ORIGINAL ARTICLE

Liver graft-to-spleen volume ratio as a useful predictive factor of the early graft function in children and young adults transplanted for biliary atresia: a retrospective study

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SUMMARY

A graft volume/standard liver volume ratio (GV/SLV) > 35% or graft/recipient weight ratio (GRWR) > 0.8% has been considered as a standard criteria of graft selection. Even if the graft size meets these selection criteria, small-for-size syndrome can still occur depending on the portal venous flow (PVF). The aim of this study was to identify other factors contributing to portal hyperperfusion and the post-transplant course, focusing on the graft volume-to-spleen volume ratio (GV/SV). Thirty-seven BA patients who underwent living donor liver transplantation were reviewed retrospectively. First, we evaluated the preoperative factors contributing to portal hyperperfusion. Second, we evaluated the factors contributing to post-transplant complications, such as thrombocytopenia, hyperbilirubinemia, and coagulopathy. The GV/SLV was >35% in all cases; however, portal hyperperfusion (≥250 ml/min/100 g graft) was found in 12 recipients (35.3%). Furthermore, although the GRWR was >0.8% in over 90% of cases, portal hyperperfusion was found in 10 recipients (32.3%). In contrast, the GV/SV showed a significant correlation with the PVF after reperfusion. If the GV/SV was <0.88, about 80% of recipients developed portal hyperperfusion. Furthermore, the GV/SV also showed a significant correlation with post-transplant persistent thrombocytopenia and hyperbilirubinemia. The GV/SV < 0.88 predicts portal hyperperfusion, post-transplant persistent thrombocytopenia, and hyperbilirubinemia.

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Key words
biliary atresia, hyperbilirubinemia, liver graft-to-spleen volume ratio, portal hyperperfusion, thrombocytopenia

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Introduction

The Kasai operation or its variants constitute the first step in the surgical treatment of infants with biliary atresia (BA). However, liver transplantation (LT) is performed secondarily when bile flow is not restored or when complications of biliary cirrhosis occur [1]. The presence of splenomegaly is likely the result of vascular disturbances that mainly relate to portal hypertension (PHT) [2].

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In living donor liver transplantation (LDLT) for large adolescents and adults with BA, small-for-size syndrome (SFSS) causing severe critical manifestations such as persistent hyperbilirubinemia, coagulopathy, and massive intractable ascites may occur [3–5]. An estimated graft volume/standard liver volume (GV/SLV) ratio < 35% or graft/recipient weight ratio (GRWR) < 0.8% has been considered as a risk factor of small-for-size grafts [4,6]. In our institution, some recipients had portal hyperperfusion, defined as a portal venous flow (PVF) ≥ 250 ml/min/100 g graft, even when an adequate graft size was used, according to the GV/SLV and GRWR criteria. Previous reports have shown that the spleen volume was significantly associated with an excessive PVF and portal venous pressure (PVP), emphasizing the graft volume-to-recipient spleen volume ratio (GV/SV) as a novel predictor of portal hyperperfusion syndrome and PHT in adult LDLT patients [7,8]. If post-transplant portal hyperperfusion can be predicted preoperatively using GV/SV, we can safely select splenectomy before LDLT and administer the 23-valent pneumococcal vaccine.

Our previous study showed that 15.8% of patients who underwent LDLT suffered from persistent thrombocytopenia and splenomegaly for several years after LDLT [9]. These patients may have relative SFSS because of splenomegaly, so GV/SV may be another factor influencing post-transplant persistent thrombocytopenia and hyperbilirubinemia.

There are no reports regarding the relationship between the graft volume and spleen volume for BA patients including children. We therefore initially evaluated the effect of the GV/SV on the PVF after reperfusion and the post-transplant course.

Patients and methods

Forty-one BA patients who underwent LDLT at our center were included in this study. A flowchart describing the recipients underwent LDLT were shown in Fig. 1. Patients who had undergone splenectomy previously ($n = 3$) and patients without sufficient data for the PVF ($n = 1$) were excluded. In Study 1, we evaluated the relationship between the GV/SLV and GRWR, which were conventional criteria, and the PVF after reperfusion. In addition, the relationship between the GV/SV and PVF was evaluated in detail.

In Study 2, we evaluated the relationship between the GV/SV and the postoperative course related to portal hyperperfusion syndrome, such as persistent thrombocytopenia, hyperbilirubinemia, coagulopathy, etc. We defined "persistent" as more than 30 days in this study. Patients who underwent splenectomy at LDLT ($n = 9$) and patients with post-transplant complications contributing to the postoperative course ($n = 8$) were excluded. Furthermore, we excluded 3 patients who died due to early complications (≤30 days), such as hepatic artery thrombosis (HAT), infection and sepsis-causing thrombocytopenia, biliary duct stenosis, etc. The periods to the normalization of thrombocytopenia, hyperbilirubinemia, and coagulopathy were evaluated. All data were verified retrospectively.

Donors were selected from among the candidates who volunteered to be living donors. They were required to be within third-degree consanguinity or the spouse of the recipient and to be between 20 and 65 years of age. Three-dimensional computed tomography (CT) was performed for the volumetric analysis and delineation of the vascular anatomy. The graft volume and spleen volume were measured before LDLT, and the volume was analyzed in this study. The standard liver volumes were calculated using Urata's formula as follows [10]: liver volume (ml) = body surface area (m^2) × 706.2 + 2.4. We determined the graft type for each recipient based on the preoperatively estimated GV/SLV. The GV/SLV was ≥35% or the GRWR was ≥0.8%. When the GV/SLV was <35% and the donor's remnant liver volume rate was <35%, the donor was rejected. The "estimated" graft volume is the preoperative volume,which is determined based on the CT findings before undergoing LDLT, while the "actual" graft volume is the weight based on measurements that have been made intraoperatively. Portal hemodynamics were measured after graft arterial reconstruction and reperfusion using an ultrasonic transit time flow meter (Transonic System™; Transonic Systems Inc., Ithaca, NY, USA) and expressed as ml/min/100 g graft.

In our institution, splenectomy at LDLT was performed for patients with a bleeding tendency because of thrombocytopenia (platelet count < 50 × 10^3/μl), with portal hyperperfusion (PVF ≥ 300 ml/min/100 g of graft), for patients more than 6 years of age and those who received preoperative vaccinations.

A SFSS diagnosis is made based on the occurrence of the following within 2 weeks after LDLT: persistent cholestasis, coagulopathy, ascites, encephalopathy, bleeding from the gastrointestinal tract, and renal failure. We defined SFSS as total bilirubin > 5.0 mg/dl and/or output of ascites > 1 l/day at within 2 weeks after LDLT.

All values were expressed as the mean ± standard deviation. The relationship between two variables was determined by a Pearson correlation analysis and

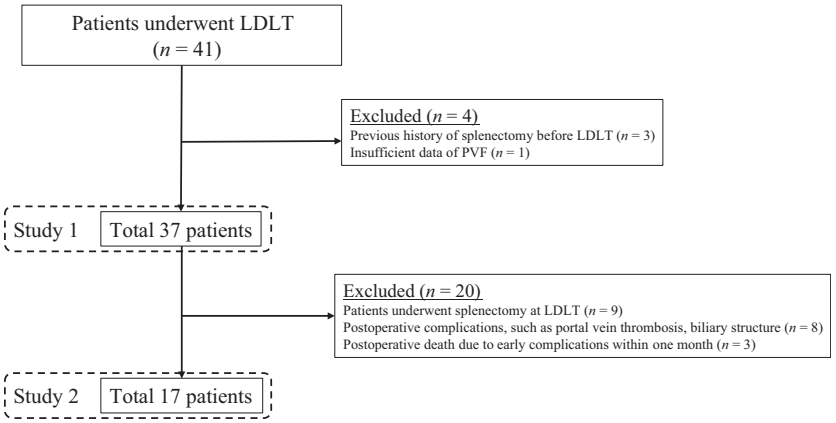

Figure 1 Flowchart describing the recipients who underwent LDLT. In Study 1, the relationship between estimated GV/SV and PVF after reperfusion was investigated in 37 patients. In Study 2, the factors contributing to post-transplant complications, such as thrombocytopenia, hyperbilirubinemia, and coagulopathy, were analyzed in 17 patients. BA: biliary atresia, LDLT: living donor liver transplantation, GV/SV: graft volume-to-spleen volume ratio, PVF: portal venous flow.

Student's *t*-test. When there were significant factors contributing to the PVF after reperfusion, the cut-off value for a PVF of ≥250 ml/min/100 g of graft was determined by the receiver operating characteristic (ROC) curve. A *P*-value of <0.05 was considered to be statistically significant. All statistical analyses were performed using the JMP 13.0 software program (SAS Institute, Cary, NC, USA).

This retrospective study was performed according to the Ethical Guidelines for Clinical Research published by the Ministry of Health, Labor and Welfare of Japan on July 30, 2003 (revised 2008) and complies with the Helsinki Declaration of 1964 (revised 2008). All parents or guardians of infants in this study gave informed consent prior to their inclusion in this study. All LDLTs were performed after obtaining approval from the Ethics and Indications Committee for LDLT in our institution. This study was approved by the ethics committee of Kyushu University (institutional review board approval number 29-85).

Results

A total of 37 BA patients were included in Study 1. There were 11 male and 26 female patients. The characteristics of recipients and grafts are shown in Table 1. The mean age was 81.2 ± 108.1 months (range 3–349), and the mean weight was 21.0 ± 20.8 kg (range 5.5–69.3). The graft type consisted of left lateral segment grafts in 23 recipients, left lobe grafts in 8, right lobe grafts in 4, and S2 monosegment grafts in 2. The mean estimated graft volume and actual graft weight were 306.1 ± 138.5 ml (range 152–687) and 288.9 ± 123.3 g (range 183–662), showing no significant differences. The mean volume of the recipient spleen was 402.3 ± 456.0 ml (range 42–2 049). The mean GV/SLV, GRWR, and GV/SV were 75.4±27.0% (range 35.9–129.6%), and 2.42±1.23% (range 0.63–4.57%), and 1.59±1.19% (range 0.20–5.26%), respectively. The PVF was measured immediately after graft arterial anastomosis, and the PVF was 225.1 ± 189.9 ml/min/100 g (range 41.9–777.8). Portal hyperperfusion (PVF ≥ 250 ml/min/100 g graft) was found in 12 recipients (35.3%). The cases with portal hyperperfusion were significantly older than those without portal hyperperfusion (201.4 ± 110.5 vs. 25.4 ± 37.4 months). Almost all patients with portal hyperperfusion were at least school age; however, one 7-month-old patient had portal hyperperfusion. The relationships between the graft type and age, graft volume, GV/SLV, GRWR, GV/SV, and PVF are shown in Table 2. The graft type increased with increasing age. For left lateral segment and S2 monosegment, the graft volume was sufficient for patients according to the GV/SLV and GRWR. The PVF was also appropriate in left lateral and S2 monosegment. In contrast, the PVF was significantly higher in left and right lobe grafts than in left lateral and S2 monosegments, even when an adequate graft size was used according to the GV/SLV and GRWR. Interestingly, the GV/SV in the left and right lobe was smaller than that in left lateral segment and S2 monosegment. These findings suggest that GV/SV might be a useful predictive factor for portal hyperperfusion.

The relationship between the GV/SLV, GRWR, and PVF after reperfusion is shown in Fig. 2. Although the GV/SLV exceeded the standard criterion (≥35%) in all cases, portal hyperperfusion was found in 12 patients

(35.3%). Furthermore, the GRWR also met the standard criterion (≥0.8%) in most patients, although portal hyperperfusion was found in 10 patients (32.3%).

In contrast, the GV/SV showed a significant negative correlation with the PVF after reperfusion, as shown in Fig. 3. Of the 12 recipients with portal hyperperfusion, the GV/SV was less than 1.0 in 11 (91.7%). This suggested that GV/SV might be a more useful predictor of portal hyperperfusion syndrome in LDLT than GV/SLV and GRWR. An ROC analysis of the GV/SV revealed that the best cut-off value for PVF ≥ 250 ml/min/100 g was 0.88 (AUC 0.86, P -value 0.0019). Of the 14 patients with GV/SV < 0.88, 11 (78.6%) developed portal hyperperfusion after reperfusion.

Seventeen recipients without splenectomy at LDLT or any postoperative complications were included in Study 2. Almost all of the graft types in Study 2 were left lateral segments (left lateral segment: 16 cases, right lobe: 1 case) because splenectomy was performed due to portal hyperperfusion in most cases in which the left or right lobe was selected. The relationship between the GV/SV and the period to the normalization of the platelet count (PLT) and total bilirubin (T-Bil) is shown in Fig. 4. Three recipients required more than 30 days until the normalization of the PLT and T-Bil after LDLT. Furthermore, two of three recipients developed persistent thrombocytopenia and hyperbilirubinemia even though they did not experience hyperperfusion after reperfusion. Splenomegaly might, therefore, affect the postoperative course even if the PVF is normal. We also evaluated other bias factors that might have played an important role in postoperative dysfunction, such as the donor's age, intraoperative blood loss and cold and warm ischemia times. However, there were no significant differences between patients with and without persistent hyperbilirubinemia or thrombocytopenia for the donor's age (33.0 ± 9.5 vs. 32.8 ± 5.9 years, P = 0.973), intraoperative blood loss (799.7 ± 461.6 vs. 535.6 ± 335.1 ml, P = 0.430), cold ischemic time (96.0 ± 13.5 vs. 105.6 ± 60.1 h, P = 0.597), or warm ischemic time (4.67 ± 3.06 vs. 3.43 ± 2.03 h, P = 0.571).

Table 1. Characteristics of recipient and graft.

Recipient's and graft's characteristics	n = 37
Age (range), month	81.2 ± 108.1 (3–349)
Gender, no	
Male	11
Female	26
Weight (range), kg	21.0 ± 20.8 (5.5–69.3)
Graft type, no	
Left lateral segment	23
Left lobe	8
Right lobe	4
S2 monosegment	2
Graft volume (range)	
Estimated graft volume, ml	306.1 ± 138.5 (152–687)
Actual graft weight, g	288.9 ± 123.3 (183–662)
Estimated spleen volume (range), ml	402.3 ± 456.0 (42–2 049)
GV/SLV (range), %	75.4 ± 27.0 (35.9–129.6)
GRWR (range), %	2.42 ± 1.23 (0.63–4.57)
GV/SV (range)	1.59 ± 1.19 (0.20–5.26)
PVF after reperfusion (range), ml/min/100 g	225.1 ± 189.9 (41.9–777.8)

Table 2. Characteristics of each graft types.

	Left lateral segment + S2 (n = 25)	Left lobe (n = 8)	Right lobe (n = 4)
Age, months	17.0 ± 18.8	196.5 ± 96.5	251.3 ± 86.2
Graft volume, ml	229.0 ± 43.3	332.6 ± 79.3	576.0 ± 89.6
GV/SLV, %	86.6 ± 18.1	38.2 ± 5.4	50.1 ± 4.1
GRWR, %	3.00 ± 0.81	0.91 ± 0.29	1.00 ± 0.10
GV/SV	2.10 ± 1.12	0.50 ± 0.24	0.57 ± 0.20
PVF, ml/min/100 g	126.7 ± 74.4	397.1 ± 183.3	495 ± 229.6

Table 3. Cut-off values of portal hyperperfusion, thrombocytopenia, and hyperbilirubinemia.

Evaluation outcome	Cut-off point of GV/SV
Predictor of portal hyperperfusion syndrome (ml/min/100 g ≥ 250 ml)	0.88
Postoperative persistent thrombocytopenia (≥30 days)	1.01
Postoperative persistent hyperbilirubinemia (≥30 days)	1.33

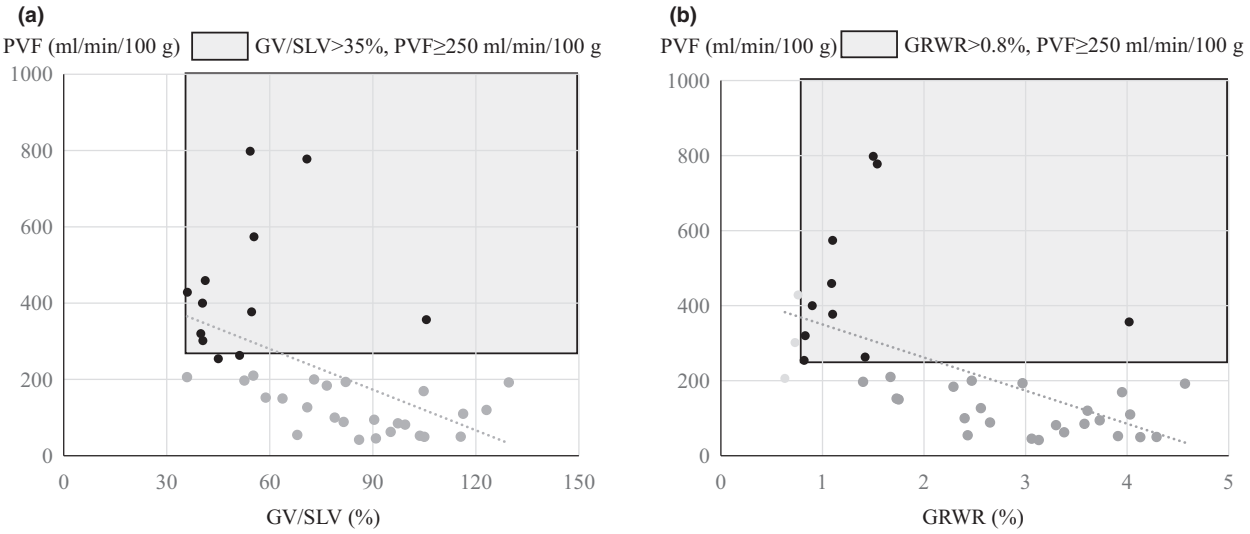

Figure 2 Relationship between GV/SLV, GRWR, and PVF after LDLT. (a) Relationship between GV/SLV and PVF. GV/SLV exceeded the conventional criterion (≥35%) in all cases. However, portal hyperperfusion was found in 12 recipients. (b) Relationship between GRWR and PVF. Three of 37 patients did not meet the standard (<0.8%) criterion. Portal hyperperfusion was found in 10 patients, even though GRWR satisfied standard criteria (≥0.8%). GV/SLV: graft volume-to-standard liver volume ratio, GRWR: graft-to-recipient weight ratio, PVF: portal venous flow, LDLT: living donor liver transplantation.

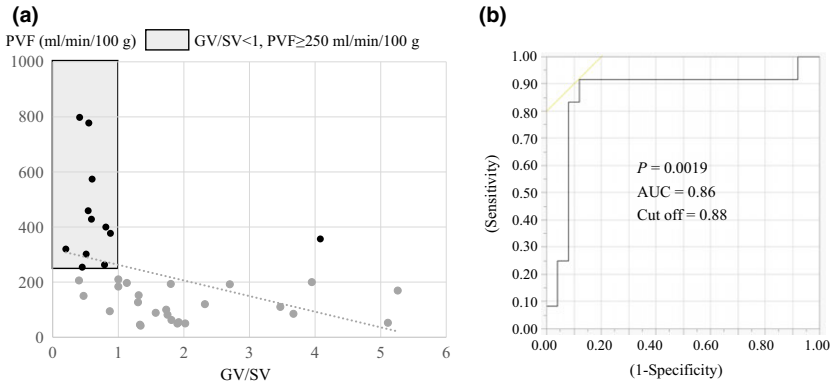

Figure 3 Relationship between GV/SV and PVF after LDLT. (a) The relationship between GV/SV and PVF. Among the 12 patients with portal hyperperfusion, the GV/SV in 11 (91.7%) was <1. (b) ROC curve of GV/SV in PVF ≥ 250 ml/min/100 g of graft after reperfusion. Portal hyperperfusion had a significant correlation with GV/SV. The cut-off value of GV/SV was 0.88. GV/SV: graft volume-to-spleen volume ratio, PVF: portal venous flow, LDLT: living donor liver transplantation.

Regarding the PLT, all three recipients required more than 4 months until it normalized. The periods of time required to achieve a normalization of the PLT in patients with persistent thrombocytopenia (≥30 days) were significantly longer than in those without it (205.7 ± 65.4 vs. 15.2 ± 7.1 days, respectively). In addition, the GV/SV in patients with persistent thrombocytopenia (≥30 days) was significantly lower than in those without it (0.91 ± 0.14 vs. 1.98 ± 1.22, respectively). An ROC analysis of the GV/SV revealed that the best cut-off value for persistent thrombocytopenia (≥30 days) was 1.01 (AUC 0.952, *P* -value 0.0016). Furthermore, the GV/SV in patients with persistent hyperbilirubinemia (≥30 days) was also significantly lower than in those without it (1.03 ± 0.29 vs. 1.98 ± 1.22, respectively). An ROC analysis of the GV/SV revealed that the best cut-off value for persistent hyperbilirubinemia was 1.33 (AUC 0.857, *P* -value 0.021). Although we also evaluated the relationship between the GV/SV and the period to the normalization of the international normalized ratio of prothrombin time (PT-INR), there were no significant differences between the values; the GV/SV in patients with persistent coagulopathy (≥30 days) and in those

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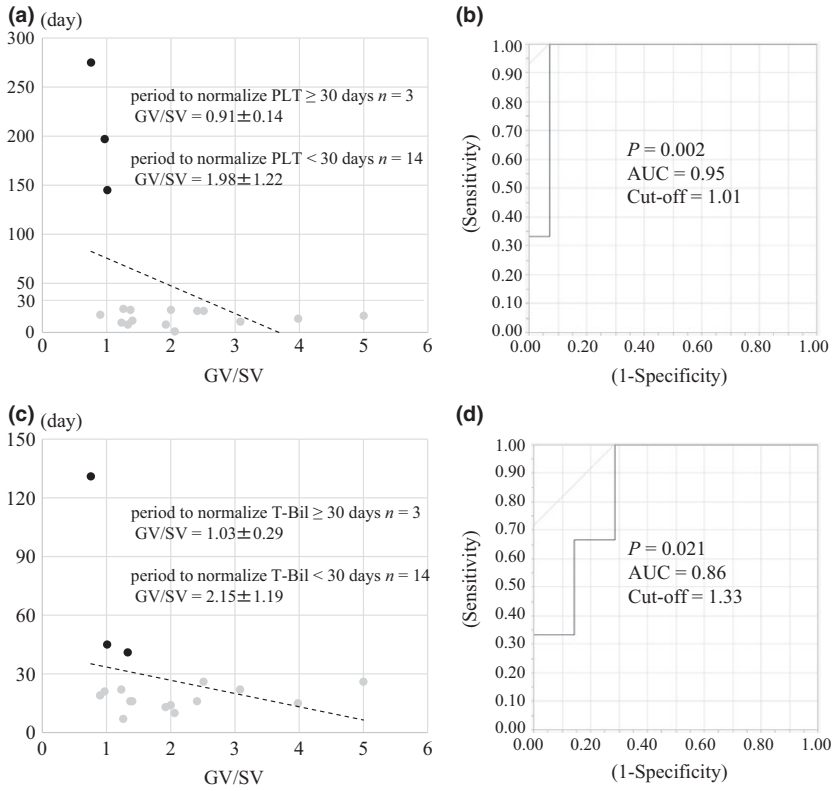

Figure 4 Relationship between GV/SV and post-transplant complications. (a) Relationship between GV/SV and the period to the normalization of PLT after LDLT. In 3 patients, it took more than 30 days to normalize the PLT after LDLT. (b) ROC curve of GV/SV with ≥30 days until normalization of PLT after LDLT. (c) Relationship between GV/SV and the period to the normalization of T-Bil after LDLT. (d) ROC curve of GV/SV with ≥30 days until normalization of T-Bil after LDLT. GV/SV: graft volume-to-spleen volume ratio, PLT: platelet, LDLT: living donor liver transplantation, ROC: receiver operating characteristic, T-Bil: total bilirubin.

without it were 1.74 ± 1.50 and 2.02 ± 1.10, respectively.

Table 3 summarizes all of the cut-off values mentioned above. The GV/SV including all three values was 0.88. Therefore, we suggested a GV/SV < 0.88 to be a new predictor of portal hyperperfusion syndrome after reperfusion and postoperative complications, especially persistent thrombocytopenia and hyperbilirubinemia, in BA patients after LDLT.

In the nine recipients who underwent splenectomy, two of them developed persistent thrombocytopenia, and five of them developed hyperbilirubinemia. However, all of them showed gradual improvement over the subsequent 3 months. Regarding other factors related to portal hyperperfusion syndrome, postoperative massive ascites were found in two cases. These patients had remarkable splenomegaly, and splenectomy was performed at LDLT. While it was difficult to control the massive ascites, the ascites were ultimately successfully managed by conservative therapy. Prolonged encephalopathy, gastrointestinal bleeding, and renal failure were not found in this study.

Discussion

Biliary atresia (BA) is characterized by the complete obstruction of all or part of the extrahepatic bile duct, leading to severe cholestasis and secondary biliary cirrhosis [11]. PHT is a major complication of BA and is present in two-thirds of long-term BA survivors. Panayotis *et al.* reported that the proportions of children with PHT after 10 and 20 years' follow-up were about the same (69% vs. 70%, respectively) [1]. In addition, the spleen size and platelet count may be useful as surrogate markers for the risk of developing complications of PHT [12].

As the number of adult recipients (≥18 years of age) of LDLT increases, graft size mismatch will become a major obstacle. The consequences of using a small graft in a cirrhotic patient with severe PHT are largely unpredictable for adult-to-adult living donor liver

transplantation (ALDLT) [13]. Furthermore, small donor grafts may induce postoperative hyperbilirubinemia and liver injury in recipients that may result in liver regeneration failure [14]. Previous reports have shown that factors other than the graft volume can influence the outcome, including recipient-related factors (disease clinical status and portal hypertension), graft-related factors (donor age, cold and warm ischemia times, and immunological factors), and technical factors (vascular reconstruction and adequate outflow, vascular inflow, and pressure gradients) [15]. In our report, there were no significant differences in other factors, such as the donor age, cold and warm ischemia time and intraoperative blood loss. We also unified the disease definition of biliary atresia and excluded postoperative complications that affected the blood examination results, like hepatic artery thrombosis, intestinal perforation and stenosis of the bile duct.

Portal hypertension following reperfusion and hyperperfusion were reported as the major triggering factors of SFSS [16]. According to systematic review about graft inflow modulation (GIM) in ALDLT, high PVP and/or PVF in the early phase of LDLT is associated with worse outcomes. Furthermore, GIM resulted in a good survival for both graft and recipients, reaching an 84% actuarial rate at 5 years; these results were statistically better than those in patients not undergoing GIM [17]. Therefore, an intraoperative liver graft hemodynamic evaluation is crucial for determining the indication of GIM. Although PVF is considered to play an important role, it is very hard to distinguish between the role of PVP and PVF. Previous reports have established PVP as a reliable predictor of graft failure. In this regard, the intraoperative measurement of PVP and PVF can help avoid potential postoperative sinusoidal damage [18]. In our institution, we evaluate the intraoperative PVP if a catheter can be inserted into the mesenteric vein. However, the PVP data were so small that we were unable to obtain them in this case.

The PVF consists of three factors: outflow, intrahepatic vascular resistance, and hemodynamic status [8]. The outflow is affected by the construction of the hepatic vein. The intrahepatic vascular resistance is related to the size and quality of the graft. The hemodynamic status is related to the spleen volume and the development of collateral vessels [8,19]. Although the GV/SLV and GRWR are generally accepted as important predictors of the adequacy of the post-transplant liver function (GV/SLV $\geq$ 35%, GRWR $\geq$ 0.08%) [4,6], we have encountered some patients whose post-transplant course was not good despite meeting these criteria. In our present study, all of the estimated GV/SLV values met the criterion ($\geq$35%), but portal hyperperfusion was still found in 12 recipients (35.3%). Furthermore, most of the estimated GRWR also met the criterion ($\geq$0.8%), but portal hyperperfusion was still found in nine recipients (26.5%). This suggests that GV/SLV and GWRW are not always adequate for selecting grafts to prevent portal hyperperfusion after reperfusion. New preoperative factors contributing to the PVF related to splenomegaly should be determined for BA patients.

Cheng *et al.* revealed that the spleen volume was significantly associated with excessive PVF as measured by intraoperative Doppler ultrasonography after reperfusion, and a graft-to-recipient spleen size ratio < 0.6 indicated a high possibility of portal hyperperfusion syndrome in ALDLT [7]. Furthermore, Gyoten *et al.* revealed that a spleen volume-to-graft volume ratio > 0.95 was a good predictor of a high PVP (>20 mmHg) after reperfusion in ALDLT, regardless of the MELD score, Child-Pugh score, or graft type [8]. However, there are no reports on the relationship between the GV/SV and PVF for recipients, including children. In our early reports for BA recipients, including children, the GV/SV showed a significant correlation with the PVF after reperfusion. The cut-off value for portal hyperperfusion of $\geq$250 ml/min/100 g was 0.88. A GV/SV < 0.88 was a good predictor of portal hyperperfusion syndrome after reperfusion and seems to be another useful parameter that takes into account the recipient's portal hemodynamic status. If the GV/SV is <0.88, we should consider splenectomy or splenic artery ligation to modulate and prevent excessive portal graft flow, as previously reported [20,21]. Although splenectomy is favorable for overcoming SFSS in LDLT, we should pay attention to overwhelming post-splenectomy infection (OPSI), which may progress from a mild flu-like illness to fulminant sepsis in a short time period. The Centers for Disease Control and Prevention recommend that patients before splenectomy receive the 23-valent pneumococcal vaccine to prevent OPSI, as this covers approximately 73–90% of strains causing OPSI [22]. In our previous study, administering the 23-valent pneumococcal vaccine before splenectomy and the oral administration of penicillin was sufficient to prevent OPSI [23].

If the possibility of splenectomy can be predicted preoperatively using GV/SV < 0.88, a 23-valent pneumococcal vaccine can be given beforehand for all patients with splenectomy. SFSS is known as a clinical condition that is associated with persistent hyperbilirubinemia and coagulopathy. Some patients have shown liver dysfunction despite meeting the graft criteria and having no complications. Furthermore, persistent thrombocytopenia has

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been found in some patients. Thrombocytopenia in patients with cirrhosis has been reported to be caused by an increased PLT pool in the enlarged spleen [24]. However, in most cases, thrombocytopenia in the early period after LT recovers with the restoration of the graft hepatic function. This is caused by portal flow recruitment due to the low-resistance vascular bed of the "new liver" [9]. In addition, the spleen volume has been reported to gradually decrease [25]. Nevertheless, we encountered some patients with persistent thrombocytopenia and splenomegaly even several years after LDLT. In our previous study, 15.8% patients suffered from persistent thrombocytopenia. Accordingly, we also evaluated the relationship between the GV/SV and the post-transplant course, such as thrombocytopenia, hyperbilirubinemia, and coagulopathy. In this way, we established predictive factors for the post-transplant course. The GV/SV showed a significant correlation with persistent thrombocytopenia and hyperbilirubinemia.

Interestingly, two of three recipients developed persistent hyperbilirubinemia and thrombocytopenia despite portal hyperperfusion after reperfusion not being found. This suggests that splenomegaly might cause adverse effects after LDLT, even if the PVF is normal. Previous reports have suggested the several causes of such deterioration in the liver function. For example, some cytokines produced in the spleen may ameliorate the liver function. In an animal model, transforming growth factor-beta 1 (TGF-β1), which is released from the spleen, was shown to inhibit liver regeneration and promote liver fibrosis and apoptosis [26]. Furthermore, platelet-derived serotonin has recently been shown to be important in liver regeneration [27]. Moreover, the expression of hepatocyte growth factor activator inhibitor (HGFAI) was enhanced in the enlarged spleen and reduced the activity of HGFA in the liver [28].

In our report for BA recipients, the cut-off values for persistent thrombocytopenia (≥30 days) was 1.01, while that for persistent hyperbilirubinemia was 1.33. In contrast, the PT-INR had no correlation with the GV/SV. Judging from our findings, GVSV < 0.88 was the most useful cut-off value for portal hyperperfusion after reperfusion and persistent thrombocytopenia and hyperbilirubinemia after LDLT, as this value covers the cut-off values for all of these complications. One limitation associated with this study is the small sample size and the fact that these findings are all based on a single center experience. To clarify the usefulness of GV/SV, the accumulation of further cases is needed in the future.

In conclusion, we initially evaluated the relationship between the GV/SV and PVF after reperfusion and the post-transplant course in BA patients who underwent LDLT, including children. The GV/SV was significantly correlated with portal hyperperfusion and persistent thrombocytopenia and hyperbilirubinemia after LDLT. A GV/SV < 0.88 predicts portal hyperperfusion of ≥250 ml/min/100 g graft and persistent thrombocytopenia and hyperbilirubinemia ≥ 30 days after LDLT.

Authorship

YT: designed research/study, performed research/study, analyzed data, and wrote the paper. TM: designed research/study, analyzed data, and revised the manuscript. KY: collected data. YY: collected data. MH: collected data. TT: revised the manuscript.

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Conflicts of interest

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