



Future liver remnant hypertrophy rate in portal vein embolization before left trisectionectomy: a retrospective cohort study

Yasuyuki Onishi¹ · Hiroyoshi Isoda¹ · Tsuyoshi Ohno¹ · Hironori Shimizu¹ · Kotaro Shimada¹ · Kojiro Taura² · Etsuro Hatano² · Yuji Nakamoto¹

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Abstract

Purpose Reports on the future liver remnant (FLR) hypertrophy rate in patients undergoing portal vein embolization (PVE) before left trisectionectomy are sparse. This study aimed to assess the FLR hypertrophy rate in patients undergoing PVE before left trisectionectomy.

Methods Between January 2010 and June 2021, 30 patients (22 men and eight women; mean age, 65.7 years) underwent PVE, mainly using gelatin sponge, before left trisectionectomy. The preoperative diagnosis was cholangiocarcinoma in 28 patients and colorectal liver metastases in two patients. The FLR hypertrophy rate, increase in the FLR volume (FLRV) ratio (the ratio of the FLRV to the total liver volume), and complications were evaluated. The patients were further divided into two groups: one group of patients with left portal vein stenosis or occlusion before PVE ($n=12$) and another without left portal vein stenosis or occlusion before PVE ($n=18$). The FLR hypertrophy rate and increase in the FLRV ratio were compared between the two groups.

Results The FLR hypertrophy rate and increase in the FLRV ratio were 31.3% and 6.9%, respectively. One major complication, cholangitis, developed; however, its association with PVE was unclear. The difference in the FLR hypertrophy rate and the increase in the FLRV ratio between the two groups of patients was statistically insignificant.

Conclusion PVE before left trisectionectomy is effective in achieving FLR hypertrophy. PVE before left trisectionectomy was equally effective in patients with left portal vein stenosis or occlusion as compared to those without. The complication rates were acceptable.

Keywords Future liver remnant hypertrophy · Interventional radiology · Left trisectionectomy · Portal vein embolization

Introduction

Curative surgery of hepatobiliary malignancies occasionally requires radical hepatic resection, and a small future liver remnant (FLR) is known to be a risk factor of postoperative liver failure [1]. Portal vein embolization (PVE) is widely accepted as an effective preoperative procedure to induce the hypertrophy of an insufficient FLR [2]. In most studies of PVE, the study population included all patients

who underwent PVE or was limited to those undergoing right lobectomy. To date, only a few studies with a small sample size have reported the FLR hypertrophy rate of patients undergoing PVE before left trisectionectomy [3, 4]. Left trisectionectomy is a challenging surgery with the highest 90-day mortality (10.3%) among the various types of hepatobiliary pancreatic surgeries [5], and postoperative liver failure is a common complication [6]. PVE before left trisectionectomy involves the embolization of the left portal vein, which seems to be technically more difficult than the embolization of the right portal vein as per our experience. Additionally, hilar cholangiocarcinoma was reported to involve the left portal vein more frequently than the right portal vein [7], which corresponds to an occasional involvement of the left portal vein in patients undergoing PVE before left trisectionectomy [4]. It is not known whether portal vein invasion has an impact on the FLR hypertrophy

✉ Yasuyuki Onishi
goforawalktoday@yahoo.co.jp

¹ Department of Diagnostic Imaging and Nuclear Medicine, Graduate School of Medicine, Kyoto University, 54 Shogoin-kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan

² Department of Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

effect of PVE. The objective of this study was to assess the FLR hypertrophy rate in patients undergoing PVE before left trisectionectomy. We also aimed to compare the FLR hypertrophy effect of PVE in patients with and without left portal vein severe stenosis or occlusion.

Methods

Patients

The institutional review board approved this retrospective study with a waiver of informed consent. We performed a retrospective cohort study on patients who underwent PVE before left trisectionectomy at our hospital from January 2010 to June 2021. Patients were excluded if their clinical information or contrast-enhanced computed tomography (CT) data, before and after PVE, were not available. During the study period, thirty patients (22 men and 8 women) underwent PVE before left trisectionectomy, and no patient was excluded or included additionally. The mean age at PVE was 65.7 years (range, 33–82 years). The preoperative diagnosis was cholangiocarcinoma in 28 patients, and colorectal liver metastases in 2 patients. In addition to left trisectionectomy, caudate lobectomy was planned in all but one patient with colorectal liver metastases, and pylorus-preserving pancreaticoduodenectomy was planned in two patients. In one patient with colorectal liver metastases, partial resection of the posterior lobe of the liver was also planned. Chemotherapy was performed in four patients before PVE; two of them had cholangiocarcinoma and the other two had colorectal liver metastases; 26 patients did not receive chemotherapy before PVE. The Child–Pugh score, peak total bilirubin level, and indocyanine green clearance rate (ICGK) before PVE were selected as indicators of liver function based on previous reports [8–10]. Detailed information on the study population is summarized in Table 1.

Indications for portal vein embolization and procedure

PVE was indicated for patients whose FLR volume ratio to total liver volume was less than 30%. When the ratio was 30% or greater, PVE was indicated in patients with decreased liver function. Decreased liver function was not clearly defined; however, one indication for PVE was an estimated ICGK value in the liver remnant of less than 0.050. Other related factors were also evaluated to determine the presence or absence of decreased liver function. These factors included the albumin and total bilirubin levels, platelet count, prothrombin time, and international normalized ratio. Hepatopancreaticoduodenectomy was another indication of PVE when major liver resection was performed. In all cases, the indication for PVE was finally confirmed by our team of surgeons, physicians, and radiologists.

PVE was performed by seven interventional radiologists with 11–33 years of experience in abdominal interventional radiology. In all patients, the right anterior or left portal vein branches were percutaneously punctured under ultrasound guidance using an 18-gauge or a 21-gauge needle, and a 4–7-French sheath with a tip marker was placed in the portal vein. A 4- or 5-French shepherd hook catheter was advanced to perform portography. A microcatheter was inserted to the right anterior and left portal vein or its branches, and embolization was performed. Branches to the caudate lobe were also embolized at the operator's discretion. From January 2010 to June 2012, the embolic agents for PVE were gelatin sponge particles (Gelpart, Nippon Kayaku) mixed with iodized oil (Lipiodol Ultra-Fluide, Terumo), and absolute ethanol ($n=4$). In this period, after selection of a target portal vein, a small amount of absolute ethanol was injected into the target portal vein until the blood flow in the branch reduced. Subsequently, 1-mm or 2-mm gelatin sponge particles mixed with iodized oil were used to occlude the target portal vein until stasis of the blood flow was obtained. After July 2012, gelatin sponge particles mixed with iodized oil

Table 1 Characteristics of patients undergoing portal vein embolization ($n=30$)

Characteristics	Value
Sex, male/female	22/8
Age (mean, range)	65.7, 33–82
Preoperative diagnosis	
Cholangiocarcinoma	28
Colorectal liver metastases	2
History of chemotherapy, yes/no	4/26
Child–Pugh score before PVE (mean, range)	5.9, 5–7
Peak total bilirubin before PVE (mean, median, range) (mg/dl)	6.5, 3.1, 0.7–41.8
Indocyanine green clearance rate before PVE (mean, range)	0.155, 0.094–0.283

PVE portal vein embolization

were used as embolic agents ($n=26$). After embolization of the target portal vein, microcoils were placed in the origin of the right anterior or left portal vein or its branches to avoid recanalization and migration of embolic agents at the operator's discretion.

CT scans before PVE revealed severe stenosis (defined as a diameter of 3 mm or less) and occlusion of the left portal vein due to tumor invasion in 10 and 2 patients, respectively. In contrast, severe stenosis or occlusion of the right portal vein or right anterior or posterior portal vein was not found in any patient. In a group of 12 patients with left portal vein severe stenosis or occlusion, embolization of the left portal vein was not performed in 6 patients because the left portal vein could not be selected with a catheter or because the left portal vein was not opacified on portography. In a patient without portal vein severe stenosis or occlusion, embolization of the left portal vein was not performed because the flow reversal of the left portal vein was observed due to a large hemangioma in the lateral segment of the liver. In the remaining 23 patients, the embolization of the left portal vein was performed. The embolization of the right anterior portal vein was performed in all patients.

Definition

The total liver volume (TLV) was defined as the total functional liver volume, which excluded tumors and other elements such as portal veins and hepatic veins. The FLRV ratio was defined as: $\frac{\text{FLRV}}{\text{TLV}} \times 100$.

The FLR hypertrophy rate was defined as : $\frac{\text{FLRV after PVE} - \text{FLRV before PVE}}{\text{FLRV before PVE}} \times 100$.

The increase in the FLRV ratio was defined as: (FLRV ratio after PVE)– (FLRV ratio before PVE).

Liver volumetry

Contrast-enhanced CT was performed both before and after PVE. Pre- and post-PVE CT studies were performed approximately 2 weeks before (mean, 15.2 days; range, 3–52 days) and 3 weeks after PVE (mean, 22 days; range, 18–34 days), respectively. CT images were obtained with a 16- to 320-detector row CT scanner (Aquilion 32, Aquilion 64, Aquilion Prime, Aquilion One; Canon Medical Systems Corporation). The contrast dose was at least 600 mgI/kg. A bolus-tracking system was used to obtain images at the appropriate time. The region of interest cursor for bolus tracking was placed over the aorta at the level of the celiac axis, and the trigger threshold was set at 200 HU. Unenhanced and multiphase contrast-enhanced images were obtained. Portal venous phase images obtained 60 s after the trigger with 1-mm slice thickness were used for liver

volumetry on a computer workstation (Synapse Vincent; Fujifilm Medical). The following elements were excluded from the liver volume: the portal vein and its branches, hepatic vein and its branches, and inferior vena cava. Hepatic tumors were also excluded when they were larger than 1 cm in diameter. The border between the FLR and non-FLR was traced by referring to the portal and hepatic veins. After PVE, the border was traced mainly based on the accumulation of iodized oil in the embolized area. To ensure consistent border tracing, pre-PVE CT images were carefully referred to during border tracing on post-PVE images. The caudate lobe was not included in the FLR in 29 patients; it was included in the FLR in one patient with colorectal liver metastasis. A board-certified radiologist with 10 years of experience in abdominal imaging performed volumetry of the liver. The TLV, FLRV, volume of the anterior liver segment, and volume of the left liver lobe were assessed on pre- and post-PVE CT scans. Patients were classified into two groups: a group with left portal vein severe stenosis or occlusion ($n=12$) and a group without left portal vein severe stenosis or occlusion ($n=18$). Liver volumes were also assessed for each group.

Study endpoints

The endpoints of this study were the FLR hypertrophy rate, increase in the FLRV ratio, complications of PVE, and changes in laboratory parameters. In addition, the FLR hypertrophy rate and the increase in the FLRV ratio were

evaluated in the two groups. Among the 12 patients with left portal vein severe stenosis or occlusion, the FLR hypertrophy rate and the increase in the FLRV ratio were evaluated in 6 patients who underwent embolization of the left portal vein and 6 patients who did not undergo embolization. Complications and changes in laboratory parameters were assessed by reviewing electronic medical records, interventional radiology records, and findings on post-PVE CT, and complications related to PVE that occurred before surgery or within 1 month after PVE were noted. Complications were categorized as minor and major based on the Society of Interventional Radiology guidelines [11]. Laboratory parameters, such as total bilirubin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels, and the percentage of prothrombin activity (PT%) were evaluated. The highest values of total bilirubin, AST, and ALT levels and the lowest value of the PT% within 1 week after PVE were also recorded. Additionally, the number of patients undergoing left trisectionectomy after PVE was recorded.

Statistical analysis

Statistical analyses were performed using JMP software (version 15.2, SAS institute, Cary, NC, USA). Statistical significance was set at $p < 0.05$. Based on pre-PVE and post-PVE CT images, the volumetric differences (the TLV, FLRV, ratio of the FLRV, ratio of the left liver lobe volume, and ratio of the right anterior liver segment volume) between patients with left portal vein severe stenosis or occlusion and those without it were calculated using the Mann–Whitney U test. Moreover, the differences in the FLR hypertrophy rate and increase in the FLRV ratio in the two groups were also calculated using the Mann–Whitney U test.

Results

Liver volume before and after portal vein embolization

The liver volume before PVE is shown in Table 2. The ratio of the left liver lobe volume to the TLV was lower in patients with left portal vein severe stenosis or occlusion (20.7%) than in patients without left portal vein severe stenosis or occlusion (26.5%), and the difference was statistically

significant ($p = 0.033$). Conversely, the ratio of the right anterior liver segment volume to the TLV was higher in patients with left portal vein severe stenosis or occlusion (45.2%) than in patients without left portal vein severe stenosis or occlusion (40.1%), although the difference was not statistically significant ($p = 0.079$).

The liver volume after PVE and changes in the liver volume are shown in Table 3. The FLR hypertrophy rate and increase in the FLRV ratio were 31.3% and 6.9%, respectively. The difference in the FLR hypertrophy rate and increase in the FLRV ratio between patients with left portal vein severe stenosis or occlusion and those without were not statistically significant ($p = 0.626$ and 0.849 , respectively) (Figs. 1, 2).

Of the 12 patients with severe stenosis or occlusion of the left portal vein, six who underwent embolization of the left portal vein had an FLR hypertrophy rate and increase in FLRV ratio of 27.5% (range, 18.4–37.6%) and 7.4% (range, 3.9–11.0%), respectively, and the remaining six who did not undergo embolization of the left portal vein had an FLR hypertrophy rate and increase in FLRV ratio of 30.7% (range, 14.9–45.8%) and 6.8% (range, 3.5–12.7%), respectively.

Table 2 Liver volumetry before portal vein embolization

	All patients ($n = 30$)	Patients with left PV severe stenosis or occlusion ($n = 12$)	Patients without left PV severe stenosis or occlusion ($n = 18$)	p
TLV (mL) (mean, range)	1229, 678–2092	1194, 678–1828	1252, 810–2092	.485
FLRV (mL) (mean, range)	384, 175–649	386, 186–605	384, 175–649	.916
Ratio of the FLRV to the TLV (%) (mean, range)	31.3, 15.8–38.8	32.2, 25.5–36.8	30.8, 15.8–38.8	.816
Ratio of the left liver lobe volume to the TLV (%) (mean, range)	24.2, 9.6–36.5	20.7, 9.6–32.8	26.5, 10.6–36.5	.033
Ratio of the right anterior liver segment volume to the TLV (%) (mean, range)	42.1, 27.1–62.5	45.2, 33.1–62.5	40.1, 27.1–54.8	.079

FLR future liver remnant, FLRV future liver remnant volume, PV portal vein, TLV total liver volume

Table 3 Liver volumetry after portal vein embolization and change in the liver volume

	All patients ($n = 30$)	Patients with left PV severe stenosis or occlusion ($n = 12$)	Patients without left PV severe stenosis or occlusion ($n = 18$)	p
Total liver volume (mL) (mean, range)	1318, 735–2372	1262, 735–1827	1356, 875–2372	.320
FLRV (mL) (mean, range)	500, 230–799	497, 230–747	503, 284–799	.849
FLRV ratio (%) (mean, range)	38.2, 21.8–48.5	39.3, 31.3–44.5	37.5, 21.8–48.5	.597
FLR hypertrophy rate (%) (mean, range)	31.3, 10.5–62.3	29.1, 14.9–45.8	32.8, 10.5–62.3	.626
Increase in the FLRV ratio (%) (mean, range)	6.9, 2.3–12.7	7.1, 3.5–12.7	6.7, 2.3–11.6	.849

FLR future liver remnant, FLRV future liver remnant volume, PV portal vein

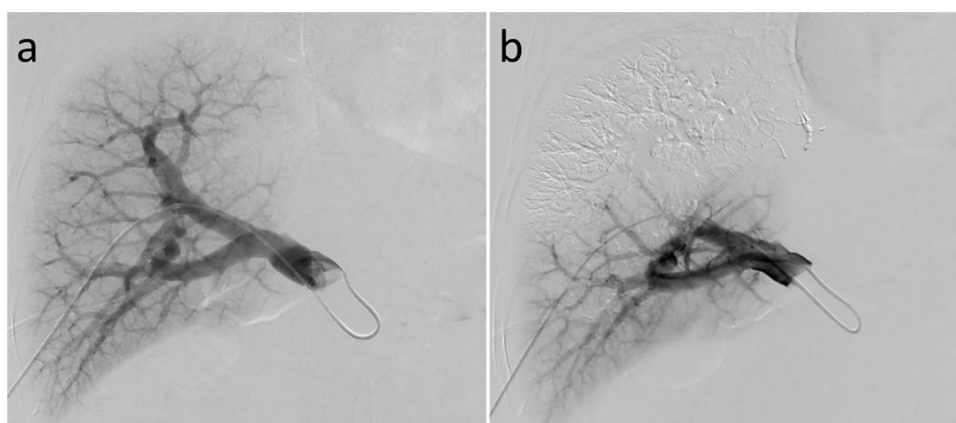


Fig. 1 50-year-old man with rectal cancer metastases to the liver who underwent portal vein embolization (PVE) before left trisectionectomy. The patient had no left portal vein severe stenosis or occlusion on pre-PVE computed tomography. **a** Portal venography before PVE reveals that the left, right anterior, and right posterior portal veins are

patent. **b** Portal venography after PVE using gelatin sponge particles mixed with iodized oil and coils reveals the occlusion of the left and right anterior portal veins. The future liver remnant hypertrophy rate is 30.3% and the increase in the future liver remnant volume ratio is 7.8%

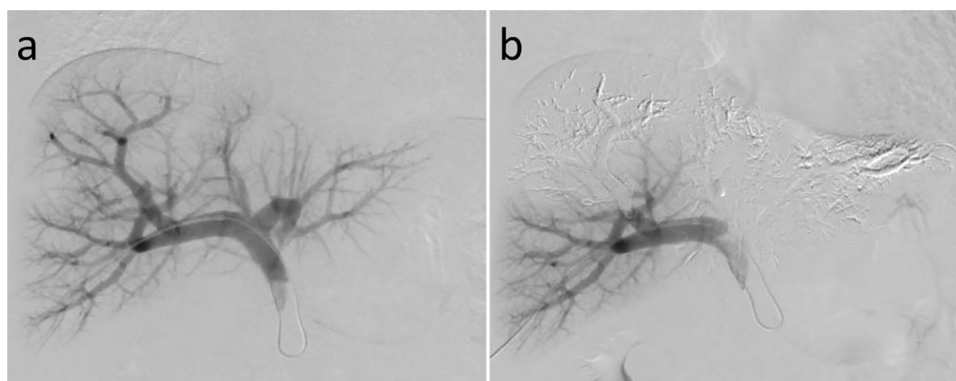


Fig. 2 77-year-old woman with cholangiocarcinoma who underwent portal vein embolization (PVE) before left trisectionectomy. The patient had left portal vein severe stenosis on pre-PVE computed tomography. **a** Portal venography before PVE reveals the right anterior and posterior portal veins. The left portal vein is not opacified

due to the invasion of cancer. **b** Portal venography after PVE using gelatin sponge particles mixed with iodized oil reveals the occlusion of the right anterior portal vein. The future liver remnant hypertrophy rate is 43.4% and the increase in the future liver remnant volume ratio is 12.3%

Change in laboratory parameters

The mean of the highest value of the total bilirubin level within 1 week after PVE was 1.3 mg/dL (range, 0.5–3.3), and that of the AST level was 67.6 IU/L (range, 23–233), and that of the ALT level was 88.1 IU/L (range, 18–230), and the mean of the lowest value of PT% was 83.7% (range, 58–127).

Transient abdominal pain and fever

Abdominal pain occurred in seven patients during and after PVE. All patients showed transient conditions and were managed with analgesics. Fever ($> 38^{\circ}\text{C}$) occurred in 13

patients on the same day or the day after PVE. All of them showed transient conditions that resolved within a few days. This transient fever was considered as post-embolization syndrome.

Major complications

In one patient, cholangitis developed 16 days after PVE, which was successfully managed by endoscopic nasobiliary drainage tube placement in the left liver lobe. The correlation between PVE and cholangitis was unclear.

Minor complications

In three patients, cholangitis developed 8 or 9 days after PVE, which was successfully managed with antibiotics. Fever ($> 38^{\circ}\text{C}$) of unknown cause occurred in three patients more than 1 week after PVE, and the fever for all of them improved with antibiotics and analgesics. In one patient, a vascular sheath was mistakenly placed into a non-drained and dilated intrahepatic bile duct during PVE. The sheath was exchanged with a percutaneous transhepatic biliary drainage (PTBD) tube to decompress the biliary system. One week later, CT revealed the dislodgement of the PTBD tube into the peritoneal cavity and was removed.

Left trisectionectomy after PVE

After PVE, 27 patients underwent surgery; of these, 21 underwent left trisectionectomy. In six patients, left trisectionectomy was not performed owing to the following intraoperative findings: peritoneal dissemination ($n=4$), lymph node metastases ($n=1$), and inflammatory reaction suggestive of benign disease ($n=1$). In two patients among the 27 who underwent surgery, the FLRV ratio after PVE was less than 30%, and recanalization of the left portal vein was observed on post-PVE CT; thus, a second PVE was performed before surgery; in the remaining 25 patients, PVE was performed once before surgery. In three patients, surgery was abandoned because of the following post-PVE CT findings: progression of cancer and low FLRV ($n=1$) and progression of cancer ($n=2$).

Discussion

Based on our experience, we have an impression that embolization of the left portal vein is more difficult than that of the right portal vein because the reflux of the gelatin sponge occurs easily during the embolization of the left portal vein. The reason remains unclear; however, we believe that it is due to the running course of the left portal vein, from dorsal to ventral, which is against the gravity when the patient is in a supine position. Thus, we speculated that the FLR hypertrophy rate of PVE before left trisectionectomy may be lower than that before right lobectomy. In this study, the FLR hypertrophy rate and increase in the FLRV ratio of PVE before left trisectionectomy were 31.3% and 6.9%, respectively. Many studies have reported various FLR hypertrophy rates of PVE before right lobectomy, ranging from 23.3 to 74% [10, 12–16], whereas the reported increase in the FLRV ratio of PVE before right lobectomy ranged from 7 to 13% [17]. This study suggests that the FLR hypertrophy effect of PVE before left trisectionectomy is not different from that before right lobectomy. One study reported an increase in the

FLRV ratio from 36.8 to 43.4% in nine patients with PVE before left trisectionectomy [4]. Another study reported an FLR hypertrophy rate of 32.8% and 42.5% in two patients who underwent PVE before left trisectionectomy [3]. These results also support the effectiveness of PVE before left trisectionectomy.

Portal vein tumor invasion or tumor thrombosis was reported to be a risk factor for a lower FLR hypertrophy rate in PVE before right lobectomy [10]. However, in this study, there was no statistically significant difference ($p=0.626$) observed in the FLR hypertrophy rate between patients with left portal vein severe stenosis or occlusion and those without. The ratio of the left liver lobe volume to the TLV was 20.7% and 26.5% in patients with and without left portal vein severe stenosis or occlusion, and both the ratios were lower than that observed in normal adults (31%) [18]. Most patients in this study had cholangiocarcinoma, and the lower values of the left liver lobe volume ratio in these patients can be explained by the left liver lobe atrophy caused by bile duct obstruction, with or without portal vein compromise, which is occasionally observed in patients with cholangiocarcinoma [19]. In contrast, the ratio of the right anterior liver segment volume to the TLV was 45.2% and 40.1% in patients with and without left portal vein severe stenosis or occlusion, and both the ratios were higher than that observed in normal adults (37%) [18]. This difference is probably due to compensatory hypertrophy of the right anterior liver segment consequential to left liver lobe atrophy. Since the ratio of the right anterior liver segment volume to the TLV (42.1%) was larger than that of the left liver lobe volume to the TLV (24.2%), and since the left liver lobe was atrophic on pre-PVE CT because of tumor invasion, it is speculated that the embolization effect of the right anterior portal vein is much greater than that of the left portal vein in PVE before left trisectionectomy. This explains why there was no statistically significant difference in the FLR hypertrophy rate between the two patient groups. Among the 12 patients with left portal vein severe stenosis or occlusion, the FLR hypertrophy rate was not much different between the 6 patients who underwent embolization of the left portal vein (27.5%) and the 6 patients who did not undergo embolization of the left portal vein (30.7%). This result is also consistent with the above speculation.

Regarding laboratory parameter changes, the mean of the highest value of total bilirubin, AST, and ALT levels were 1.3 mg/dl, 67.6 IU/L, and 88.1 IU/L, respectively. The mean of the lowest value of the PT% was 83.7%. This result shows a mild inflammatory reaction induced by gelatin sponge particles, which is consistent with the findings of a previous report [20].

A major complication, cholangitis, was observed in one patient (3.3%). However, cholangitis developed 16 days after PVE, and its association with PVE remains unclear. The

reported incidence of a major complication related to PVE was 0.76–1.9%, and the most frequent complications were portal vein thrombosis, hepatic abscess, and bleeding [9]. This study indicates that the complication rate of PVE before left trisectionectomy is not much higher than that of right hepatectomy.

This study has some limitations including its retrospective design and small sample size. It was conducted at a single center, and the embolic materials used for the surgical procedures were inconsistent. In this study, gelatin sponge was the main embolic agent used; other agents such as ethanol and N-butyl cyanoacrylate, were not used. Therefore, further studies are needed to evaluate the FRL hypertrophy rate when other embolic agents are used and to identify the factors that affect FLR hypertrophy rate.

In conclusion, in patients who underwent PVE before left trisectionectomy, the FLR hypertrophy rate was 31.3%, and the increase in the FLRV ratio was 6.9%. There was no significant difference observed in the FLR hypertrophy rate and increase in the FLRV ratio between patients with left portal vein severe stenosis or occlusion and those without, showing that PVE was equally effective in the two groups. All complications were managed successfully, and the complication rates were acceptable.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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