed to the inferior vena cava in an end-to-side fashion. The middle hepatic vein in the right lobe graft was anastomosed to the inferior vena cava using an autologous venous patch: the portal vein of the extirpated native liver, ovarian vein, and inferior mesenteric vein of recipients. In right lobe grafts without middle hepatic vein, all drainage veins from segments 5 and 8 larger than 5 mm were basically reconstructed.¹³ Reconstruction of the portal veins and the hepatic arteries was performed with end-to-end anastomosis. Intraoperative Doppler ultrasound was used

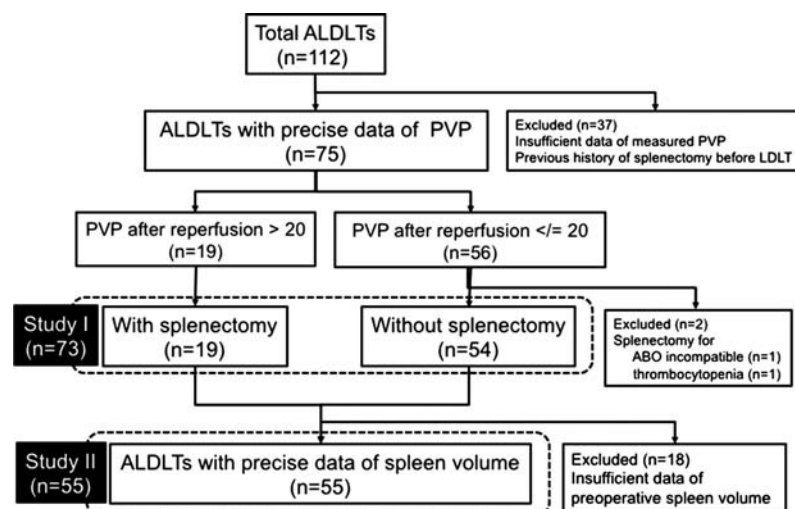


FIGURE 1. Flow chart detailing recipients who underwent ALDLTs. In study 1, efficacy of splenectomy was investigated in 73 recipients whose precise records of PVP were preserved. In study 2, factors contributing to PVP after reperfusion were analyzed in 55 recipients whose preoperative spleen volumetry was available.

TABLE 1.**Backgrounds of the 55 recipients**

Recipient	Age, y	56.1 (34-70)
	Male/Female	34:21
	BMI	23.4 (15.4-33.8)
	Albumin, mg/dL	2.8 (1.5-4.4)
	Total bilirubin, mg/dL	5.1 (0.5-39.9)
	Creatinine, mg/dL	1.0 (0.4-4.3)
	PT-INR	1.5 (0.98-4.07)
	Platelet count, $\times 10^3/\mu\text{L}$	77.9
	Mild or severe ascites	34
	Encephalopathy > grade I	30
	Preoperative EIS or EVL for esophageal varix	22
	Gastrointestinal bleeding	9
	Child-Pugh score	9.3 (5-15)
	MELD score	15.7 (6-33)
	Estimated graft volume, mL	599 (316-944)
	Actual graft weight, g	565 (320-980)
	Estimated GRWR	0.882 (0.464-1.291)
	Recipient SLV, mL	1182 (932-1437)
	Estimated spleen volume, mL	430 (62.6-923)
	Graft type	Rt 30:Lt 24:Pos 1
Donor	Age, y	37.4 (19-65)
	Male/Female	30:25

EIS, endoscopic injection sclerotherapy; EVL, endoscopic variceal ligation; PT-INR, prothrombin time-international normalized ratio; SLV, standard liver volume; Rt, right lobe; Lt, left lobe; Pos, posterior segment; BMI, body mass index.

to confirm the flow in the hepatic vein, portal vein, and hepatic artery. The bile duct was reconstructed with duct-to-duct anastomosis.

Monitoring and Regulation of PVP

For monitoring PVP, a 16-gauge antithrombotic catheter (Medicut UK-LCV Kit; Nippon Sherwood Medical Industries, Tokyo, Japan) was inserted via the inferior mesenteric vein before the recipient's liver was removed. The tip of the catheter was positioned in the recipient's portal vein or splenic vein and fixed in place by ligation and 2 rubber bands. The other end was drawn outside the body via the surgical wound as described elsewhere.³ A transducer was used to monitor PVP continuously during the operation. Routinely, PVP was modulated only by splenectomy when PVP after reperfusion remained more than 20 mm Hg until abdominal closure. Construction of a portosystemic shunt was not performed even if PVP after splenectomy was more than 20 mm Hg. Central venous pressure (CVP) was also monitored during the operation.

CT Volumetry of Liver Graft and Spleen and Measurement of Actual Liver Graft

Serial transverse enhanced CT scan images were obtained at 2.0-mm intervals. The total liver volume, graft volume, and spleen volume of the patients were estimated by tracing the liver and spleen on each CT image during the preoperative survey period. Estimated graft weight was preoperatively calculated using a correlation coefficient of 0.91 from the graft volume estimated by MeVis Distant Service (MeVis software; MeVisLab, Bremen, Germany). Standard liver volume was calculated according to the formula proposed by Urata et al.¹¹ Estimated GRWR was calculated by estimated

graft weight/body weight $\times 100$. The actual liver grafts removed from donors were flushed with histidine-tryptophan-ketoglutarate solution ex situ via the portal vein, and then weighed on the back Table 1.²

Evaluation of Spontaneous Portosystemic Shunts

We evaluated the presence of spontaneous portosystemic shunts by preoperative CT scan. The coronary and umbilical vein was determined to be engorged if its size was greater than 5 mm by CT measurement. The evaluation of an engorged vein in all the CT scans was made by the same medical doctor in this series.

Statistical Analysis

The results for continuous variables were expressed as mean values with ranges and standard deviations. The relationship between 2 variants was determined by Pearson correlation analysis and Student *t* test. Cumulative survival according to PVP was analyzed by the Kaplan-Meier method, and prognostic factors were estimated by log-rank analysis. Stepwise multiple regression analysis of factors contributing to PVP after reperfusion was carried out using SPSS version 21.0 (SPSS, Inc., Chicago, IL). When there were significant factors contributing to PVP after reperfusion, the best of cutoff value for PVP of more than 20 mm Hg was determined by the receiver operating characteristic (ROC) curve. *P* value less than 0.05 was considered to be statistically significant. *R* greater than 0.4 was considered to be a coefficient relation.

RESULTS

Study 1

Efficacy of Splenectomy According to PVP After Reperfusion

In the 73 recipients, PVP after reperfusion was 18.3 ± 5.7 mm Hg. Splenectomy was performed in 19 recipients because PVP was more than 20 mm Hg (25.8 ± 4.7) after reperfusion, and PVP decreased to 20 mm Hg or less (16.7 ± 4.0) in 17 of them, but was still more than 20 mm Hg in the other 2 recipients (23 and 25 mm Hg, respectively) (Figure 2). The 2 recipients with PVP of more than 20 mm Hg even after splenectomy had prolonged

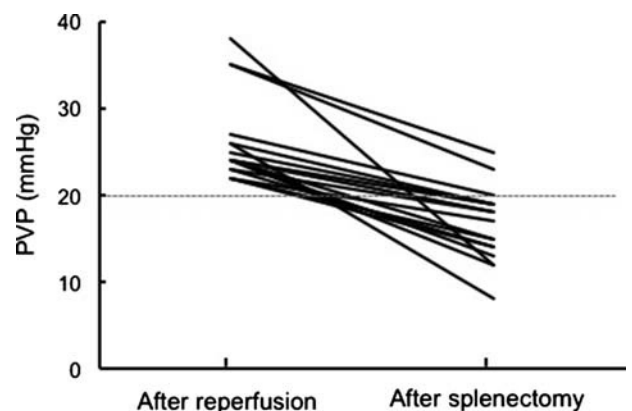


FIGURE 2. Change of PVP after splenectomy. Splenectomy was performed in 19 (26%) of the 73 recipients. After splenectomy, mean portal pressure significantly decreased from 25.8 ± 4.7 to 16.7 ± 4.0 mm Hg (mean \pm SD).

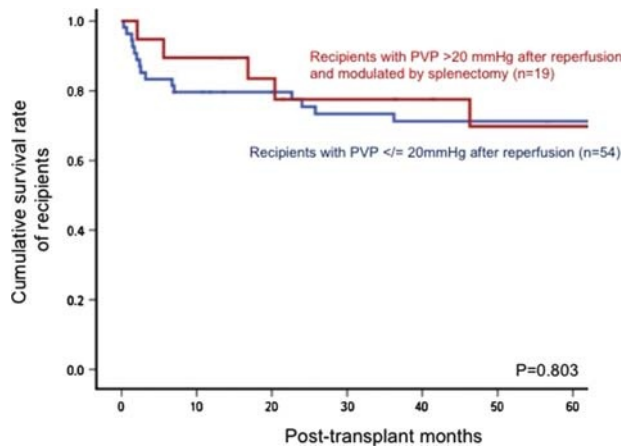


FIGURE 3. Cumulative survival rate according to PVP after reperfusion with a threshold of more than 20 mm Hg. Survival rate of 19 recipients who underwent splenectomy for PVP > 20 mm Hg after reperfusion was as favorable as that of 54 recipients with PVP ≤ 20 mm Hg after reperfusion.

hyperbilirubinemia but recovered in the postoperative acute phase. One of them especially, had complications with massive ascites and sepsis. The 1-, 3-, 5-year cumulative survival rates were 79.6%, 73.3%, and 71.2%, respectively, in the 54 recipients with PVP of 20 mm Hg or less after reperfusion and 89.5%, 77.5%, and 69.8% in the 19 with PVP of more than 20 mm Hg followed by splenectomy, showing no significant difference between the 2 groups ($P = 0.803$) (Figure 3). In 54 patients with PVP of 20 mm Hg or less after reperfusion, 9 recipients (16.7%) died within 6 months after LT, despite the large graft volume: the median GRWR was 1.12 (0.67-1.32). However, the median MELD score was high: 28 (9-44), and the causes of death were not related with the graft size (sepsis in 3 recipients, pneumonia in 2, fibrosing cholestatic hepatitis of HCV in 1, cerebral bleeding in 1, rupture of splenic arterial aneurysm in 1 and gastrointestinal bleeding in 1). Additionally, precise records on CVP measured at the same time as PVP after reperfusion were available for 53 recipients, whose CVP was 7.0 ± 2.8 mm Hg. Portal venous pressure after reperfusion had no correlation to CVP after reperfusion ($R = 0.057$).

When PVP was reanalyzed according to graft type, PVP after reperfusion was 21.4 ± 6.3 mm Hg in left lobe grafts ($n = 27$) and 16.2 ± 4.2 mm Hg in right lobe grafts ($n = 45$), showing a significant difference ($P < 0.001$). Among the right lobe grafts, PVP was 15.6 ± 4.0 mm Hg in the grafts with MHV ($n = 15$) and 17.2 ± 4.7 mm Hg in the grafts without MHV ($n = 30$), showing no significant difference ($P = 0.265$). Portal hypertension of more than 20 mm Hg occurred in 26.7% (4/15) of the grafts with MHV and in 10% (3/30) of the grafts without MHV (not a significant difference, $P = 0.145$).

Study 2

Patients' Background and Underlying Disease

Backgrounds of the 55 recipients in whom PVP and spleen volume could be measured are shown in Table 1. There were 34 men and 21 women. The mean age was 56.1 years (34-70 years). The mean Child-Pugh score was 9.3 (5-15).

The mean MELD score was 15.7 (6-33). Mean estimated graft volume and actual graft weight were 599 mL (316-944) and 565 g (320-980), showing a significant linear correlation between them ($R = 0.778$, $P < 0.0001$). Estimated spleen volume was 430 mL (62.6-923). Underlying diseases for liver transplantation were hepatitis B- or C-related cirrhosis in 34 recipients (26 of whom had complications of hepatocellular carcinoma), fulminant hepatitis B in 2, cryptogenic liver cirrhosis in 7 (one of whom had complications of hepatocellular carcinoma), alcoholic liver cirrhosis in 2, primary biliary cirrhosis in 7, secondary biliary cirrhosis in 1, autoimmune hepatic cirrhosis in 1, and glycogen storage disease type III in 1.

Spontaneous portosystemic shunt was found in 31 (56.3 %) of the 55 recipients: engorged coronary vein in 14, splenorenal shunt in 10, paraumbilical vein shunt in 6 and gastrosplenic shunt in 4 (overlapped).

Graft type consisted of left lobe grafts in 24 recipients, right lobe grafts in 30 and posterior graft in 1. Right lobe grafts without MHV were selected for 16 recipients, on whom the reconstruction of V5, V8, or both V5 and V8 was performed in 2, 6, and 3 recipients, respectively. The recipient with a posterior graft (actual graft weight, 620 g; GRWR, 1.04) died of prolonged infection at 168 days after LDLT, although PVP after reperfusion was 27 mm Hg, the final PVP was 20 mm Hg after splenectomy and his early hemodynamic status was stable.

Relationship Between Estimated GRWR and PVP After Reperfusion

Estimated GRWR had no correlation to PVP after reperfusion ($R = 0.360$) (Figure 4). In the 19 recipients with estimated GRWR of less than 0.8, 8 (42%) had PVP of more than 20 mm Hg after reperfusion. In the 35 recipients with GRWR of 0.8 or more, 9 (25%) had PVP of more than 20 mm Hg.

Multivariable Analysis of Factors Contributing to PVP After Reperfusion

For multivariate analysis of PVP after reperfusion, we evaluated the following factors: age, sex, hepatocellular carcinoma, liver cirrhosis, albumin, total bilirubin, creatinine,

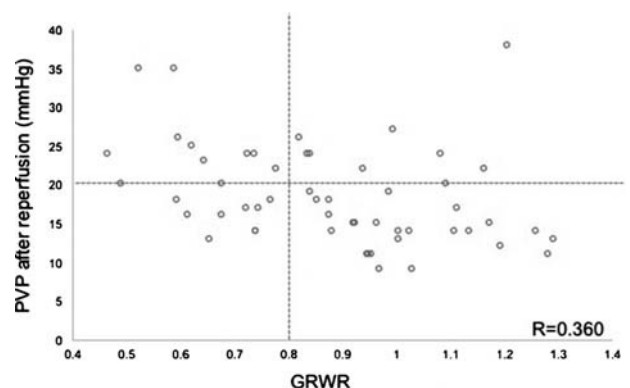


FIGURE 4. Relationship between estimated GRWR and PVP after reperfusion. Estimated GRWR had no correlation with PVP after reperfusion ($R = 0.360$). In 19 recipients with estimated GRWR < 0.8, PVP > 20 mm Hg occurred in 8 (42%). In 36 recipients with estimated GRWR ≥ 0.8, PVP > 20 mm Hg occurred in 9 (25%).

TABLE 2.
Multivariable analysis of factors contributing to PVP after reperfusion

	Regression coefficient	95% CI	P
Estimated graft volume	-0.021	-0.030 to -0.012	<0.0001
Estimated spleen volume	0.013	0.008 to 0.0019	<0.0001

prothrombin time, body mass index, the presence of ascites or encephalopathy (≥ Grade I), previous gastrointestinal bleeding, platelet counts and endoscopic treatments of esophageal varices, Child-Pugh score, MELD score, estimated graft volume, estimated GRWR, %GV/standard liver volume, estimated spleen volume, spontaneous shunt, graft type, and age and sex of donor. As a result, estimated graft volume and spleen volume were independent factors contributing to PVP after reperfusion ($P < 0.0001$ and $P < 0.0001$, respectively) (Table 2). This result was derived following the calculating formula to predict PVP after reperfusion: PVP after reperfusion (mm Hg) = $25.40 - 0.021 \times GV + 0.013 \times \text{spleen volume}$ ($R = 0.68$).

The Cutoff Value of Estimated Graft and Spleen Volumes for PVP of More Than 20 mm Hg

A significant negative correlation was observed between estimated graft volume and PVP after reperfusion ($R = 0.509$). Furthermore, a significant positive correlation was observed between spleen volume and PVP after reperfusion ($R = 0.483$). ROC analysis of estimated graft volume revealed that the best cutoff value for PVP of more than 20 mm Hg was 557 mL (area under the curve [AUC], 0.784, 95% confidence interval [95% CI], 0.662-0.906; $P = 0.001$; sensitivity, 78.9%; specificity, 70.6%). Therefore, the optimal cutoff level of graft volume for PVP of 20 mm Hg or more after

reperfusion was set at 560 mL. ROC analysis of estimated spleen volume revealed that the best cutoff value for PVP of more than 20 mm Hg was between 488 and 510 mL (AUC, 0.734; 95% CI, 0.587-0.880; $P = 0.006$; sensitivity, 58.8-52.9%; specificity, 78.9-84.2%). Therefore, the optimal cutoff level of estimated spleen volume for PVP of more than 20 mm Hg after reperfusion was set at 500 mL (Fig. 5).

Because both estimated graft and spleen volumes were significantly correlated with PVP after reperfusion, it was considered that their ratio, that is, spleen volume graft volume ratio (SVGVR), reflected PVP after reperfusion more accurately. Estimated SVGVR showed a more significant positive correlation with PVP after reperfusion ($R = 0.652$) (Figure 6). ROC analysis of SVGVR revealed that the best cutoff value for PVP of more than 20 mm Hg was between 0.923 and 0.968 (AUC, 0.820; 95% CI, 0.689-0.952; $P < 0.0001$; sensitivity, 70.6-64.7%; specificity, 77.1-92.1%). Therefore, the optimal predictive SVGVR cutoff level of PVP of more than 20 mm Hg was set at 0.95. Of the 15 recipients with SVGVR of more than 0.95, 11 (73.3%) developed PVP of more than 20 mm Hg after reperfusion.

Evaluation of SVGVR According to MELD Score, Child-Pugh Classification, and Graft Type

As shown in Figure 7, in recipients with a high MELD scores of 15 or more ($n = 23$) as well as less than 15 ($n = 32$), there were significant correlations between SVGVR and PVP after reperfusion ($R = 0.58$ and $R = 0.69$, respectively). In addition, in the recipients with Child-Pugh B ($n = 21$) and Child-Pugh C ($n = 26$), there was a significant correlation between SVGVR and PVP after reperfusion ($R = 0.76$ and $R = 0.51$, respectively); however, in 8 recipients with Child-Pugh A, there was no significant correlation ($R = 0.34$). As shown in Figure 8, SVGVR had a significant correlation with

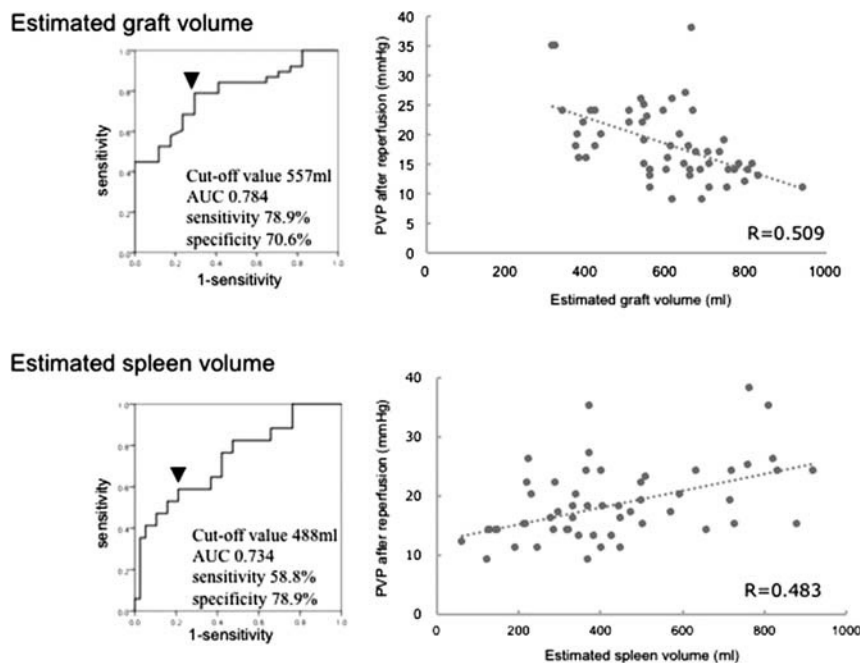


FIGURE 5. ROC curve of graft volume and spleen volume in portal hypertension of 20 mm Hg or more after reperfusion. The cutoff value of graft and spleen volume was 557 and 488 mL, respectively. PVP after reperfusion had a significant correlation with graft and spleen volume.

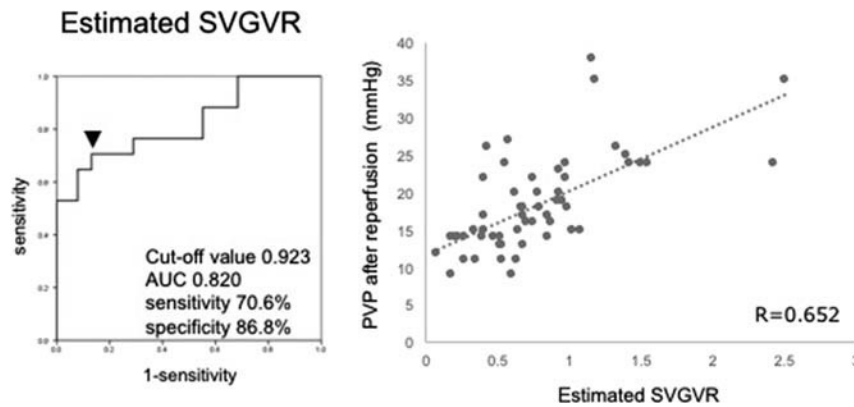


FIGURE 6. ROC curve of estimated SVGVR in portal hypertension of more than 20 mm Hg after reperfusion, and the relation between SVGVR ratio and PVP after reperfusion. The cutoff value of SVGVR was set as 0.95. In 15 recipients with SVGVR of 0.95 or more, 11 (73.3%) had portal hypertension.

PVP after reperfusion in left lobe grafts ($n = 24$, $R = 0.573$) as well as in right lobe grafts ($n = 30$, $R = 0.735$), respectively.

DISCUSSION

In ALDLT, small-for-size grafts, generally defined as GRWR of less than 0.8, often cause an imbalance between liver regeneration and function, showing clinical manifestations of SFSS, such as prolonged cholestasis, coagulopathy, and massive intractable ascites, leading to septic complications and higher mortality.^{14,15} Although the mechanism of SFSS is not clear, the sinusoidal excessive shear stress of the graft liver due to the elevated PVP is considered to be a main cause. To reduce the elevated PVP in small-for-size grafts, portal modulations have been proposed. The Kyoto group previously reported that an elevated PVP of more than 20 mm Hg in the early phase was strongly associated with poor patient survival.³ Thereafter, they reported that achievement of a PVP of less than 15 mm Hg by the combination of splenectomy and portosystemic shunt contributed to a successful outcome even in small-for-size grafts.^{1,16} In our institution, PVP of 20 mm Hg has been set as an important prognostic factor and the threshold for portal modulation since we reported previously.¹⁷ As for portal modulation, we prefer splenectomy to portosystemic shunting because the latter has a risk of causing excessive diversion of the portal flow into the systemic circulation, the so-called portal steal phenomenon, requiring closure of the shunt.^{7,18} In fact, the PVP of most of the recipients in the present study was reduced to below 20 mm Hg by splenectomy.

Because we thought that small-for-size grafts caused posttransplant portal hypertension, we first examined the relationship between estimated GRWR and PVP after reperfusion, revealing no significant correlation. Graft to recipient weight ratio is not always adequate for selecting grafts to prevent portal hypertension after reperfusion.^{1,19} In recipients with a GRWR of more than 0.8, posttransplant massive ascites associated with portal overperfusion into the graft liver can develop.²⁰ Therefore, the occurrence of portal hypertension could be determined by graft volume and other factors. Graft to recipient weight ratio reflects just graft size, but PVP reflects 3 factors: outflow from the hepatic vein, size and quality of the graft, and portal hemodynamic status. In liver cirrhosis, the elevation of PVP is generated by increased intrahepatic vascular resistance and hyperkinetic splanchnic blood flow.^{21–23} As a result, splenomegaly and collateral circulation develop. In liver transplantation, PVP is influenced by graft size and hyperkinetic hemodynamic splanchnic circulation persisting in patients with cirrhosis. After whole-liver transplantation, normal portal resistance and liver function are restored, and the amount of splanchnic blood decreases rapidly. As a result, a rapid improvement of splenomegaly and closure of collateral circulation is observed.²⁴ In partial liver transplantation, however, the reduction of the liver vasculature increases PVP in the early phase, but in the later phase, the liver graft regenerates to adapt to the persisting recipient hemodynamic environment with gradual improvement of splenomegaly.²⁴ Therefore, spleen volume and the development of collateral circulation reflect the portal hemodynamic status of the recipients.

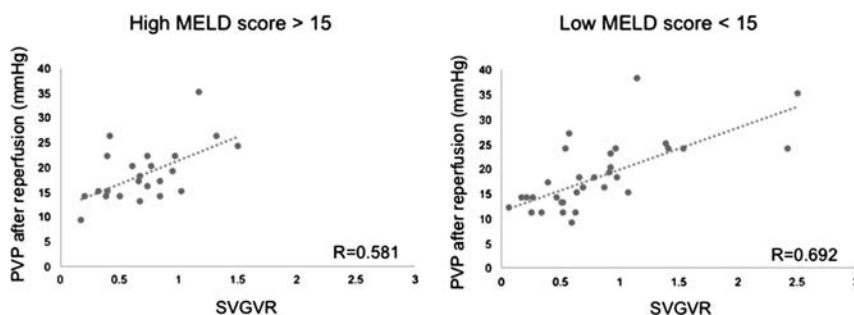


FIGURE 7. Relationship between SVGVR and PVP after reperfusion according to MELD score. In high and low MELD, SVGVR showed a positive correlation with PVP ($R = 0.581$ and $R = 0.692$, respectively).

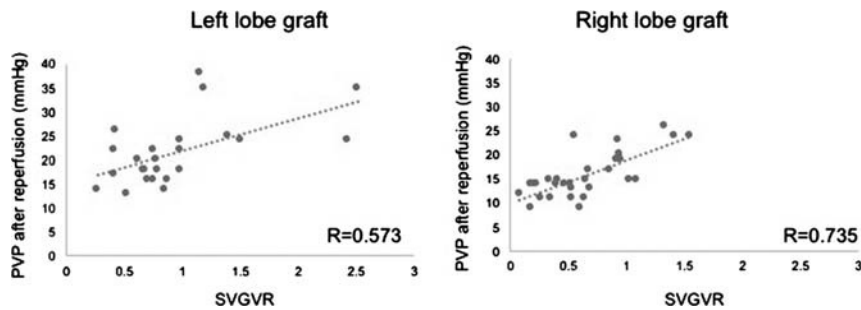


FIGURE 8. Relationship between SVGVR and PVP after reperfusion according to graft type. In left lobe grafts ($n = 24$) as well as right lobe grafts ($n = 30$), SVGVR had a significant correlation with PVP after reperfusion ($R = 0.57$ and $R = 0.73$, respectively).

Accordingly, we evaluated various preoperative factors contributing to PVP after reperfusion, paying special attention to graft weight, spleen volume, and collateral circulation. In multivariate analysis, graft volume and spleen volume were independent significant factors. The development of collateral circulation was not a significant factor. Platelet count, which is generally affected by spleen size, had a negative correlation with spleen volume, but it had no correlation to PVP after reperfusion. Cheng et al¹⁰ previously reported that the spleen volume was significantly associated with excessive portal venous flow and that a graft-to-recipient spleen size ratio of less than 0.6 might predict the development of posttransplant portal hyperperfusion. In their study, however, the definition of posttransplant portal hyperperfusion was more than 260 mL/min per 100 g graft liver weight measured by Doppler ultrasonography, which was associated with posttransplant hyperbilirubinemia and longer hospital stays, but was not a factor in patient survival.²⁵ The definition of portal hyperperfusion varied from 190 to 500 mL/min per 100 g according to previous reports.²⁶⁻²⁸ Moreover, the measurement of portal flow using Doppler ultrasonography has the potential to be underestimated because portal flow might be diverted to the splenic vein and/or collateral vessels in excessive portal flow.

In ALDLT, PVP after reperfusion is determined by graft and spleen volume, which means that intrahepatic vascular resistance and portal hemodynamic status existing in recipients. In the present study, estimated graft and spleen volume showed a significant correlation to PVP after reperfusion, whose cutoff values for high PVP of more than 20 mm Hg were 560 mL for graft volume and 500 mL for spleen volume, respectively. The estimated graft and spleen volumes could be precisely calculated by preoperative CT scan. Although these 2 factors were good predictors for PVP after reperfusion, we set SVGVR to increase the correlation with PVP after reperfusion. It is considered that SVGVR reflects a relationship between vascular resistance in the graft and portal hemodynamic status in the recipient. Spleen volume-to-graft volume ratio of more than 0.95 was a good predictor of high PVP of more than 20 mm Hg after reperfusion, regardless of MELD score, Child-Pugh score, or graft type.

Preoperative prediction of portal hypertension using SVGVR is considered useful from a clinical point of view, because the modulation procedures of PVP are usually performed after confirming the presence of high PVP status, which may cause graft damage. We had usually performed

splenectomy only when PVP of more than 20 mm Hg was measured just after reperfusion. In such situations, the graft liver is exposed to shear stress of high PVP and has an accumulation of splenic inflammatory cells which produce inflammatory cytokines after reperfusion and may accelerate liver damage. In our rat model using small-for-size liver grafts, splenectomy before transplantation attenuated hepatic sinusoidal endothelial injury, increased hepatic hemoxygenase-1 expression and decreased plasma endothelin 1 levels, exerted antiapoptotic effects, and improved liver regeneration.²⁹ Referring to the results of our basic research, we have performed splenectomy before reperfusion in 5 ALDLTs with SVGVR of 0.95 or more. In 4 of 5 recipients, PVP after reperfusion could be evaluated: 10, 19, 21 and 22 mm Hg, respectively; however, PVP of 1 recipient could not be assessed. If splenectomy had not been performed before reperfusion, PVP would exceed 20 mm Hg, which could cause graft dysfunction or failure. The mean posttransplant peaked aspartate aminotransferase levels in these recent 5 recipients were 214 ± 102 U/L, which were slightly lower than 268 ± 150 U/L in the 19 recipients who underwent splenectomy after reperfusion in the present study, although there was no significant difference. To clarify the usefulness of splenectomy before reperfusion, further study is needed.

In ALDLT, PVP after reperfusion is significantly correlated to graft and spleen volume. Spleen volume-to-graft volume ratio of more than 0.95 predicts portal hypertension of more than 20 mm Hg, in which case graft selection splenectomy before reperfusion is favored. Preoperative assessment of SVGVR is a good predictor of PVP after reperfusion and can be used to indicate the need for splenectomy before reperfusion.

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