Original Article

Portal vein embolization with ethylene-vinyl alcohol copolymer for contralateral lobe hypertrophy before liver resection: safety, feasibility and initial experience

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Background: To report our preliminary experience with preoperative portal vein embolization (PVE) using liquid ethylene vinyl alcohol (EVOH) copolymer.

Methods: Retrospectively review of patients with primary or secondary liver malignancies scheduled for extensive hepatectomy after the induction of future liver remnant (FLR) hypertrophy by right or left PVE with EVOH as the only embolic agent between 2014 and 2018 at two academic centers. Cross-sectional imaging liver volumetry data obtained before and 3–6 weeks after PVE were used to assess the FLR volume (FLRV) increase, degree of FLR hypertrophy and the FLR kinetic growth rate (KGR).

Results: Twenty-six patients (17 males; mean age, 58.7±11 years; range, 32–79 years) were included. The technical and clinical success rate was 100%. PVE produced adequate FLR hypertrophy in all patients. Embolization occurred in all targeted portal branches and in no non-target vessels. The %FLRV increased by 52.9%±32.5% and the degree of FLR hypertrophy was 16.7%±6.8%. The KGR was 4.4%±2.0% per week. Four patients experience minor complications after PVE which resolved with symptomatic treatment. The resection rate was 84.5%. One patient died during surgery for reasons unrelated to PVE.

Conclusions: Preoperative PVE with EVOH copolymer is feasible, safe, and effective in inducing FLR hypertrophy.

Keywords: Portal vein embolization (PVE); Ethylene vinyl alcohol copolymer; Onyx®; hepatectomy; liver cancer; future liver remnant (FLR)

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Introduction

The optimal treatment for patients with primary or secondary liver malignancies is tumor resection with negative margins (1). However, extensive hepatectomy carries a risk of life-threatening liver failure (2). Portal vein occlusion performed before hepatectomy takes advantage of the unique regenerative potential of hepatic tissue by redirecting blood toward the liver that will remain after surgery, or future liver remnant (FLR), which then undergoes hypertrophy (3). This technique has made

hepatectomy possible in patients with very small pre-occlusion FLRs. Occlusion can be achieved by portal vein ligation or portal vein embolization (PVE). PVE has produced high technical and clinical success rates with low morbidity and, compared to ligation, larger FLR increases and shorter hospital stays (4-7).

No randomized trials are available to determine which embolic agent is optimal for PVE. A mixture of *N*-butyl-cyanoacrylate (NBCA) and ethiodized oil is safe and effective according to a 2018 review of Level IIa cohort studies (8). However, the rapid polymerization and strong adhesive properties of NCBA may result in unpredictable embolization, with a risk of complications such as non-target vessel occlusion, venous migration, and catheter blockage or retention (9). Moreover, the strong inflammatory reaction induced by NBCA may raise challenges during the surgical resection (10).

Ethylene-vinyl alcohol (EVOH) copolymer (Onyx® LES, Covidien, Plymouth, MN) is a non-adhesive liquid embolic agent whose slower solidification rate compared to NBCA may improve embolization predictability. EVOH is dissolved in dimethyl sulfoxide (DMSO), and micronized tantalum powder is suspended in the mixture to provide contrast for fluoroscopy. The occlusion obtained is permanent. EVOH has been found effective and safe for treating cerebral arteriovenous malformations, type II endoleaks, hemoptysis, renal angiomyolipomas, and for peripheral hemostasis (11-17). When used for PVE, EVOH seemed to result in faster growth of FLR compared to other embolic agents (18).

Here, our objective was to assess the efficacy and safety of PVE performed with EVOH only, based on a retrospective review of patients managed at two centers.

Methods

Ethical statement

According to institutional policy, approval from our Institutional Review Board was not required and the informed patient consent requirement was waived owing to the investigation's retrospective nature. All methods were carried out in accordance with relevant guidelines and regulations.

Patients

The databases of two academic centers were searched for patients scheduled between April 2014 and June 2018 for major hepatectomy to treat primary or secondary liver cancer, with previous PVE due to a small FLR. In each patient, the decision to perform hepatic resection surgery after PVE was taken by a multidisciplinary tumor board including a radiologist, a surgeon, and an oncologist. At both centers, the smallest acceptable FLR was 25% in patients without and 40% in patients with an underlying liver disease (19-23).

Investigations related to PVE

Pre-embolization workup

Abdominal computed tomography (CT) or magnetic resonance imaging (MRI) was performed in each patient before PVE (24) (*Figure 1*). The portal phase was used to assess portal vein anatomy, hepatic segmentation as described by Couinaud, the extent of hepatic and extra-hepatic involvement by the malignancy, and the presence of tumor in the FLR (25). Total tumor volume (TV), FLR tumor volume (FLRTV), embolized liver tumor volume (ELTV), FLR volume (FLRV), total liver volume (TLV), and embolized liver volume (ELV) were measured after exclusion of the large vessels and major fissures. The percentage of FLR (%FLR) was computed as the tumor-free FLR volume over the tumor-free liver volume according to the following formula (26).

Post-embolization liver volumetry

The above-defined volumes were measured again by CT or MRI 3 to 4 weeks after PVE (*Figure 1*). Two parameters were used to assess the hypertrophy response (7): the degree of FLR hypertrophy (DH) and the %FLRV increase were calculated by the following formulas (27):

$$DH = (\%FLR\,after\,PVE - \%FLR\,before\,PVE) \quad [1]$$

$$\%FLRV\,increase = \frac{(\%FLR\,after\,PVE - \%FLR\,before\,PVE)}{\%FLR\,before\,PVE} \times 100\% \quad [2]$$

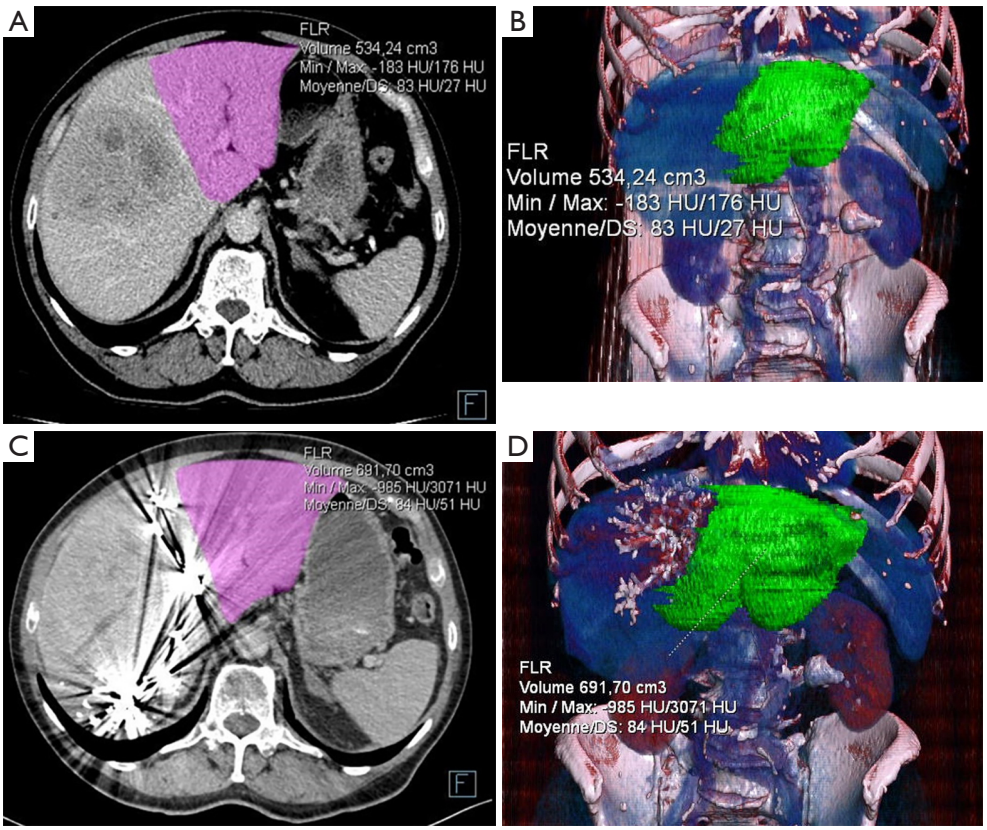

Figure 1 CT-based liver volumetry calculation before/after PVE with EVOH in a 74-year-old man with right-sided hepatocellular carcinoma showing important FLR hypertrophy after PVE. FLR was manually delimited on axial images at the portal venous phase and an automated algorithm interpolated all slices to obtain the volume of the region of interest (in pink) and a 3D volume rendering reconstruction (in green). (A,B) FLR before right PVE procedure was 534 mL (22% of the total liver volume). (C,D) FLR after right PVE procedure was 691 mL (41.6% of the total liver volume). The %FLR increase was 87.6% and the degree of hypertrophy of FLR was 19.4%. Beam hardening white artifacts after PVE related to EVOH copolymer liver distribution are well visualized in the right portal vein branches on axial images. No complication following PVE occurred. PVE, portal vein embolization; EVOH, ethylene-vinyl alcohol; FLR, future liver remnant.

The pace of FLR growth was assessed by computing the kinetic growth rate (KGR) as DH over the time elapsed since PVE, as follows (28):

$$KGR = \frac{DH}{\text{time elapsed since PVE}} \quad [3]$$

PVE technique

Patients were admitted for 2 days and PVE was performed under light general anesthesia. The PVE procedures in the study patients were done by two experienced hepatobiliary interventional radiologists. The Onyx® liquid embolization system included a 1.5-mL vial of Onyx®, a 1.5-mL vial of DMSO, and three 1-mL delivery syringes. Before use, the vial contents were homogenized on a mixer for at least 15 minutes by gentle rotation according to the manufacturer's instructions. The vial was used immediately after mixing to ensure even distribution of the tantalum and, therefore, reliable fluoroscopy visualization. Depending on the required depth of EVOH penetration into the embolization site, either Onyx®-18 (6% EVOH) or Onyx®-34 (8% EVOH) was used.

A 21-Gauge Chiba needle was introduced into a peripheral branch of the contralateral portal system under ultrasound guidance. According to the Seldinger technique, a 6-French introducer sheath was inserted into the main portal vein, which was then opacified to show the venous anatomy and look for a fistula, whose presence

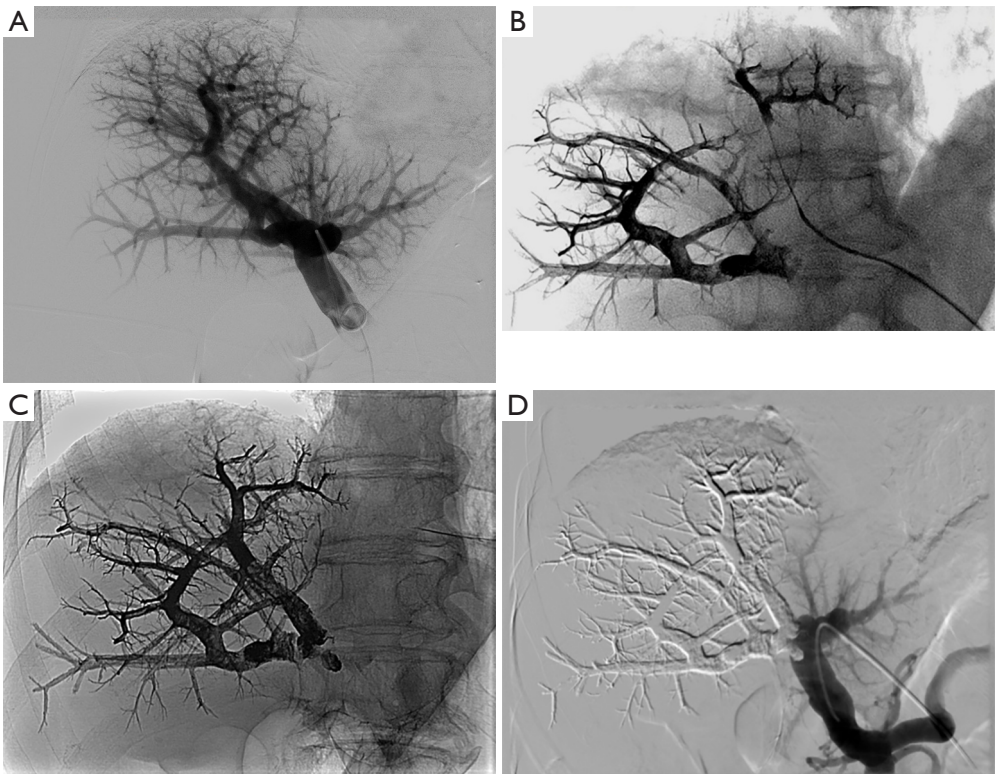

Figure 2 Preoperative right PVE in the same 74-year-old man with right-sided hepatocellular carcinoma. (A) Initial portography from the main portal vein through the left side showing normal anatomy; (B) fluoroscopic image during selective embolization of portal vein branches through a microcatheter showing filling of portal branches with EVOH; (C) fluoroscopic control demonstrating the distribution of highly radiopaque EVOH copolymer into the right portal vein branches; (D) final post-PVE portography from the main portal vein showing complete and successful occlusion of all right portal vein branches. PVE, portal vein embolization; EVOH, ethylene-vinyl alcohol.

would contraindicate the procedure. A standard coaxial system composed of a guidewire and a DMSO-compatible 2.7-French microcatheter (Progreat®, Terumo, Japan) was used to selectively catheterize target second-order portal vein branches. The microcatheter was flushed with saline and DMSO was injected to fill the microcatheter dead space, thus preventing EVOH solidification in the catheter lumen. As soon as the microcatheter reached the most distal portal branches, EVOH was injected under fluoroscopic guidance, at a rate below 0.3 mL/min (*Figure 2*).

The EVOH first traveled in the anterograde direction, along the normal venous flow, then occluded the vein downstream of the microcatheter, inducing reflux along the microcatheter, which ensured embolization of narrow portal vessels without requiring selective catheterization. Catheter removal was achieved easily as long as the EVOH reflux along the tip did not exceed 1 cm. After occlusion of all the small branches, the microcatheter tip was moved to a more proximal position, and a further EVOH injection was performed. This procedure was repeated in each target portal segmental branch. EVOH was administered until all target portal vessels were occluded. The proximal trunk (left or right) was occluded last, leaving a 1-cm non-occluded segment to facilitate surgical ligation during hepatectomy. Portal venography was then performed to check completeness of embolization. Finally, during removal of the sheath, the puncture track was embolized with sterile absorbable gelatin sponge to ensure hemostasis (Curaspon® Cura Medical, Assendelft, The Netherlands).

After the procedure, patients underwent thorough physical examinations for evidence of adverse events, as well as liver function tests and blood cell counts (4,29). Further investigations were performed as dictated by the clinical situation.

Table 1 Baseline characteristics of the 26 study patients

Data	No. of patients (%) or mean SD (range)
Demographics	26 (100.0)
Age (years)	58.711 [32–79]
Male gender	17 (65.4)
Liver tumor type	26 (100.0)
Primary tumor	12 (46.1)
Hepatocellular carcinoma	8 (30.8)
Healthy liver	4 (15.4)
Viral hepatitis C	2 (7.7)
Non-alcoholic steatohepatitis	1 (3.8)
Alcoholic cirrhosis	1 (3.8)
Cholangiocarcinoma	3 (11.5)
Extrahepatic	2 (7.7)
Intrahepatic	1 (3.8)
Hemorrhagic hepatic adenoma	1 (3.8)
Secondary tumor	14 (53.8)
Metastases	13 (50.0)
Colorectal cancer	10 (38.5)
Kidney cancer	1 (3.8)
Breast cancer	1 (3.8)
Malignant paraganglioma	1 (3.8)
Peribiliary cysts	1 (3.8)
Underlying liver disease	10 (38.5)
Chemotherapy	5 (19.2)
Cirrhosis	2 (7.7)
Fibrosis	1 (3.8)
Steatosis	1 (3.8)
Diabetes	1 (3.8)
Preoperative bile duct drainage	2 (7.7)
Future liver remnant segments	26 (100.0)
1+2+3	17 (65.4)
1+2+3+4	6 (23.1)
2+3+4	1 (3.8)
2+3	1 (3.8)
6+7	1 (3.8)

No., number; SD, standard deviation.

Assessment criteria

Technical success was defined as complete occlusion of all portal branches feeding the liver segments to be resected (23). Clinical success was defined as achieving an FLR of at least 25% in patients without, and at least 40% in patients with, underlying liver disease (23).

Clinical symptoms and laboratory parameter alterations after PVE were recorded. The following post-hepatectomy data were collected: resection margins, hospital stay length, postoperative complications, and day-90 mortality due to liver failure.

Statistical analysis

Statistical Triomphe® software developed at the medical statistics unit of our university was used. Volumes were described as mean ± SD and categorical variables as n (%). Liver volumetry variables before and after PVE were compared by applying Student's *t* test. P values <0.05 were considered significant, and 95% confidence intervals (95% CIs) were computed.

Results

We identified 26 patients (male, 17; mean age, 58.7± 11 years; range, 32–79) meeting our selection criteria. Twenty-two patients were managed in the 1st academic center and 4 patients in the 2nd center. Twelve patients with primary liver malignancy and 14 patients with secondary liver malignancy were treated. *Table 1* reports their main characteristics before PVE.

Table 2 provides details on the PVE procedures and the numbers of patients managed with Onyx®-18 and Onyx®-34. Complete embolization of the right portal tree was performed in 25 patients. In the remaining patient, the embolization involved the left portal tree with extension to segments V and VIII. Simultaneous endoscopic bile duct drainage was performed in 2 patients with hilar cholangiocarcinoma (30,31). *Figure 3* reports the number of Onyx® vials used (mean, 12.0±4.8; range, 5–25).

PVE outcomes

Both the technical success rate and the clinical success rate of PVE were 100%. Mean time from PVE to post-embolization liver volumetry was 28.5±9.5 days (range,

Table 2 PVE procedure and follow-up after PVE

Data	No. of patients (%) or mean SD (range)
PVE procedure	26 (100.0)
Side	
Right PVE	25 (96.2)
Right PVE	23 (88.5)
Right PVE extended to segment 4	2 (11.5)
Left PVE	1 (3.8)
Type of Onyx® used	26 (100.0)
Onyx®18 only	16 (61.5)
Onyx®34 only	5 (19.2)
Both	5 (19.2)
Complications	3 (11.5)
Minor complications	4 (15.4)
Transient fever	2 (7.7)
Transient pain	2 (7.7)
Non-target embolization	0 (0)
Major complications	0 (0)
Hepatic surgery procedure	22 (84.6)
Type of surgery	22 (84.6)
Right hepatectomy	6 (27.3)
Right hepatectomy extended to S4	14 (63.6)
Right hepatectomy extended to S1	1 (4.5)
Left hepatectomy extended to S5/S8	1 (4.5)
Cancellation of hepatic resection	4 (15.4)
Tumor progression on CT	2 (7.7)
Metastases at laparotomy	2 (7.7)
Inadequate FLR growth	0 (0)
Resection margins	22 (84.6)
R0	20 (90.9)
R1	1 (4.5)
Rx	1 (4.5)
Complications	
Major complications	
Death during surgery	1 (4.2)
Minor complications	5 (20.9)
Abscess	4 (16.7)
Biliary peritonitis	1 (4.2)
Postoperative hospital stay (days)	12.8±13.8 [8–27]
Mortality rate at 3 months	1 (3.8)

†, resection margins were not examined because the patient died during surgery. PVE, portal vein embolization; S, segment; No., number; SD, standard deviation; CT, computed tomography; FLR, future liver remnant.

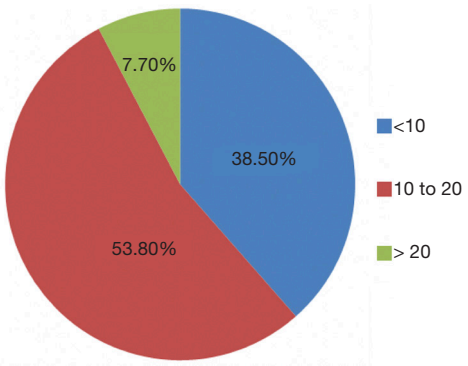

Figure 3 Number of Onyx's vials used for PVE in the study. Mean number of vials was 12.0±4.8 (range, 5–25). PVE, portal vein embolization.

9–47 days). FLRV increased from 704.6±248.2 mL (median, 640.5 mL; range, 434.0–1,265.0 mL) before PVE to 956.9±270.5 mL (median, 915.0 mL; range, 521.0–1,904.0 mL) after PVE. The %FLR increased from 35.5%±9.2% (median, 33.8%) to 52.2%±8.1% (median, 51.2%). The %FLRV increase was 52.9%±32.5% (median, 44.2%; range, 11.8–153.3%). DH was 16.7±6.9 (median, 15.6; range, 5.6–36.5). The mean KGR was 4.4%±2.0% per week (median, 3.6%; range, 1.9–11.1%). In the 10 patients who had an underlying hepatopathy, the %FLRV increase was 45.4%±39.7% (median, 39.7%; range, 13.9–153.3%), the DH was 14.5±8.4 (median, 14.5; range, 10.0–17.1) and the mean KGR was 3.6%±1.9% per week (median, 3.2%; range, 1.9–4.4%). Data are summarized in *Table 3*.

Safety data

During the 2-day hospital stay, 4 patients experienced minor symptoms of post-embolization syndrome (grade B in the Society of Interventional Radiology classification) (32): 2 had low-grade fever and 2 others mild abdominal discomfort (*Table 2*). Acetaminophen was sufficient to control the symptoms in all patients. No major complications were recorded. *Table 4* shows the main liver function test results before and after PVE. No significant change was noted.

Liver resection

Data are summarized in *Table 2*. Resection was not performed in 2 patients, due to extensive disease in the FLR or to the development of extrahepatic disease between the

Table 3 Radiological liver volumetry results of PVE

Parameters (mL)	Before PVE	After PVE	Δ±SD	95% CI	P value
TLV	2,000.3±511.5	2,032.8±540.4	32.5±295.3	−86.17 to 151.25	0.579
ELTV	195.0±294.6	186.9±265.6	−8.2±79.4	−40.14 to 23.69	0.602
FLRTV	5.3±18.0	5.6±15.6	0.3±3.4	−1.14 to 1.63	0.718
TV	200.4±300.9	192.5±269.3	−8.0±81.2	−40.63 to 24.68	0.621
ELV	1,302.9±401.0	1,075.9±420.6	−227.0±245.9	−325.82 to −128.11	$7.97.10^{-05}$*
FLRV	704.6±248.2	956.9±270.5	252.3±200.0	171.94 to 332.67	$9.71.10^{-07}$*
%FLR	35.5±9.2	52.2±8.1	16.7±6.9	13.93 to 19.47	$3.85.10^{-12}$*

Data before and after PVE, available in all patients, are expressed as means ± SD. *, P<0.05 was considered significant. PVE, portal vein embolization; TLV, total liver volume; ELTV, embolized liver tumor volume; FLRTV, future liver remnant tumor volume; TV, total tumor volume; ELV, embolized liver volume; FLRV, future liver remnant volume; %FLR, percentage of FLR; Δ, difference between after and before PVE; SD, standard deviation; CI, confidence interval.

Table 4 Liver laboratory function tests before and after PVE

Parameters	Before PVE	After PVE	95% CI	P value
ALT (U/L)	135±221	110±173	−28.13 to 80.13	0.320
AST (U/L)	113±198	86±143	−30.18 to 82.98	0.334
Total bilirubin (umol/L)	19±23	21±29	−8.11 to 3.84	0.457

Data before and after PVE, available in 15 patients only, are expressed as means ± SD. P<0.05 was considered significant. ALT, alanine transaminase; AST, aspartate transaminase; PVE, portal vein embolization; SD, standard deviation; CI, confidence interval.

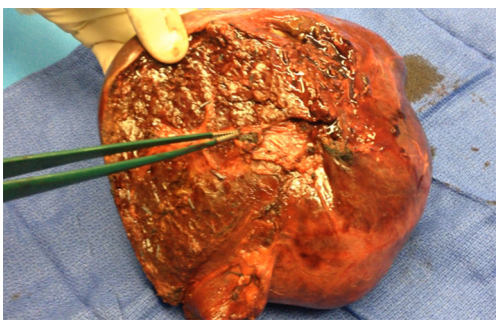

Figure 4 Macroscopic view of right hepatectomy. The tip of the tissue plier shows blackish material occluding right portal vein corresponding to EVOH. EVOH, ethylene-vinyl alcohol.

PVE procedure and the post-PVE imaging studies. Mean time from PVE and surgery was 44.5±18.3 days (range, 19–85 days). Of the 24 patients who had surgery, 2 had previously unsuspected metastases identified during the procedure and consequently did not undergo the planned hepatectomy procedure. Thus, 4 (15.4%) patients did not undergo major hepatectomy.

Four patients had postoperative complications classified as grade III according to Dindo-Clavien, i.e., requiring radiological or surgical intervention (33). One patient died during surgery due to extensive bleeding from a vena cava injury unrelated to the PVE procedure. No patient experienced fatal liver failure.

Pathological examination of the embolized liver showed dark blue-to-black material in the lumen of the targeted portal tree with no evidence of recanalization in all patients. An inflammatory reaction was evidenced in the tissue surrounding the embolized vessels (*Figure 4*).

Discussion

In our retrospective review of 26 patients with liver malignancies managed between 2014 and 2018, PVE performed using EVOH to induce FLR hypertrophy was technically successful in every case and consistently increased the FLR volume to at least 40% or 25% of total liver volume in patients with and without underlying liver disease, respectively. No major complications of

PVE were recorded. Four patients experienced mild post-embolization symptoms that responded to acetaminophen. To our knowledge, this is the largest study reporting results of preoperative PVE with the use of EVOH as the only embolic agent.

Several agents are available for PVE. Recommendations issued by the Cardiovascular and Interventional Radiological Society of Europe indicate that some embolic agents should be avoided due to a high rate of portal vein recanalization or to limited efficiency in inducing liver hypertrophy (23). A mixture of NBCA and ethiodized oil induced substantial FLR hypertrophy with low morbidity rates in several studies (4,5,8,34). Onyx® has produced good outcomes when used for various peripheral interventions (15,17). A study in a pig model reported in 2012 established the feasibility of PVE with Onyx® (35). During PVE with NBCA, EVOH has been found useful for occluding portal vein branches for which the use of NBCA was deemed to carry a high risk of non-target embolization (36). Our 84.5% surgical resection rate is consistent with the 75.9% rate reported in a recent meta-analysis of PVE with NCBA (8). The %FLRV increase was also similar in our study and the meta-analysis. In a study of 41 patients, EVOH, used in 11 patients, produced faster growth of the S2/3 segments compared to ethiodized oil (n=10), polyvinyl alcohol (n=8), and ligation (n=12) (18). In keeping with this finding, KGR values above 2% have been reported to correlate with favorable surgical outcomes, and the KGR of 4.4±2.0 per week in our study was thus well into the safety zone (28). Thus, EVOH, with a FLRV increase of 52.9% in our study, might be among the most effective agents for inducing liver hypertrophy as compared to the existing literature (*Table 5*) (37-55). One explanation could be the distal and inflammatory nature of EVOH embolization. It is worth noting that 2 of our patients underwent post-PVE imaging early, on day 9, yet had %FLRV increases of 13.9% and 31.3%, indicating a very short PVE response time, in keeping with earlier data (56). Finally, a good response to PVE was seen in the 10 patients who had an underlying liver disease predicted to slow the pace of liver regeneration.

Minor complications of PVE have been reported in 20% to 25% of patients, compared to 15% in our population (4,5,8,23). No major PVE-related complications were recorded. More specifically, no patient experienced post-hepatectomy liver failure or fatal liver failure within 90 days after surgery.

EVOH copolymer is a plastic polymer that is used dissolved in DMSO and solidifies gradually upon contact with blood. DMSO is potentially toxic, and its metabolites are excreted through the lungs and kidneys. A case of acute respiratory distress syndrome related to DMSO has been reported (57). A slow Onyx® injection rate of 0.3 mL/min is recommended to avoid vasospasm. However, vasospasm does not occur at the portal vein, and the amount of DMSO contained in the microcatheter dead space is well below the toxic threshold. Therefore, an injection rate of up to 0.5 mL/min can be used for PVE. Advantages of EVOH over NBCA include a slower time to solidification of about 5 min that improves embolization predictability, absence of adherence to the vessel or catheter walls allowing multiple injections to achieve full penetration, greater cohesiveness, less endothelial inflammation, and better fluoroscopic visibility (58). These properties virtually eliminate the risk of non-target embolization. No cases of catheter adhesion, obstruction, or trapping were recorded in our study. As with NBCA, vessel occlusion is permanent. Furthermore, PVE with EVOH could be more standardized and homogeneous than with NBCA. Indeed, when using glue, the NBCA/lipiodol ratio varies from center to center depending on operator comfort. This might potentially lead to discrepancies in liver hypertrophy.

Compared to Onyx®-34, Onyx®-18 has lower viscosity and therefore penetrates deeper into the portal tree. Onyx®-34 is useful for embolizing more proximal sites near the portal trunk. The high radiodensity of Onyx® can generate beam-hardening artifacts that may interfere with the quality of post-PVE CT imaging. However, no artifacts occur with MRI, which visualizes EVOH as low endoluminal signal on T1- and T2-weighted sequences, without artifacts.

Onyx® has three main disadvantages. The DMSO injection is painful, and complete immobility of the patient must be maintained during fluoroscopy. However, PVE is usually performed under light general anesthesia regardless of the embolic agent used, with no pain. Second, Onyx® is considerably more expensive than NBCA (59). Finally, the fluoroscopy time may be longer with Onyx® than with other embolic agents but general anesthesia allows for faster injection.

Two methods can be used for PVE with Onyx®. In the first method, after the first injection, the reflux along the catheter solidifies within 2–3 min, after which a second injection can only travel in the anterograde direction into the target vessels. In the second method, the catheter tip is advanced as far as possible in the portal tree and a continuous Onyx® injection at a steady rate is then

Table 5 Impact of embolic agent used for PVE on the hypertrophy of FLR reported in the literature

Embolic agent	Author/year	No. of patients	%FLRV increase
Fibrin glue	Liem *et al.* 2005; (37)	15	31.4
	Nagino *et al.* 2006; (38)	105	27.4
NBCA	de Baere *et al.* 2010; (20)	107	57.8
	Barbaro *et al.* 2009; (39)	26	53
	Capussotti *et al.* 2008; (40)	31	48.5
	Elias *et al.* 2002; (41)	68	59.1
	Giraudo *et al.* 2008; (42)	146	41.7
	Sirichindakul *et al.* 2007; (43)	29	27.5
	Guiu *et al.* 2013; (44)	20	48
	Broering *et al.* 2002; (6)	17	69.4
Gelatin sponge	Fujii *et al.* 2005; (45)	30	17.8
	Imamura *et al.* 1999; (46)	84	30.7
	Kakizawa *et al.* 2006; (47)	14	23.8
	Makuuchi *et al.* 1991; (48)	54	37.9
	Nanashima *et al.* 2009; (49)	30	29.4
	Sugawara *et al.* 2002; (50)	66	35.8
PVA + coils/plugs	Covey *et al.* 2008; (51)	100	24.3
	Libicher *et al.* 2010; (52)	10	26.4
	Camelo *et al.* 2019; (53)	64	40
Microparticles + coils	Guiu *et al.* 2013; (44)	14	29
STS foam	Fischman *et al.* 2014; (54)	35	48.8
Ethanol	Sofue *et al.* 2014; (55)	83	43
EVOH copolymer	Our study	26	52.9

NBCA, N-butyl cyanoacrylate; PVA, polyvinyl alcohol; STS, sodium tetradecyl sulfate; EVOH, ethylene-vinyl alcohol; No., number; PVE, portal vein embolization; %FRLV, percentage of future liver remnant volume.

performed until reflux along the catheter and retrograde penetration of the EVOH into the portal tree branches occur, producing a smooth lava-flow like pattern with no fragmentation. The catheter tip is then retracted along about 1 cm and a further injection is performed. Thus, the EVOH does not need to be injected directly into the target site, and both small and large vessels of any configuration can be embolized without selective catheterization (36).

Lastly, the use of EVOH was as easy to use ipsilaterally as it was contralaterally. Indeed, the site of puncture did not matter for using EVOH. By contralateral approach, tract embolization with gelfoam is the rule, as with any other embolic agents. By ipsilateral approach, the portal branch which is initially punctured for PVE has to be embolized last, with no risk of sticking the catheter as compared to NBCA.

The main limitations of our study are the retrospective design and small sample of patients. Body mass index was not available for computing the standardized FLR volume (60). Hepatobiliary scintigraphy was not performed, limiting the amount of information on liver function (56). Nevertheless, the 100% technical and clinical success rates and the absence of major complications deserve note and warrant further studies of EVOH for PVE compared to other embolic agents.

Conclusions

In conclusion, PVE with EVOH alone was feasible, safe, and effective in inducing FLR hypertrophy. Despite higher cost, this liquid embolic agent is very promising in such a setting. Further work is needed to determine the role for EVOH PVE in the treatment strategy for patients with liver malignancies.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/qims-20-808). RL serves as a Deputy Editor for *Quantitative Imaging in Medicine and Surgery*. The other authors have no conflicts of interest to declare.

Ethical Statement: According to institutional policy, approval from our Institutional Review Board was not required owing the retrospective nature of the study. Written informed consent from the patient for publication of this study and any accompanying images was waived.

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