

The impact of portal vein embolization on the future liver remanent prior to major hepatectomy surgery: a single center study.

Elshaimaa M. Mohamed^{1*}, Ahmed Elaryan², Turki A. Alhazmi³, Mohamed Hamed Zidan⁴, Ahmed Mohamed Alsowey¹, Mona Mohammed Refaat Ismail¹, Ibrahim M. Eladl¹, Mona M. Eladl¹

1 Radiology Department, Faculty of Medicine, Zagazig University, Egypt

2 Radiology Department, International Medical Center Hospital, Saudi Arabia

3 Interventional Radiology Department, Faculty of Medicine, Umm Al Qura University, Saudi Arabia

4 Surgery Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding author:

Elshaimaa M. Mohamed

Email:

bosy.radiology@gmail.com

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ABSTRACT

Background: Liver resection is the gold standard curative procedure for primary or secondary hepatobiliary cancers. It produces the best predictive results. An efficient technique carried out before substantial hepatic resection is portal vein embolization (PVE). Our study's purpose is to inquire about PVE indications, patient selection criteria, technique, post-procedural problems, and clinical results prior to right hepatectomy.

Methods: Twenty-five participants who underwent right portal vein embolization before partial hepatectomy between May 2019 and June 2022 were the subjects of this retrospective analysis. Following the diagnosis of hepatic respectability, all participants were admitted for PVE. The selection criteria involved the accessibility of patient records. Records were analyzed. Excluded cases were those future liver remnants (FLR) prior to and following PVE, or hypertrophy was not documented.

Results: Most of RPVE (72%) was carried out on patients with hepatocellular carcinoma. A large percentage of patients (88%) had definitive surgical excision after PVE. Four participants (16%) experienced complications related to PVE. More severe consequences were also seen by three (12%) of the patients who underwent right hepatectomy, such as postoperative liver failure, bacteremia, and small intestine ischemia.

Conclusions: Preoperative PVE is an effective way to boost FLR volume and has an excellent technical and clinical success rate. This method increases the ability of liver tumors resection that were previously deemed unsuitable for resection due to insufficient FLR volume.

Keywords: Portal vein embolization, future liver remanent, and polyvinyl alcohol particles.

INTRODUCTION

Liver resection is the gold standard curative procedure for primary or secondary hepatobiliary cancers. It produces the best predictive results. However, postoperative liver failure is a serious consequence that is primarily correlated with liver remnant size and function [1].

An efficient technique carried out before substantial hepatic resection is portal vein embolization (PVE). It seeks to stop the passage of portal venous blood to the liver segments that are about to be removed, which will cause their atrophy and, eventually, cause the healthy liver to grow more quickly in response. This will result in an increase in the

functioning liver volume post-surgically, also described as the future liver remnant (FLR) [2].

PVE is often indicated when the predicted remnant liver volume (FLR/total estimated liver volume (TELV ratio) is less than 25% of the total liver volume in otherwise healthy liver and 40% in cirrhotic or impaired liver. Two to six weeks following embolization, liver resection is subsequently carried out [3]. Even though PVE can encourage hypertrophy of either lobe, left PVE is infrequently carried out because left hepatectomy produces a substantial amount of post-hepatectomy remaining liver volume, making liver failure improbable. Volumetric investigations

revealed that the standardized FLR (sFLR) is often greater than 33% even with a left hepatectomy that extends to segments 2, 3, and 4 with extension to the caudate. After extended right hepatectomy, the average sFLR is 20%, unfortunately [4,5].

There have been a few observed PVE restrictions that could reduce the approach's advantages: Patients with unresectable metastatic disease, like distant metastases or periportal lymphadenopathy, tumor ingrowth of the portal vein, portal hypertension, and, to a lesser extent, systemic disease, like diabetes mellitus, may be able to restrict hepatic growth because insulin is a comedogenic factor with hepatocyte growth factor (HGF), resulting in sluggish renewal [6].

In 20% to 25% of instances, minor problems including a little fever and abdominal ache are noted. Only 2% of cases involve infection, subcapsular hematoma, haemobilia, and portal vein thrombosis. Deaths attributed to PVE have not been documented [7].

For PVE, a number of different procedures are used, such as intraoperative portal branch ligation, ipsilateral or contralateral percutaneous transhepatic embolization, and trans-ileocolic PVE [8].

Additionally, a variety of embolization materials can be employed, including polyvinyl alcohol particles (PVA), non-absorbable gelatin, coils, fibrin glue, n-butyl cyanoacrylate, and lipiodol [9].

Our study's goal is to discuss PVE's indications, technique, post-procedural problems, and clinical results prior to right hepatectomy.

METHODS

Twenty-five participants who underwent right PVE before partial hepatectomy between May 2019 and June 2022 were the subjects of this retrospective analysis. They were found to have a variety of primary and secondary hepatobiliary tumors that required hepatic resection, the most prevalent of which were liver metastases and hepatocellular carcinoma. Following the diagnosis of hepatic resectability, all participants were admitted for PVE from the Hepatobiliary unit to the Department of Interventional Radiology. The availability of patient records who performed

RPVE prior to major right hepatic resection between 2019 and 2022 served as the selection criterion. Our local picture archiving and communication system (PACS) were analyzed to extract patient characteristics, PVE indications, pre/post-PVE liver volumes or percentage of FLR, the technique employed, the interval between PVE and CT-associated PVE complication, and hepatectomy results. Our institutional review board (number 10075/20-11-2022) gave the study their approval. Excluded cases were those where the patient features, FLR prior to and following PVE, or hypertrophy were not documented.

Technique:

Hepatobiliary surgeons, hepatologists, radiologists, and interventional radiologists all participated in the multidisciplinary discussion that led to the decision to perform PVE prior to resection. After carefully examining the data from the chosen cases, our multidisciplinary team agreed that RPVE should be performed before right hepatectomy. The current study decided to perform RPVE without segment intravenous (IV) embolization as the access to the left portal vein carried a minuscule chance that stray embolic material would affect one of the veins in the targeted remnant. There are technical difficulties with segment IV embolization.

The day before the procedure, patients were admitted, and they were not given any food or drink (NPO). In most cases, IV antibiotic prophylaxis was necessary. Fentanyl and midazolam were used to moderately sedate the patient during PVE. Just before the procedure, an ultrasound was used to make sure the targeted access branch of the portal vein remained patent.

Either the contralateral transhepatic approach or the ipsilateral transhepatic approach could be used for percutaneous PVE. The main factor influencing the choice of approach in the current study is the operator's preferences. Although the ipsilateral approach could be more difficult technically, it does not involve puncturing the FLR. The contralateral strategy is quicker and provides easy access to the portal vein, but it might occasionally injure the FLR, making curative resection impossible [10-13].

Involved interventional radiologists chose an ipsilateral technique for every patient that was included. Under real-time ultrasound guidance, a 22-gauge Chiba needle was inserted into a peripheral portal venous branch of the non-FLR.

The needle was used to introduce a 0.18-in. guidewire, which was subsequently swapped out for a dilator of the proper size using fluoroscopy. A 5 Fr. or 6 Fr. vascular sheath was placed into the right portal vein branch. Under the Angio suite, the procedure was performed. A 5 Fr. angiographic flush catheter placed within the primary portal vein was used to perform portography (Figure 1 A).

Anteroposterior and oblique projections are used to capture pictures via digital subtraction. To best characterize variation anatomy, selective right and left portograms are obtained.

The preferred embolic agents were spherical microparticles (like PVA particles, for example). Under fluoroscopy, the microspheres, which ranged in size from 100 to 1000 micron, were introduced incrementally (Figure 1B).

In order to further restrict portal inflow, promote hypertrophy, and lower recanalization rates, fibered microcoils were placed in the more proximal segmental branches of the portal vein after particulate material embolization was finished and the portogram showed a state of near stasis (Figure 2). The flush catheter was inserted into the main portal vein to get the final portography (Figure 3). The working catheter and vascular sheath were removed after the embolization was complete, and the access tract was sealed off with gel foam.

Reviewing patient complaints, clinical indicators, and laboratory results are all parts of post-procedure monitoring for evidence of postembolization syndrome or liver insufficiency (such as elevated white blood cell count, increasing transaminase levels, or prothrombin time), vigorous hydration up till appropriate oral intake. For the treatment of pain, nausea, and fever, opioids, antiemetics, and antipyretics were available as needed. As oral intake is sufficient and parenteral opioids are not necessary for pain control (although

pain is unusual after PVE), patients were discharged, typically the following day [14].

Triphasic computed tomography (CT) protocol was used to do a follow-up imaging procedure after PVE 2-4 weeks later (Figure 4). The disappearance of the right portal vein opacification on subsequent imaging was used to determine if embolization was fully achieved. The radiological indicator of disease overgrowth between PVE and follow-up imaging was an increasing tumor load on the follow-up scan.

A volumetric evaluation was carried out (Figure 5). On contrast-enhanced CT, liver volumes were assessed both before and after PVE using special software for volume calculation. A formula developed by Vauthey et al. [15] was used to compute the sFLR by dividing the FLR-V (measured by CT volumetry) by the total liver volume (TL-V): $Cal\ TL-V = -794.41 + 1267.28 \times BSA$ (body surface area).

$$BSA = \sqrt{height\ (cm) \times weight\ (kg) / 3,600}$$

It was initially established how the FLR (mL) and TLV (mL) changed before and after PVE. Afterwards, the percentage change in FLR volume relative to TLV was used to calculate the degree of hypertrophy (DH%): $DH\% = (FLR/TLV\ post\ PVE - FLR/TLV\ pre\ PVE) \times 100\%$.

$$\%FLR\ volume\ increase = \frac{\%FLR\ post\ PVE - \%FLR\ pre\ PVE}{\%FLR\ pre\ PVE} \times 100\%$$

Statistical analysis:

Continuous data were expressed as median and range and compared using Mann-Whitney U test. Categorical data were compared using chi-square test or Fisher’s exact test as appropriate. P values < 0.05 were considered statistically significant.

RESULTS

Table 1 lists the clinical characteristics of twenty-five patients who had RPVE at our facility between 2019 and 2022. Ultimately, 72% of these techniques were carried out on patients with colorectal metastasis. A large percentage of patients (88%) had definitive surgical excision after PVE. The disease progressed in three patients making them unfit for surgical resection (Table 1).

Volume measurements both before and after PVE were computed for each subject. Table 2 shows the median sFLR volumes pre- and post-PVE.

Four participants (16%) experienced complications related to PVE. A subcapsular hematoma that occurred in two patients (8%) necessitated hospitalization to the intensive care unit. Even though the first one required a blood transfusion, the planned surgical excision was carried out right away. As there was significant tumor progression, the hepatectomy surgery for the second one was cancelled. The final two cases (8%) required hospital admission, had pain and nausea, and

had planned hepatectomy surgery in due time (Table S1).

Table S2 contains a list of complications following liver resection. Thirty-six percentage (n = 9) of postoperative complications overall. The majority of the problems were modest and comprised one pleural effusion with aspiration pneumonia, three wound infections, and two urinary tract infections.

Three patients (12%), each of whom received right hepatectomy, suffered more severe side effects, including one incident of postoperative liver failure, one incidence of bacteremia, and one instance of small intestinal ischemia requiring bowel resection.

Table 1: Clinical characteristics of patients.

Characteristic	Participants
Age years (mean ± SD)	50±9.7
Gender	
Male	17
female	8
Aetiology	
Colorectal cancer hepatic metastasis	18 (72%)
Hepatocellular carcinoma	5 (20%)
Others	2 (8%)
Preoperative chemotherapy	20
Cirrhosis	4
Operation	
Resection	22 (88%)
No resection	3 (disease progression) (12%)

Table 2: Comparison of future liver remanent (FLR) volume before and after portal vein embolization (PVE).

	Pre PVE	Post PVE
FLR volume, ml, median	439.0 (256.9–513.0)	578.6 (420.0–703.3)
sFLR, %, median	23.5 (18.8–29.5)	35.5 (24.5–42.3)

%FLR volume increase =31.8 (26.0-87.0)

The standardized FRL (sFRL), which was calculated by dividing FRL-V (measured by CT volumetry) by total liver volume (cal TL-V), which was calculated using a formula described by Vauthey et al. [15]:

Cal TL-V= -794.41 + 1267.28 x BSA (body surface area).

$BSA = \sqrt{\text{height (cm)} \times \text{weight (kg)} / 3,600}$

$\%FLR \text{ volume increase} = \frac{\%FLR \text{ post PVE} - \%FLR \text{ pre PVE}}{\%FLR \text{ pre PVE}} \times 100\%$

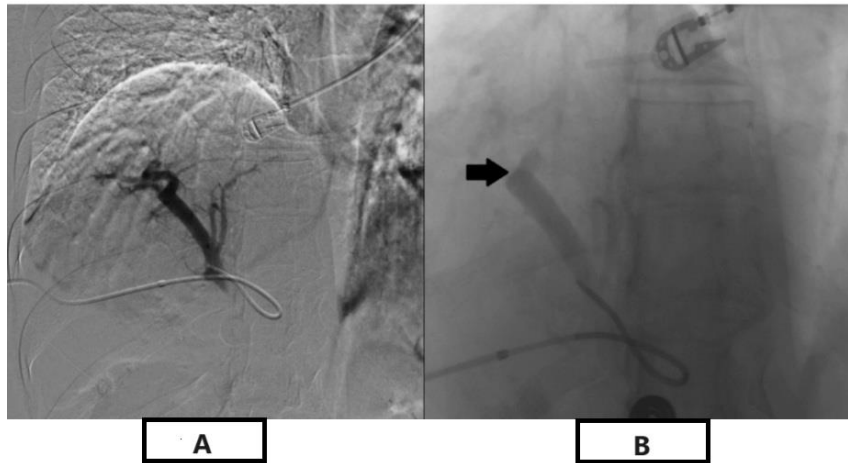


Figure 1: Male patient 50 years old with colorectal metastasis. **A:** Right anterior portal vein ipsilateral transhepatic percutaneous portography. **B:** Following the injection of PVA particles, the opacified flow in the right anterior portal vein slowed down (black arrow).

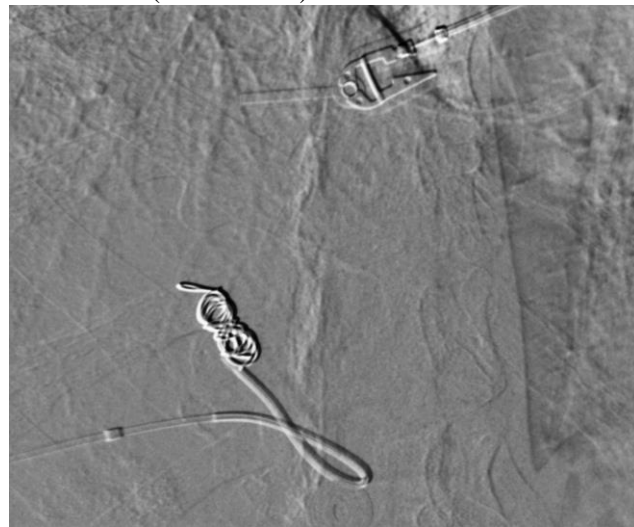


Figure 2: Female patient 56 years old with colorectal metastasis. Portography following RPVE; right anterior and posterior portal vein branches were embolized with coils as shown by the white arrows.

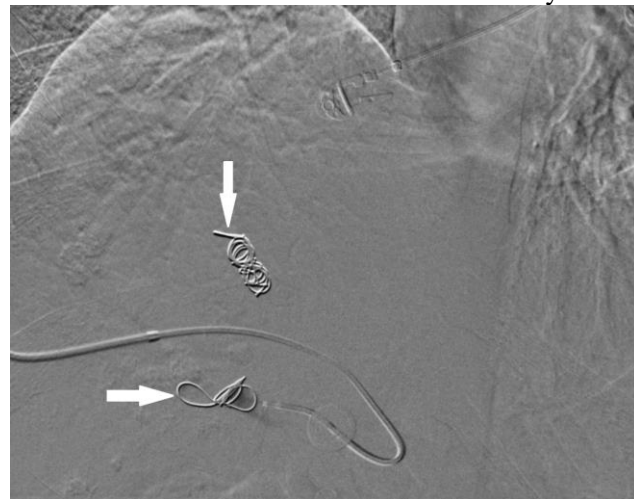


Figure 3: Male patient 49 years old with colorectal metastasis. Portography following RPVE and the main left portal vein is clearly and effectively opacified. However, the segmental branch where the access sheath was introduced was not embolized adequately by coil, so further recoiling was done before ending the procedure.



Figure 4: Follow-up CT after PVE procedure for a 55 years old male patient. In the portal venous phase of the post-PVE CT coronal picture, the right anterior and posterior portal venous branches are adequately coiled, and the left main portal vein is patent (black arrows). Calcific hepatic metastatic deposit observed (white arrow).

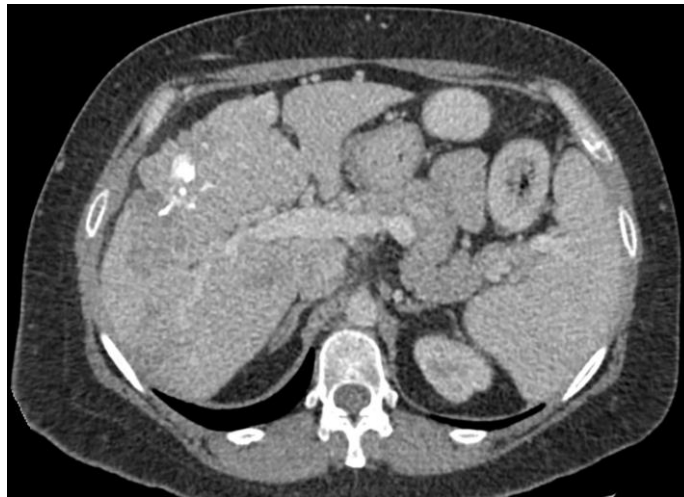


Figure 5: CT software processing for same patient on follow up after PVE procedure. The FLR's post-PVE CT volumetry is about 821.27 ± 11.12 (before was 560.11 ± 15.15).

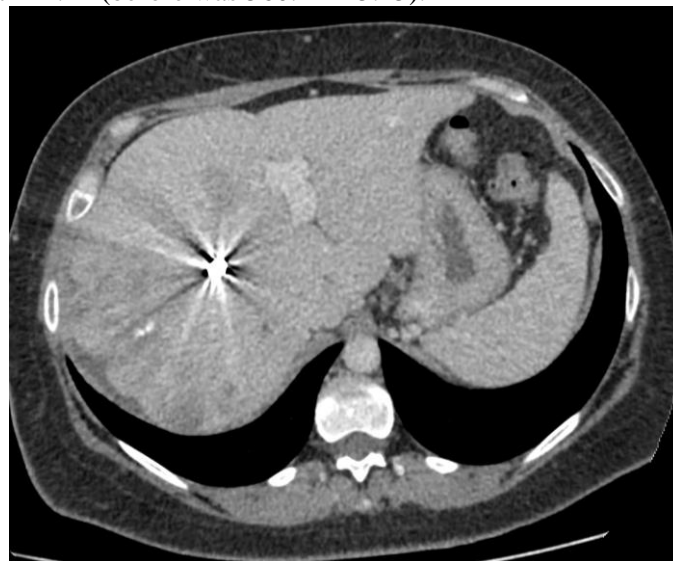


Figure (6)



Figure (7)

DISCUSSION

In the current investigation, colorectal cancer hepatic metastases were the commonest indication. For PVE in 18 cases (72%) followed by hepatocellular carcinoma in 5 instances (20%), and other liver diseases in 8% of cases. Based on the predicted postoperative volume of the FLR, liver function, and the presence of underlying liver disease, the clinical decision to conduct PVE is made [16]. In most trials, a resection of more than 70–75% of the total liver volume in normal livers and more than 60–65% in impaired livers served as the fundamental cut-off point for preoperative PVE (i.e., cirrhosis, fibrosis) [17, 18, 19]. Using the Vauthey calculation [15], the proportion of FLR volume increase in our study was equal to 31.8 (26.0-87.0). The foundation for our surgical resection planning was a CT volumetric assessment. The average period between PVE and liver resection in our study was 33 days, which is comparable to the findings of Huang's meta-analysis, which indicated a time delay of up to 38.9 days. Our understanding is that a longer period following PVE permits more FLR development. However, some surgeons contend that PVE also promotes tumor growth [18]. The intervention radiologists at our institution opted to use PVA particles, and fibered microcoils were positioned in the more proximal areas to further reduce portal inflow. PVA particles are generally available, have trustworthy side effects, and effectively block the portal lumen for an extended period of time. PVA is therefore indicated for usage

either alone or in conjunction with other materials in the vast majority of centers [19, 20].

The portal venous system can be blocked for a very long time with PVA particles, which are convenient to utilize. Little inflammation is visible in the liver tissue after PVA application [16].

Twenty-two instances (88%) required further hepatic resection, whereas only three cases (12%) were abandoned due to disease progression. 100% of technical attempts were successful.

This study's resection rate (88%) is comparable to Sakuhara et al. [21], Sofue et al. [22], Yamamoto et al. [23], Alvarez et al. [24] and Santhakumar et al. [25].

14.2% of the planned resections in 37 studies (1,464 patients) in the Lienden metanalysis [7] were abandoned due to newly formed FLR metastases, extrahepatic tumor spread, or local intrahepatic tumor progression making resection unfeasible.

In 8% of instances, there were significant PVE-related problems, including subcapsular hematomas. The condition only progressed in one patient with subcapsular hematoma, leading to cancelled liver resection. This information matched with Santhakumar et al. [25] and Di Stefano et al. [26]. The frequency of these issues was in line with the 6% cut-off point for serious PVE-related complications suggested by the Society of Interventional Radiologists quality improvement standards [27].

Post-resection complications (36%), six cases of minor complications, including two cases of urinary tract infections, three cases of wound infections, and one case each of aspiration pneumonia and pleural effusion.

One bacteremia, one liver failure, and one small bowel ischemia were three cases of significant consequences. This mirrored the study by Alvarez et al. [24] postoperative liver failure rates, which ranged from 5.6 to 14.0%. Our study has some restrictions. First, the FLR estimate was influenced by how subjectively the CT-based volumetric assessment was performed. Second, different intervals were employed between the time of the embolization and the follow-up imaging modalities. Third, the small sample number was an obstacle in the statistics, as the financial and technical challenges restricted the ability to widespread preoperative PVE in our center. Last but not least, the current study's retrospective and non-randomized methodology prevented additional investigation and introduced a bias in selection.

Conclusions

Preoperative PVE is an effective way to boost FLR volume and has an excellent technical and clinical success rate. Liver tumors that were previously thought to be unsuitable for resection because of insufficient FLR volume are now more resectable owing to this technique. However, some side effects could make it more difficult for a patient to endure future treatments or surgery.

Therefore, the procedure should be handled by a multidisciplinary team that includes interventional radiologists and hepatobiliary surgeons. This will guarantee that the right patients receive the procedure's benefits and that it is performed safely.

Conflict of interest

The authors declared that they have no conflicts of interest with respect to the authorship and/ or publication of this article.

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Table S1: PVE-associated complications

Patient number	Indications	PVE complications	PVE outcomes	Surgical outcomes
2	Colorectal cancer metastasis	Pain and nausea	Hospital admission	Complete resection
1	Hepatocellular carcinoma	Subcapsular hematoma	ICU admission and blood transfusion	Complete resection
1	Colorectal cancer metastasis	Subcapsular hematoma	ICU admission	No resection secondary to disease progression.

Table S2: Post-hepatic resection complications

Complications	Percentage
Minor complications	24%
<ul style="list-style-type: none"> • Urinary tract infection • Wound infection • Pleural effusion/pneumonia 	8% 12% 4%
Major complications	12%
<ul style="list-style-type: none"> • Small bowel ischemia • Bacteremia • Liver failure 	4% 4% 4%



Figure S1

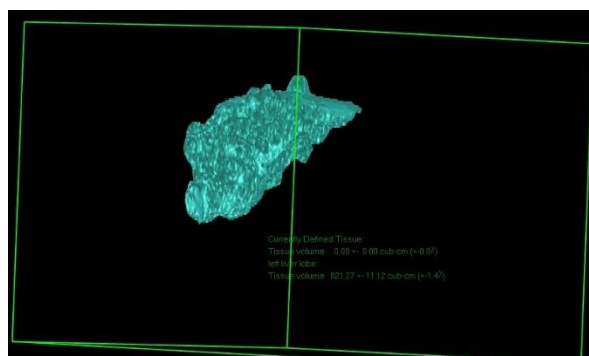


Figure S2