

Quality Improvement for Portal Vein Embolization

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Introduction

Major hepatectomy carries a significant risk of mortality. In patients with normal liver bearing metastases, mortality after major hepatectomy ranges from 0.5% to 4%, but in patients [1] with chronic liver disease, such as cholestatic or cirrhotic liver, mortality increases up to 4 to 12% [2, 3]. The main cause of mortality as well as post-operative morbidity after major hepatic resection is liver insufficiency often due to an insufficient liver remnant volume [4, 5]. It has been demonstrated from animal experiment and clinical data that redirection of the portal flow towards a part of the liver will induce hypertrophy of this part. This redirection of portal flow can be obtained by surgical ligation or percutaneous embolization. Today, percutaneous portal vein embolization (PVE) is preferred to surgical ligation in order to avoid additional surgery. However, when surgery is performed, usually for resection of the primary tumor, and portal vein flow redistribution is required, no clear recommendations can be given regarding if it is preferable to carry out percutaneous PVE in a second step or ligation at the time of surgery. Some papers report higher hypertrophy after PVE [6] and others report no differences in hypertrophy [7]. The aim of PVE is to pre-operatively increase the volume of the future liver remnant in order to enable surgery and decrease postoperative morbidity when the only contraindication to surgery is an initially insufficient remnant liver.

Definition

Future liver remnant (FLR) is the liver that will be left in place after surgery and which was not targeted by embolization. The FLR must hypertrophy after portal vein embolization. Most teams will wait 4 weeks before surgery. FLR hypertrophy must be measured by means of a CT examination after injection of iodine with volumetric measurements of the future remnant segments and compared to the measurements performed before portal vein embolization using the same technique.

Hypertrophy can be quantified as FLR hypertrophy which is defined as the difference between FLR after a waiting period from 3 to 6 weeks post PVE minus FLR before PVE divided by the FLR before PVE. The waiting period must be long enough to allow hypertrophy and as short as possible to avoid tumor growth precluding surgery. Hypertrophy can also be quantified by the increase of the FLR ratio. The FLR ratio is defined as: $(\text{FLR volume} - \text{tumor in the FLR}) / (\text{total liver volume} - \text{total tumor volume})$ [8].

Technical success of portal vein embolization is defined by a complete occlusion of portal branches feeding the future resected liver segments. Branches of the future liver remnant

must be patent with hepatopetal flow. In the late phase of the control portography, parenchymography must be visible only in the future liver remnant.

Clinical success is considered successful if the patient reaches the volumetric criteria for liver resection.

Major hepatic resection (or major hepatectomy) is defined as a resection of at least 4 out of 8 segments of the liver. Right hepatectomy is defined as a resection of segments V to VIII. Extended right hepatectomy additionally includes segment IV.

Resection rate is defined as the number of embolized patients that will ultimately be resected.

Patient selection

Patients must be candidates for major hepatectomy or major hepatectomy associated to radiofrequency ablation on the future liver remnant. This decision should be taken in a tumor board meeting including surgeons, hepatologists, oncologists and interventional radiologists. The only contraindication to the liver resection must be the initially insufficient volume of the future liver remnant.

PVE indication is determined by the liver volumetry obtained from a liver CT [9]. Liver volumetry is done manually from CT slices after injection of contrast media, preferably in the portal or equilibrium phase in order to have all the portal and hepatic veins opacified. Slice thickness of 5mm or below is recommended. The future liver remnant is determined according to the future resection plane in collaboration with the surgical team. If RFA is planned on a tumor in the future liver remnant, the expected volume of radiofrequency ablation must be taken into consideration and subtracted from the future liver remnant volume. Any tumor tissue must not be taken into consideration for volumetric evaluation, as volumetry must evaluate liver tissue only.

Blood tests including liver enzyme, bilirubin level, PTT, PT and platelet count must be obtained before PVE.

Criteria to propose PVE are different according to the liver status and to the tumor involvement:

A. Patients with tumors that have developed in normal underlying liver parenchyma:

PVE is recommended when the FRL to total liver ratio is below 25-30 [7, 10, 11]. The indication of PVE can be extended to a 40% FLR ratio in patients having received chemotherapy or showing abnormal indocyanine green test results (or other abnormal liver function tests) [10, 12, 13].

B. Patients with tumors developed in chronic liver disease and cirrhosis:

In such cases the decision is based either on liver volume or on liver volumes plus estimation of the overall liver function by indocyanin green retention rate at 15 minutes (ICCG 15). An FRLR of 40% is recommended when the ICCG 15 is between 10% and 20%. When the ICCG 15 is above 20%, an FRLR of 50% is recommended [12-14].

C. Patients with tumors invading the biliary tree associated with cholestasis:

As biliary obstruction has impaired liver regeneration and hypertrophy, the biliary tree of the FRL must be drained first and the PVE can be performed secondarily. The indication is an FRLR below 40% [15].

Contraindication for PVE [11]

PVE is contraindicated in patients with:

- Tumors invading the portal vein
- Portal hypertension (blocked to free hepatic vein pressure gradient over 12mm HG)
- Coagulation disorders (PT<60%, platelet count <50G/l)
- Even if a previous TACE may improve results of PVE [16], a minimum of 3 weeks delay between TACE and PVE is recommended.

Patient information before treatment

Patient should be informed that this procedure is not an anti-tumoral treatment, but a treatment made to increase safety or enable a surgical procedure.

Minor complications are encountered in 20-25% of cases, mainly with the association of slight fever and abdominal discomfort and pain. Major complications are infrequent and mainly include infection and subcapsular hematoma, hemobilia and portal vein thrombosis (in less than 2% of cases). Mortality due to PVE has not been reported.

When tumors (usually small nodules) are present in the non embolized lobe, it must be explained to the patient that those lesions might increase in size more quickly due to PVE [17].

Patients must be told that the efficacy of the procedure can be estimated about 4 weeks after PVE by mean of another CT with injection of contrast media and liver volumetry.

Embolization method

Access to the portal system should be done under US guidance in order to puncture a peripheral branch [8]. Access can be obtained from a contralateral approach (i.e. puncture of the left portal branch and embolization of right portal branches) or an ipsilateral approach (puncture of the right to embolize right portal branches. The advantage of the contralateral approach is easier catheterization, but there is a risk of damage to the FLR.

Five French materials (catheter or introductory sheath) are usually recommended. The catheter should be placed at the splenomesenteric confluence to perform a portography in order to visualize portal anatomy including its variations and localize segment IV branches. Measurement of portal pressure is not routinely performed in patients with normal liver. In cirrhotic patients measuring the portal pressure and central venous pressure is useful to determine if the patient has a porto-systemic gradient superior to 12 mmHg in which case he/she is at major risk of complications occurring during surgery [18, 19]. These patients are not eligible for PVE.

The aim of embolization is complete obstruction of the targeted branches and redistribution of the flow to FLR branches only. A final portography is mandatory to verify this objective. A final pressure measurement should be obtained at the end of the procedure in patients with chronic liver disease in order to document the portal pressure increase which is usually around 3mmHg. Embolization of segment 4 branches is recommended in patients with tumors undergoing extended right hepatectomy. However, if embolization of that segment

causes the risk of reflux into the portal branch of the FRL, such embolization must not be performed, as any major reflux into FRL portal branches might preclude surgery.

Various embolic materials have been used.

Some products are not recommended due to reported recanalization or lower induced hypertrophy

Gelfoam is associated with a high rate of portal vein recanalization and seems less efficient than other products [8].

Non spherical poly-vinyl alcohol particles have been used, but are less efficient than spherical particles [20].

Alcohol Direct intra-portal injection has been described. Although efficient, it is hard to control and has been associated with a significant morbidity (liver necrosis, portal vein thrombosis) [21].

Drug loadable embols have not been reported in PVE and cannot be recommended

Recommended products [14, 20, 22] are

A Mixture of n-butyl-cyanoacrylate (NBCA) and iodized oil has been described extensively, showing good results and low morbidity. Usually a mixture of 1 part NBCA to 1 or 2 parts of Lipiodol is used. Injections of small aliquots in between abundant flushing with non ionic liquid such as dextran or glucose 5% is the most commonly reported technique.

Spherical microparticles associated with coil embolization, which is mostly described in North American reports, have been reported to be superior to non spherical PVA. It seems as efficient as NBCA, although never compared in randomized trials. Most teams start with 300-500 micron particles and finish with 700-900 micron particles. Coils are used at the end of the procedure to allow for complete occlusion of the proximal trunk. It is advisable to avoid all too proximal occlusions and rather leave 1cm unembolized segment of the right portal branch in order to facilitate surgical ligation at the time of liver resection.

Association of fibrin glue with iodized oil has mostly been described in Japan and has the drawback of requiring special catheters which are only available in Asia.

Medication and periprocedural cure

PVE can be carried out as an out-patient procedure when conscious sedation is used. A one or two day hospital stay is recommended, as reported by most teams using either conscious sedation associated with local anesthesia or general anesthesia.

There is no consensus on the use of antibiotics, and the type of antibiotics and the length of treatment vary from one report to another [11], excepted in patients with an associated biliary procedure. Due to the fact that very little to no liver tissue necrosis is found after PVE if an antibiotic is given, it must be for a very short period of time, single dose to 48 hours. Post

PVE mild to moderate abdominal pain is reported in 20% to 30% of patients, usually easily controlled by oral analgesia. Use of pure alcohol as embolic material is associated with more severe abdominal pain.

Biological tests are not mandatory after the procedure. A slight elevation of AST and ALT with a peak at day 3 after the procedure have been reported, but without clinical significance.

Results [14]

Technical success rate should be close to 100%. Very few cases of failures or repeated procedures have been reported in the literature.

Resection rate should be around 85%. This rate may decrease to 70% in case of cirrhotic patients. Reasons for non resection are tumor progression, peritoneal metastases or unsuspected metastases discovered at laparotomy. Absence of hypertrophy is rare – less than 10% in metastatic liver – but can reach 20% in cirrhotic patients.

In patients with normal liver and liver metastases, the increase of the FLR ratio is between 8% and 25% and regeneration is always observed after PVE. In cirrhotic patients, PVE fails to induce a left lobe hypertrophy in 20% of cases. The increase rate of the FLR ratio in this population is slightly lower – between 6% and 20%.

Recent studies have demonstrated that hypertrophy is inversely proportional to the FRL ratio before PVE, meaning that the smaller FRL before PVE will have the larger hypertrophy. Consequently there is no lower limit for the FRL ratio to perform PVE.

Complications [14, 23]

In terms of complications (Table 1) a rate of minor complications (20-25%) is accepted. With major complications this rate should be below 5% and should not preclude further liver resection. Except for inadvertent embolization, most complications will occur in the punctured lobe, which is an argument in favour of a homolateral approach. However, complication rates for homolateral and controlateral approaches are the same. Reported in the literature the only factor increasing complications is puncture of the posterior segment versus puncture of the anterior segment [24], thus advocating puncture of the anterior segment when compatible with the location of the PVE to be performed.

Table 1: Portal vein embolization procedure

Minor complications	Mean reported rate %	Suggested procedure threshold %
Abdominal pain	20	40
Fever	25	50
Nausea	2.5	5
Embolic material displaced in the FRL without portal thrombosis	0.2	0.4
Major complications		
Liver abscess	0.3	0.6
Cholangitis	0.2	0.4
Main or left portal vein thrombosis	0.2	0.4
Subcapsular hematoma	0.2	0.4

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