

# Safety and outcomes of pre-operative portal vein embolization using N-butyl cyanoacrylate (Glue) in hepatobiliary malignancies: A single center retrospective analysis

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## Abstract

**Aims and Objectives:** To evaluate the outcome of preoperative portal vein embolization (PVE) using N-butyl cyanoacrylate (NBCA) for change in future liver remnant (FLR) volume, biochemical changes, and procedure-related complications. The factors affecting FLR hypertrophy and the rate of resection was also evaluated for this cohort. **Materials and Methods:** From 2012 to 2017, PVE utilizing NBCA mixed with lipiodol (1:4) was performed using percutaneous approach in 28 patients with hepatobiliary malignancies with low FLR. All patients underwent volumetric computed tomography (CT) assessment before and at 3–5 weeks after PVE and total liver volume (TLV), FLR volume, and FLR/TLV ratio, changes in portal vein diameter and factors affecting FLR were evaluated. Complications and the resectability rate were recorded and analyzed. **Result:** PVE was successful in all 28 patients. The mean FLR increased by  $52\% \pm 32\%$  after PVE ( $P < 0.0001$ ). The FLR/TLV ratio was increased by  $14.2\% \pm 2.8\%$  ( $P < 0.001$ ). Two major complications were encountered without any impact on surgery. There was no significant change seen in liver function test and complete blood counts after PVE. Eighteen patients (64.28%) underwent hepatic resection without any liver failure, and only three patients developed major complication after surgery. Remaining ten patients did not undergo surgery because of extrahepatic metastasis detected either on follow-up imaging or staging laparotomy. Patients with diabetes showed a lower rate of hypertrophy ( $P < 0.05$ ). **Conclusion:** Preoperative PVE with NBCA is safe and effective for increasing FLR volume in patients of all age group and even in patients with an underlying liver parenchymal disease with hepatobiliary malignancy. Lesser hypertrophy was noted in patients with diabetes. A reasonable resectability was achieved despite having a high rejection in gall bladder cancer subgroup due to rapid disease progression.

**Key words:** Future liver remnant; N-butyl cyanoacrylate glue; Portal vein embolization

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## Introduction

Complete resection of hepatic tumors remains the first choice for curative treatment of primary and secondary liver malignancies, giving the patient the only chance of long-term survival.<sup>[1,2]</sup> The variable deciding the extent of resection include tumor size, tumor location, and tumor burden. Often extensive liver parenchymal resection may be needed for curative treatment making the tumor unresectable. The reason for unresectability may be insufficient remnant liver volume to support postoperative liver function, which itself is the principal cause of postoperative death after major hepatectomy. It has been demonstrated that liver failure is directly related to the size of a remnant functional liver volume.<sup>[3]</sup>

Portal vein embolization (PVE) to induce hypertrophy of an insufficient future liver remnant (FLR) prior to hepatic tumor resection is currently recognized as a standard practice to minimize the risk of postoperative failure as well as increase the number of resectable patients.<sup>[4-13]</sup>

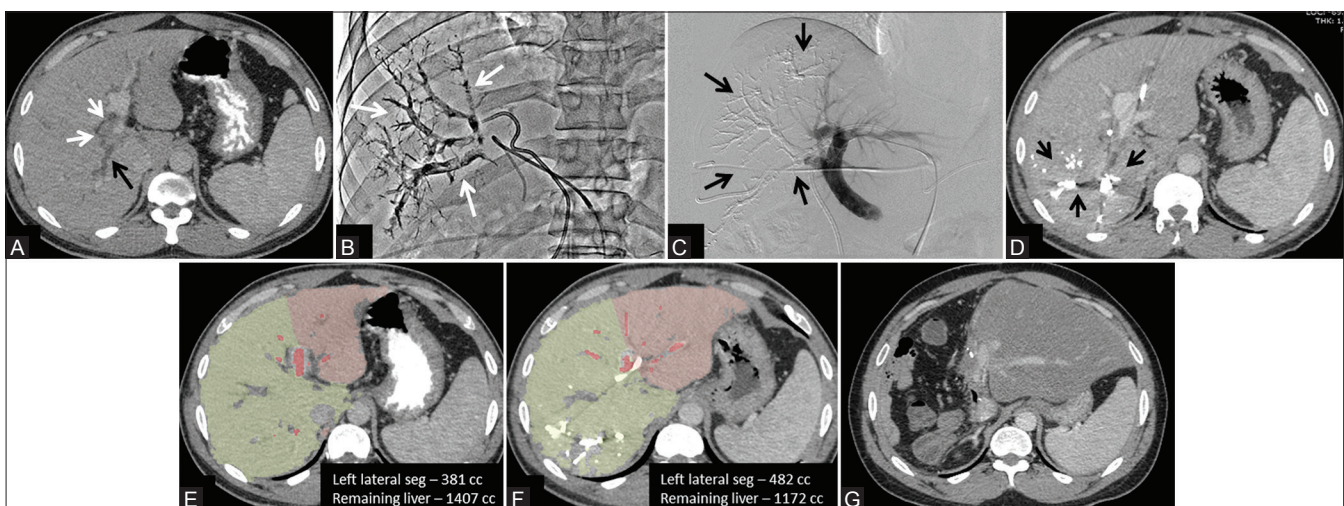
Currently, various embolic agents, including gel-foam, coils, polyvinyl alcohol (PVA) particles, absolute alcohol, and N-butyl-cyanoacrylate (NBCA) glue, have been used for PVE.<sup>[14-16]</sup> However, there is no consensus in the most effective and safe embolic agents for PVE.<sup>[17]</sup> The ideal embolic agent is one that causes permanent embolization without recanalization. In previous studies, NBCA has been used for PVE because it causes permanent embolization without recanalization.<sup>[18-21]</sup> However, NBCA is difficult to control because of its liquidity and rapid polymerization. In this study, we analyzed the outcome of PVE using NBCA. The primary objective was to evaluate the post PVE change in

future liver remnant (FLR) volume, biochemical parameters, and procedure-related complications. The factors affecting the FLR hypertrophy with emphasis on patients with liver parenchymal disease. The rate of resection was also evaluated.

## Materials and Methods

A retrospective review of our hospital electronic database was performed to search all patients who underwent PVE between January 2012 and December 2017 for primary hepatobiliary malignancies requiring right hepatectomy. The study protocol was approved by our institutional review board and conducted according to the standards of the declaration of Helsinki. The indications of right hepatectomy or extended hepatectomy and pre-resection PVE were elaborated through a case-by-case discussion at a multidisciplinary team meeting (including hepatologists, hepatobiliary surgeons, and interventional radiologists). Pre-embolization computed tomography (CT) was performed to evaluate the extent of hepatobiliary disease, the portal vein anatomy, and biliary obstruction [Figure 1A]. The PVE was suggested according to the hepatic volumetry and underlying disease. For healthy liver, the FLR should be at least 25% of the total liver volume (TLV); whereas in case of liver cirrhosis, the FLR must be at least 40% of the TLV. For the patients undergoing preoperative chemotherapy, the FLR should be at least 30% of TLV. The exclusion criteria were as follows: unresectable tumor, patients who had any type of liver resection before PVE, PVE done with embolic agents other than NBCA, portal vein thrombosis, and renal failure.

Percutaneous biliary drainage was performed in patients with biliary obstruction before PVE either previously or same day of PVE procedure.



**Figure 1 (A-F):** (A) Contrast-enhanced CT, axial image showing hilar mass (white arrows) with minimal biliary dilatation (black arrow) and small left lobe of the liver. (B) Fluoroscopic image showing NBCA-lipiodol cast (white arrows) in the right portal vein branches. (C) Post PVE portal venogram showing non-opacification of right portal vein branches (black arrows) suggestive of complete embolization of all right portal vein branches. (D) Follow-up axial CECT image showing lipiodol deposition in right portal vein branches (black arrows) with right lobe atrophy and hypertrophy of left lobe of the liver. Comparative liver volumetry images, pre PVE (E), and post PVE (F) showing hypertrophy of the left lateral segments of the liver. Post right hepatectomy follow-up axial CECT image (G) showing remnant left lobe of liver

### Portal vein embolization technique

PVE was usually performed 4–5 weeks before the planned surgery. Percutaneous PVE was performed under conscious sedation (induced with intravenous administered midazolam and fentanyl citrate) and a local anesthetic (1% lidocaine hydrochloride) at the skin puncture site for local pain control.

The portal venous system was accessed percutaneously under ultrasound and fluoroscopic guidance using either contralateral approach (puncture of the left portal vein branch and embolization of the right portal vein branches) or ipsilateral approach (puncture of the right portal vein branch to embolize the right portal vein branches). A 22 gauge Chiba needle (Neff Percutaneous Access Set, Cook, Bloomington, Indiana, USA) was used to puncture the distal selected portal vein, and the Neff set assembly was advanced in the main portal vein thereafter replaced by a 0.035" hydrophilic guidewire (Terumo, Tokyo, Japan). After that, a 6F vascular sheath was placed into the portal vein over the wire to facilitate subsequent catheter exchange. Flush portography was performed with a 5F KMP catheter in the main portal vein to identify variations of the intra-hepatic portal tree. KMP catheter was used to cannulate segmental portal vein branches in the contralateral approach, and a combination of SIM 1, C1/2, and KMP catheter was needed to achieve complete embolization in the ipsilateral approach.

Before embolization, contrast venogram of selected right portal vein branches was performed using a 5F angiographic catheter. Further, NBCA (glue) mixed with lipiodol (1:4 ratio) was injected under fluoroscopic guidance into each selected portal vein branch in small aliquots (0.5 to 1.0 ml) [Figure 1B]. The catheter was flushed with 5% dextrose solution (5% DW) both prior to glue injection and after the glue injection to prevent polymerization of NBCA within the catheter. If a right extended hepatectomy (including segment IV) was planned, then additional embolization of segment IV portal vein branches was also done. In contralateral approach, a final flush portography was done with 5F KMP catheter placed in the main portal vein to assess the completeness of the embolization [Figure 1C]. At the end of the procedure, while removing the access sheath, the punctured portal vein radicle was embolized with NBCA and coils in ipsilateral approach; whereas in contralateral approach, the catheter and sheath were removed under manual compression for 10 min, without tract embolization owing to the anterior and superficial location of the left lobe of liver.

### Follow-up

Patients were kept under observation with monitoring of vitals for 3–6 h after the procedure. Clinical and laboratory findings were evaluated for post-embolization syndrome, liver dysfunction, or catheter-related complications. Patients

were discharged when they were clinically stable and without any complaints. Liver function tests and complete blood counts were assessed prior to the procedure, on day 2 and at 3–4 weeks of PVE.

The complications were recorded and classified according to the Society of Interventional Radiology complication guidelines. Technical success rate was defined as the successful occlusion of the targeted branches of portal veins after PVE.

### Assessment of hypertrophy

A follow-up CT scan of the abdomen was performed 3–4 weeks after PVE to determine the degree of liver hypertrophy [Figure 1D]. A triple-phase CT scan protocol (non-contrast scan, acquisitions at arterial phase, obtained 35 s after injection, and venous phase obtained 75–90 s after injection) was used to define the liver segments precisely. All measurements were obtained on the venous phase to delineate both portal vein and the hepatic veins.

Volumetric measurements were performed using liver volumetry software (Myrian XP, Intrasure, France) on serial transverse scans at 2.5 mm interval from the dome of the liver to the most inferior part of liver. These measurements included total liver volume (TLV), future liver remnant (FLR) volume, and ratio of FLR/TLV, the ratio before and after PVE and increase of FLR hypertrophy [Figure 1E and F].

### Statistical analysis

All data were expressed as mean  $\pm$  standard deviation (SD). The paired student *t* test or the Mann-Whitney test was used to compare continuous variables depending on the distribution of data, and the Fisher exact test was used for categorical variables. Statistical significance was set at a *P* value  $< 0.05$ . All analyses were performed using the SPSS software version 16.

## Results

From January 2012 to December 2017, total 29 patients underwent PVE prior to right hepatectomy for hepatobiliary malignancies. One patient was excluded from the study as PVA and coil were used as embolic agents. Hence, the data of 28 patients (20 male and 8 female) was included and analyzed in this study. Twenty-two patients underwent PVE through contralateral approach, whereas in the remaining six, PVE was done using ipsilateral approach. Out of 28 patients, embolization of segment IV was done in six patients. The demographic details are presented in Table 1.

### Technical success of PVE

The technical success was achieved in all patients with complete occlusion of all targeted portal vein branches throughout both contralateral and ipsilateral approach.

**Assessment of hypertrophy [Table 2]**

All post-embolization volumetric CT scans were performed from 20 days to 30 days (mean 24 days  $\pm$  6 days) after PVE. The mean TLVs were 1602  $\pm$  328 cm<sup>2</sup> before and 1537  $\pm$  323 cm<sup>2</sup> after PVE and showed no significant changes ( $P < 0.71$ ). The mean absolute FLR volumes were 371  $\pm$  87 cm<sup>3</sup> before and 567  $\pm$  142 cm<sup>3</sup> after PVE. The mean absolute FLR volume was increased by 52% $\pm$ 32%. The pre-embolization FLR/TLV ratio was 23.33% $\pm$ 4.7% and the post-embolization was 37.4% $\pm$ 8.1%, and this difference was statistically significant ( $P < 0.0001$ ). The mean increase in the FLR/TLV ratio after PVE was 14.1% $\pm$ 2.8%.

**Biochemical changes after PVE**

Mild transient transaminitis was noted in the majority of patients after PVE, which required no treatment. There was no significant change seen in bilirubin, hemoglobin, and WBC value after PVE. Similarly, the mean platelet count and the international normalized ratio (INR), (indicating hepatic failure), measured prior to the procedure, on day 2 and at 3-4 weeks did not show any significant change ( $P > 0.05$ ). The laboratory values before and after PVE are summarized in Table 3.

**Complications of PVE**

No patient in this cohort developed post-embolization syndrome or liver failure after PVE. The median length of hospital stay was 2 days (range 1 day to 16 days). Four patients experienced mild abdominal pain after PVE, which was managed by administering intravenous analgesics. Three patients developed mild fever on the next day of the

procedure but was self-limiting and required no treatment. In four patients, minor non-targeted migration of NBCA into left lobe was noted. This partial non-target embolization was not symptomatic and did not prevent from sufficient hypertrophy in these patients. Major complications were noted in two patients out of 28 patients. One patient developed bile leak after PVE with the formation of biloma along left epigastrium, however, it subsided after aspiration and percutaneous biliary drainage of the affected segment, and the patient was discharged after 16 days. One patient developed partial thrombus in the main portal vein, however, no signs of portal hypertension was seen on clinical examination and imaging findings. All patients with above-cited complications did undergo surgery except one owing to extra-hepatic peritoneal metastasis on staging laparotomy.

**Resection rate and outcome**

Of the 28 patients who underwent PVE, 18 patients (64.28%) underwent successful hepatectomy [right hepatectomy ( $n = 9$ ), modified right hepatectomy ( $n = 5$ ), and extended right hepatectomy ( $n = 4$ )] after 4 to 8 weeks of PVE. However, 10 patients did not undergo resection because of extrahepatic metastasis detected either on follow-up imaging or staging laparotomy, and most of these patients ( $n = 5$ ) had gall bladder cancer as the primary disease. Among the patients who were operated, one patient developed transient postoperative liver failure on day 5 of surgery but recovered by day 10. One patient died after 7 days of surgery owing to severe cholangitis leading to sepsis. One patient having diabetes mellitus and coronary artery disease developed perihepatic and abdominal collections and ultimately died after 30 days secondary to sepsis and cardiac failure. Remaining 15 patients did not show any postoperative complication or any other complication up to 3 months follow-up.

**Factors affecting FLR volume [Table 4]**

Clinical parameters including age, sex, underlying liver damage such as chronic liver disease and previous chemotherapy, and underlying diabetes mellitus were studied in relation to the mean FLR volume. The patients were grouped below 60 years and above 60 years to study the variation in hypertrophy according to the age. However, both groups showed a similar rate of FLR hypertrophy. Hypertrophy rate was similar in male and female. Surprisingly, in our study, even the underlying liver parenchymal damage (cirrhosis or preoperative

**Table 1: Patient demographics**

Parameters	Patient numbers ( $n=28$ )
Sex (M/F)	22/6
Age (mean, range)	55.6 years (35-72)
Tumor type ( $n$ %)	
Cholangiocarcinoma	14
Hepatocellular carcinoma	5
Gall bladder carcinoma	9
Underlying liver damage/Systemic disease	
Cirrhosis	19
Neoadjuvant chemotherapy	5
Diabetes mellitus	6
PVE approach	
Ipsilateral PVE	6
Contralateral PVE	22

**Table 2: Change in liver volume (CT volumetry values) before and after PVE**

Parameters	Before PVE (mean $\pm$ SD) (range)	After PVE (mean $\pm$ SD) (range)	$P$
TLV (cm <sup>3</sup> )	1602 $\pm$ 328 (2250-1050)	1537 $\pm$ 323 (2128-1090)	0.71
FLR (cm <sup>3</sup> )	371.18 $\pm$ 87 (228-650)	567.3 $\pm$ 142 (303-922)	<0.0001
FLR/TLV (%)	23.33 $\pm$ 4.7 (15.5-32.3)	37.4 $\pm$ 8.1 (26.9-51.2)	<0.0001
Hypertrophy of FLR (%)		52 $\pm$ 32	
Increase of the FLR/TLV ratio (%)		14.1 $\pm$ 2.8	

chemotherapy) did not significantly affect the enlargement of FLR. However, patients with diabetes mellitus showed a lower rate of FLR hypertrophy than non-diabetic patients [statistically significant ( $P < 0.005$ )].

## Discussion

PVE has been proposed to increase the size of the FLR after major hepatectomy, thus reducing the risks of postoperative liver insufficiency.<sup>[4-13]</sup> Permanent embolization of portal branches is frequently preferred because the liver after embolization is resected in most cases. Some authors consider NBCA to be the most effective for PV embolization because it induces proximal and distal PV occlusion and incites a periportal inflammatory reaction that may also play a role in liver regeneration stimulation.<sup>[6]</sup>

Previous literature showed that NBCA is effective for PVE to induce FLR.<sup>[18-21]</sup> Few previous studies reported that hardening of vein and difficulty in tissue resection occurred after PVE with NBCA because of its strong inflammatory reaction and subsequent fibrosis.<sup>[5,6,22]</sup>

**Table 3: Change of laboratory parameters before and after PVE**

Parameters	Mean (range)		
	Before PVE	After PVE (2 days)	After PVE (3-4 weeks)
AST (U/L)	48.2 (18.2-404)	68.51 (22.5-512)	50.2 (16.7-466)
ALT (U/L)	46.3 (12.7-388)	69.33 (14.2-566)	54.6 (12-390)
ALP (U/L)	319.04 (81-951)	289.11 (66-699)	238.44 (54-530)
Bilirubin	2.9 (0.4-12.7)	2.69 (0.3-10.4)	2.8 (0.6-14.1)
HB	11.68 (7.9-15.7)	11.82 (8.9-15)	11.92 (8.5-15.3)
WBC	9.2 (18.2-5.4)	10.3 (5.7-22.1)	9.8 (5.7-16.5)
Platelet count $\times 10^3$ /ml	293.44 (607-96)	265.92 (552-81)	272.18 (100-520.22)
INR	1.25 (0.8-2.4)	1.44 (0.7-2.8)	1.34 (0.7-2.8)

**Table 4: Factors affecting change in FLR**

Clinical Parameters	Future Liver Remnant (FLR) (mean- $\text{cm}^3$ )			P*
	Pre PVE	Post PVE	FLR hypertrophy (%)	
Age				<0.72
$\leq 60$ years ( $n=15$ )	393 $\pm$ 101	585 $\pm$ 153	53 $\pm$ 29	
$> 60$ years ( $n=13$ )	349 $\pm$ 62	543 $\pm$ 121	51 $\pm$ 37	
Gender				<0.029
Male ( $n=22$ )	380 $\pm$ 90	587 $\pm$ 139	56 $\pm$ 37	
Female ( $n=6$ )	343 $\pm$ 67.4	483 $\pm$ 120	46 $\pm$ 28	
Chronic Liver Disease				<0.04
Cirrhotic ( $n=19$ )	363 $\pm$ 73	508 $\pm$ 138	46 $\pm$ 34	
Non cirrhotic ( $n=9$ )	374 $\pm$ 92	590 $\pm$ 191	57 $\pm$ 30	
Chemotherapy				<0.27
No-chemotherapy ( $n=23$ )	382 $\pm$ 87	572 $\pm$ 111	55 $\pm$ 31	
Adjuvant Chemotherapy ( $n=5$ )	324 $\pm$ 68	546 $\pm$ 228	49 $\pm$ 34	
Diabetes Mellitus				<0.005
Non-diabetic ( $n=22$ )	350 $\pm$ 68	572 $\pm$ 137	59 $\pm$ 36	
Diabetic ( $n=6$ )	450 $\pm$ 102	549 $\pm$ 155	44 $\pm$ 31	

\*Statistical difference of increased FLR after PVE was compared between different groups

Limited literatures have been published for PVE using appropriate dilution of NBCA for effective FLR hypertrophy and causing no difficulty in resection. Our study shows that percutaneous transhepatic PVE using NBCA mixed with lipiodol (1:4) is feasible and safe, along with low morbidity and no mortality. The technical success rate of PVE in this study was 100%, which is similar to previous studies.<sup>[18,21,22]</sup>

The dilution of the NBCA with lipiodol reported in the literature varies, is often not clearly quantified, and ranges from 1 ml of NBCA mixed with 1–9 ml of lipiodol.<sup>[11,18,20,21]</sup> Optimal NBCA penetration is governed by several factors; however, the three main variables include a choice of NBCA dilution, portal venous flow, and rate of injection. In the current study, we used 1: 4 ratio of NBCA with lipiodol resulting delayed polymerization of NBCA mixture leading to more peripheral embolization. In the present study, minor non-target NBCA embolization was seen in left lobe in four patients but did not hinder for effective FLR hypertrophy.

In this study, marked FLR hypertrophy was found after PVE using NBCA with lipiodol (ratio 1:4). We found a mean increase of FLR  $194 \pm 64 \text{ cm}^3$  in absolute volume and 52% in percentage (statistically significant,  $P < 0.0001$ ). The increase of FLR/TLV ratio was  $14.1 \pm 2.8$  (statistically significant,  $P < 0.0001$ ). Our results showed equivalent efficacy compared to previous large cohort studies.<sup>[20-23]</sup>

The main principle of PVE is occlusion of ipsilateral portal vein to induce hypertrophy of contralateral lobe of the liver. Several techniques of portal vein occlusion have been proposed and broadly divided into two main category – surgical (including operative ligation, trans-ileocolic PVE) and percutaneous (ipsilateral and

contralateral PVE). In comparison to the surgical approach, percutaneous PVE is a minimally invasive method and preferable. One previous study compared the PVE and surgical portal vein ligation for FLR hypertrophy and observed a more effective increase in FLR volume and shorter hospital stay after percutaneous PVE. PVE seems to be more effective than surgical ligation of portal vein branch by preventing the development of other collateral circulation to the right lobe of liver because of distal occlusion of the portal vessels.<sup>[24]</sup> Moreover, PVE keeps the hilum free of adhesion caused by the hilar dissection required for ligation and reduced the complication during liver resection.<sup>[10]</sup>

In our study, most of the PVE was done through the contralateral approach. The contralateral approach has several advantages such as easy cannulation of anterior and posterior right portal branches, absence of sharp angulation, and no risk of tumor seeding. In current study, a mild transient increase of hepatobiliary enzyme was found after 2 days of PVE. It is reported that aspartate aminotransferase and alanine aminotransferase reach a peak level at 1–3 days after PVE, usually rising to less than three times the baseline values. There was no statistically significant change seen in hemoglobin, platelet counts, INR, and albumin level after PVE in our study. Major complications were noted in only 2 (7.1%) patients of 28 patients. This result is comparable to the other previous study.<sup>[18,21-23,25,26]</sup> Most of our patients had no fever except three patients following PVE. Partial main portal vein thrombosis in one patient, bile leak causing biloma in one patient, and minor non-target embolization in three patients were found in our study. However, all patients who had complications showed clinical improvement after conservative treatments and survived, and these did not hinder in surgery. From our study, we experienced that non-target embolization can be reduced through a slower rate of injection of NBCA. To reduce the risk of embolic agent migration in the left branches, NBCA was injected selectively in the segmental branches. With this technique, refluxed embolic material is less likely to migrate to the left portal branches. Moreover, the contralateral approach allows better control of glue release starting distally in the right portal vessels with flow directed embolization leading to less chance of non-target embolization. Further, from contralateral approach, we can perform a final portography and can be used as a good tool to measure intra-portal pressure before and after portal vein embolization if needed. The contralateral approach could, however, induce injury to the future remnant segments, but in our study, we did not find any such complication. The primary parameter used to evaluate the efficacy of PVE is the resectability rate after PVE and post-resection liver insufficiency. The limiting factors in performing a curative hepatic resection after PVE

are the final volume of FLR and the absence of disease progression. In the current series, the resectability rate was 64.28% (18/28). This low resectability may be attributable to high rejection of patients with gall bladder cancer having aggressive behavior with rapid progression (only 4 of 9 making to surgery). Although the resectability rate appears low, it is similar to previous literature.<sup>[20-23]</sup> In this study, adequate FLR hypertrophy after PVE was achieved in all patients before surgery. Only one patient with cirrhosis developed transient liver insufficiency after extended right hepatectomy for hilar cholangiocarcinoma. Remaining ten patients (35.72%) did not undergo resection because of extrahepatic metastasis found on follow-up imaging or peritoneal metastatic deposit seen on preoperative laparotomy. Different authors have shown that similar observation.<sup>[20,23]</sup> The previous few literatures demonstrated that differences in age, gender, underlying liver disease, and diabetes may cause differences in increased FLR hypertrophy.<sup>[6,7,10,27]</sup> In the present study, patients of age group <60 years, male gender, patients without cirrhosis, and those who have not received chemotherapy had better mean FLR hypertrophy than age group >60 years, female patients, and those with underlying cirrhosis or receiving chemotherapy. However, these results were not statistically significant ( $P > 0.05$ ). Moreover, noteworthy hypertrophy was noted in patients with underlying liver parenchymal disease as well. However, we found that non-diabetic patient achieved higher FLR hypertrophy than patients with diabetes mellitus, and it was statistically significant ( $P < 0.001$ ). Our study had several limitations. First, it is a retrospective single-center study. Second, total number of patients in this study is relatively small, which may limit statistical power. Third, it is not randomized and lacks comparison with other embolic material. Fourth, as this study is retrospective comparing the different groups, this could result in selection bias.

## Conclusion

In our experience, PVE using NBCA (Glue) mixed with lipiodol (ratio1:4) is safe and highly effective in inducing future liver remnant hypertrophy in all age group and even in patients with underlying liver parenchymal disease before right hepatectomy in the patients with hepatobiliary malignancies. Lesser hypertrophy was noted in patients with diabetes. A reasonable resectability was achieved despite having a high rejection in gall bladder cancer subgroup owing to rapid disease progression.

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## Conflicts of interest

There are no conflicts of interest.

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