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Review Article

Major Hepatic Resection Following Portal Vein Embolisation: Indications, Technique and Peri-Operative Outcome

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ABSTRACT

Major liver resections are limited by the volume of future liver (FLR) remnant with the risk of subjecting patient to post surgery liver failure. This increases morbidity and mortality of the patients. However, the technique of ipsilateral portal vein embolisation (PVE) has given surgeons extra mileage to consider major liver resections previously thought to be unresectable. All cases should be discussed in a multidisciplinary setting. A good knowledge of portal anatomy and variations should be known as part of selection procedure for PVE. Base liver functional status should be reviewed before consideration given to PVE. CT volumetry assessment should be made before and after PVE to assess for resectability. Multiple embolic materials are used in current practice, but none have shown superiority. Several complications are related to application of PVE, however it is generally regarded a safe procedure. At least four weeks are required to assess for FLR with repeat abdominal cross-sectional imaging. Patients with normal liver function tests achieve maximum hypertrophy in four weeks versus patients with underlying liver disease. Liver surgery is scheduled upto 2 to 6 weeks following embolisation. The aim of this article is to provide an overview of current indications, technique, complications and outcomes following PVE.

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Introduction

Liver resection is the only option for long term survival for patients with primary or metastatic liver disease. The resectability rate for patients with hepatocellular carcinoma and metastatic liver disease is 20 – 30% and 10 – 20% respectively [1]. The incidence of liver failure post liver resection varies from 0 to 30% and is a major cause of post-operative mortality. Initial unresectable disease because of insufficient future liver remnant can be made potential resectable by employing technique of portal vein embolisation (PVE) [2]. This helps to increase the volume of future liver remnant (FLR) and therefore increasing the possibility of liver resection. PVE is mainly indicated in two situations when future FLR is too small to support body metabolic needs or FLR is borderline

and high risk of post-operative liver failure with increased morbidity and mortality. PVE underlying principle is to stop portal blood flow to the segments of the liver to be resected and increase flow to the FLR which causes hypertrophy of contralateral liver segments. Several techniques for portal vein inflow occlusion have been described in the literature including trans-ileocolic, percutaneous transhepatic and intra-operative ipsilateral portal branch ligation [3-6]. Different embolisation materials have been employed e.g coils, gelatine sponge, lipidol, microspheres and fibrin glue [1]. PVE is a safe procedure and large case series have reported 0% mortality related to the procedure [7].

The first reported PVE was performed by Makuuchi *et al* 1990 for management of hilar cholangiocarcinoma [8]. Their initial objective was

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to avoid increased portal venous pressure following liver resection and achieving hypertrophy in the FLR. Following the initial success with hilar cholangiocarcinoma the subsequent reported series expanded the criteria for PVE. The indications expanded to include patients with colorectal liver metastases and non-cirrhotic HCC [9, 10]. Initial indication were multiple lesions limited to the right lobe of the liver and Central lesions located at the peri-hilar region. Especially for patients requiring extended right trisectionectomy, PVE was an opportunity to offer them liver resection safely and achieving FLR to achieve remnant liver synthetic function.

I Assessment of Liver Synthetic Function to Predict the Outcome

Before liver resection the synthetic function of the liver is assessed by the Child-Pugh Class A, B or C. Major liver resection is contraindicated in Child Pugh B and C patients. The PVE results will be impaired in patients with underlying liver disease and cirrhosis and it is advised to proceed with caution because of increased risk of acute decompensation [11]. All patients with liver cancer and normal liver functions with FLR < 20% are recommended to be considered for PVE [2].

II Contraindications for PVE

Multiple factors can preclude PVE. Some conditions can be considered as relative risk guided by individual patient factors and underlying disease conditions. Any factors that can precipitate liver failure are considered absolute contraindication for proceeding for PVE. A portosystemic gradient > 12 mm of Hg is a significant contraindication against PVE [12]. Child Pugh B and C cirrhosis patients will not be considered for major liver surgery hence will not proceed for PVE [13]. Presence of hepatic artery stenosis and thrombosis are significant risk factors for liver failure and PVE should not be considered.

III Planning for PVE

All patients will undergo triphasic computed tomographic scan to assess the liver anatomy. A detailed mapping of the portal vein along with its variations are outlined. The FLR is calculated to pre-determine outcome following PVE. The length of the right portal vein and its intra-hepatic branching pattern is identified to achieve access from the distal branches. Initial evaluation of tumour is performed to avoid access traversing through the tumour. Landing zone for the embolisation material e.g coils,

gelfoams is mapped avoiding migration to the contralateral side (FLR). The size of the portal vein is measured to pre-determine the size of the occlusion balloon to prevent migration of the embolic material.

IV Approaches for PVE

Multiple approaches have been described for performing portal vein embolization namely trans-ileocolic, contralateral and ipsilateral approach. (Table 1) describes the procedures, advantages and disadvantages of each approach. Trans-ileocolic approach was the first technique which involved direct cannulation of ileocolic vein to reach the portal tract. It had an additional advantage of peritoneal visualisation but involves laparotomy with impact on overall morbidity. The transhepatic contralateral approach involves puncturing the portal vein on the FLR side under ultrasound guidance and gaining antegrade access in the contralateral portal tract which is mostly the right portal vein. The ipsilateral transhepatic approach employs ultrasound guided access to the portal vein branches on the side of the diseased liver and crossing the full length of the portal vein branch to reach to the bifurcation. This is associated with less risk of disrupting the FLR but can lead to tumour seeding and spillage [14].

Regardless of which transhepatic approach is applied, the PVE will comprise of following steps.

1. Ultrasound or fluoroscopy to cannulate the portal venous system.
2. Portography to assess the position of the catheter and reposition to achieve the pre-determined landing zone.
3. Measurement of portal pressure to determine the porto-systemic gradient.
4. Injecting the embolic material and reconfirming the position of the site of embolisation followed by repeat portal pressure measurements and withdrawal of catheter.

Types of Embolic Materials

Multiple types of embolic materials are used in routine clinical practice. They comprise of fibrin glue, absolute alcohol, gelatin sponge, metal coils and microparticles (microspheres). There are no randomized clinical trials which have shown clinical superiority of one agent over the other [13]. However, a combination of coils and absolute alcohol is a preferred combination of agents for inducing hypertrophy in the normal liver remnant [15].

Table 1: Approaches to portal vein embolization.

| Approach | Method | Advantages | Disadvantages |
|---------------------------------------|---|--|--|
| Ipsilateral | Cannulation of diseased liver to puncture the portal vein | Decreased risk of injury to the future liver remnant | Risk of seeding the tumour Migration of embolic material to the contralateral segment |
| Contralateral | Cannulation of the portal vein from the normal liver (FLR) | Anatomical easy route to gain access to portal vein | Injury to the FLR Embolic material migration to the left lobe of the liver |
| Laparotomy and Ileo-colic- SMV | Puncture of ileo-colonic vein to gain access to portal vein | Visualisation of peritoneal cavity Assessment of gross liver architecture and FLR | Risk from laparotomy Injury to bowel Portal vein thrombosis |

FLR: Future liver remnant, SMV: Superior mesenteric vein.

I Pathophysiology of PVE

Structural and histological changes are viewed in the liver following PVE. The scale of changes following PVE are different following hepatectomy. Because of compensatory hypertrophy in the FLR, liver rotates around the axis towards the atrophic lobe. The degree of cellular proliferation is unevenly distributed in the future FLR. Periportal region shows maximum cellular expansion versus central vein. The underlying replication at any given time in hepatocytes is limited to only 0.01% of the total cell volume however this persistent pattern helps to achieve the liver volume in a short period of time. Following PVE, increase in the cell number (hyperplasia) is the main contributor versus increase in cell size (hypertrophy) [16]. The phenomenon of increase in volume in non-PVE part of liver initiates well before the atrophy ensues in the occluded segment of the liver [17].

Several theories have been proposed to explain the mechanism of hypertrophy and hyperplasia resulting following PVE. Increase in portal pressure drives endothelial cells to generate nitric oxide which inhibits methionine adenosyltransferase and activates extracellular signal-regulated kinases (ERK 1, 2) members of the mitogen-activated protein kinases. Traditionally, ERK are linked with the regulation of cellular proliferation and differentiation [18]. Hepatocyte swelling from increased portal flow activates mitogen-activated protein kinase (MAPKs). Also, systemic growth factors may also significantly contribute to the hypertrophy in the FLR. Hepatocyte growth factor (HGF) is a potent mitogen that binds the HGF receptor, c-met, and can induce hepatocyte DNA synthesis both in vitro and in vivo. HGF is produced by nonparenchymal cells in the liver and acts as a paracrine factor on hepatocytes. Animal studies have shown significant increase in HGF-RN in the non-PVE lobe of the liver versus the embolised lobe. This change was observed within 6 hours of ligation and also associated with significant increase in hepatocyte DNA synthesis [19].

II Complications Following PVE

The complication rate following PVE is between 9 to 12% [20, 21]. Immediate complications include bleeding, migration of embolus to the FLR vein and portal vein thrombosis of the main trunk. Also, if ipsilateral approach is employed there is risk of guide wire passing through part of the tumour causing tumour spread. Hemobilia, cholangitis, pneumothorax and subcapsular haematoma have all been observed following PVE [2].

III Post PVE Assessment of Future Liver Remnant

Child Pugh class A patients will regenerate liver at a rate of 12- 21 cm³/day and will achieve significant hypertrophy in one month. While patients with liver cirrhosis has significantly lower hypertrophy rate at 9 cm³/day and will take > one month to achieve hypertrophy a volume required in the FLR [2]. Following one-month patients will undergo repeat CT scan for volumetric analysis and determination of FLR. A repeat PVE can be considered to the ipsilateral side if the first embolisation failed to completely occlude the first order branching of the portal vein. The indications for repeat ipsilateral PVE are few and success in achieving the desired outcome is limited.

Clinical Overview

PVE is a safe and well tolerated procedure. It is routinely performed as a day case procedure. In 50% of cases there is no significant change observed in liver function tests (LFT's) following PVE. Even if change in LFT's is observed is temporary and returns back to baseline. There is minimal effect on patient coagulation profile and synthetic function of the liver is preserved [22]. PVE causes minimal side effects when compared to trans-arterial embolisation (TACE). Its major effect is caused by cellular apoptosis versus necrosis hence causing limited release of inflammatory mediators [2]. Assessment for patients for suitability for PVE is multifactorial. It includes type of tumour, tumour size, assessment of liver function, associated liver disease, extent of liver resection and size of FLR.

Segment 4 embolisation in patients undergoing extended right trisectionectomy has been advocated. This is in addition to full right portal vein embolization. It can be achieved by both contralateral and ipsilateral approaches. It helps in further hypertrophy of left lateral segments in achieving the FLR [23]. Not all patients will proceed to surgery following PVE and will be considered for resection. Approximately 15% of patients will not proceed for surgical resection. This is either due to inadequate FLR size, tumour recurrence in FLR and systemic spread of tumour rendering any type of surgical resection futile [7]. The cytokine driven hyperplasia and hypertrophy of hepatocytes has been identified as a potential promoter of tumour growth both intra- and extrahepatic [24]. The new procedure associating liver partition and portal vein ligation is being promoted to induce contralateral lobar hypertrophy in a short period of time [25]. However, it is not a widely practiced surgical technique at present and results are limited to only few case series [8].

Conclusion

PVE is a safe procedure which can be considered in patient's requiring major liver resection but are limited by the tumour volume. This technique can help to achieve FLR volume required to meet post-resection metabolic demands of the patient. Previously labelled unresectable tumours can be considered for resection and will help to improve post-operative outcomes. PVE should only be conducted in a multi-disciplinary setting where both surgeon and the interventional radiologists are fully aware of options available; portal anatomy has been extensively reviewed and CT volumetry has been employed in calculation of FLR both before and after PVE.

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