Portal Vein Embolization of Indications and Contraindications

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Preoperative portal vein embolization (PVE) via the purposeful occlusion of select portal vein branches to promote contralateral hepatic lobar hypertrophy has become the accepted standard for liver regeneration. Advances in embolic materials, selection of treatment approaches, and PVE with hepatic venous deprivation or concurrent transcatheter arterial embolization/radioembolization are all active areas of research. The primary indication for pre-operative PVE is centered on the inability of the pre-embolization future liver remnant (FLR) to support whole liver function post-resection. Contraindications to PVE are severe portal hypertension, uncontrollable intrahepatic portal-to-hepatic vein shunts, tumor thrombus in the portal vein, and occlusion of the portal vein in the FLR.

portal vein embolization | future liver remnant | liver hypertrophy

1. Introduction

1.1. Hepatectomy

Rates of both primary and secondary liver cancer has been increasing in incidence over the past few decades [1], with hepatocellular carcinoma (HCC) being the fourth most common cause of cancer-related mortalities worldwide [2]. Liver transplantation and surgical resection are the only two therapies that offer long term survival, and because of the strict criteria for transplantation in addition to the finite number of available organs, resection, when possible, remains the mainstay treatment in both HCC and confined metastatic disease [3][4]. Additionally, patients must meet certain criteria in order to be amenable to surgical resection [5]. Large-volume tumoral liver resections carry the substantial risk of post-hepatectomy liver failure (PHLF) due to the inability of the residual hepatic tissue to handle the workload of the previous whole organ.

1.2. Future Residual Liver Volume

The percentage of liver that remains post-resection, known as the future liver remnant (FLR), is an independent and reliable predictor of post-resection hepatic dysfunction [5][6]. The expected absolute FLR volume alone is not enough to predict a good prognosis for patients post-resection. Patients with larger body mass indices (BMI) and body surface areas (BSA) will require a larger FLR to achieve appropriate compensation to avoid hepatic insufficiency. Therefore, the concept of the standardized FLR (sFLR) emerged to standardize the FLR relative to a patient's size [7]. The sFLR, expressed as a percentage of the patient's liver volume, is determined by taking the

FLR as a ratio of a patient's total functional liver volume (TLV). Multiple studies have shown that post-resection complications are significantly reduced in patients with an sFLR > 20% in normal livers [8]. Interventional oncologists offer a unique procedure to achieve this, and thereby expand resection indications, limiting dropouts from curative treatment and improving management algorithms.

A second associated concept referred to as kinetic growth rate (KGR) has been shown to be a promising factor in determining mortality from hepatic insufficiency [9]. KGR is calculated by degree of hypertrophy at first post-portal vein embolization (PVE) volume assessment (%) ÷ time elapsed since PVE (weeks) at the first post-PVE volume assessment. A recent study demonstrated KGR > 2.0% growth per week was associated with zero cases of hepatic insufficiency post-resection. The authors concluded KGR may be a better predictor of postoperative morbidity and mortality after liver resection than conventional volume parameters.

1.3. Portal Vein Ligation

The role of portal vein ligation (PVL) in inducing hypertrophy of the liver has been clearly demonstrated in an experimental study studying liver hypertrophy in rat models [10]. However, another report has suggested that PVL was significantly less efficient than portal vein embolization (PVE) in inducing hypertrophy of the left lateral segments [11]. Pandanaboyana et al. took this a step further and published a meta-analysis comparing PVL with PVE for elective liver resection. A total of 218 patients were included, and they found no significant difference in FLR hypertrophy between the two groups (PVE: 39%, PVL: 27%, mean difference 6.04, 95% confidence interval −0.23, 12.32, p = 0.06). This procedure achieves liver hypertrophy by surgically ligating the desired extrahepatic branch of the portal vein, thereby re-directing the entire portal vascular flow into the FLR. A common topic of discussion is the relative efficacy of PVL versus PVE for inducing FLR hypertrophy [12]. Capussotti et al. demonstrated that PVL is just as efficacious as PVE in inducing FLR hypertrophy [13]. A larger systematic review by Vyas et al. found that PVL induced a mean FLR hypertrophy rate of 64.65%, with a receptibility rate of 63.68% versus a PVE hypertrophy and resectability rate of 39.75% and 76.88%, respectively [14].

1.4. Portal Vein Embolization

Since its inception almost 30 years ago, PVE has now become the standard of care treatment to prevent post-hepatectomy liver failure (PHLF). During PVE, embolic material is administered intra-vascularly into select intrahepatic portal veins to decrease the portal vascular flow to the targeted liver segments with tumoral involvement. Occlusion of the portal veins ultimately deprives the embolized segments of liver of the blood flow required to sustain growth, while subsequently inducing a physiologic response to hypertrophy in the non-embolized liver segments. PVE leverages the unique dual vascular supply of the liver, with the liver parenchyma being fed by both hepatic arteries and from the portal venous system which reduces the risk of infarction.

To date, multiple studies have proved PVE to be safe and effective in down-staging tumoral liver tissue, optimizing future liver remnant (FLR) and ultimately increasing the number of patients eligible for major liver resection [15][16][17].

However, there is also published evidence that points towards PVE having controversial results in overall survival (OS) rates, as well as on disease-free survival (DFS) rates. Giglio et al. performed a systematic review analyzing the oncological outcomes of patients who underwent major liver resection following PVE, and they reported on postoperative hepatic recurrence (PHR) and 3-year and 5-year OS rates between patients who received PVE and those who did not [18]. They found that no difference in PHR (p = 0.41), 3-year OS (p = 0.22), and 5-year OS (p = 0.82) was noted between the two groups. These results were consistent with other published literature [19][20][21]. In reference to DFS, Ardito et al. analyzed liver-specific DFS curves for two groups, one receiving PVE and one not [21]. They found that at 5 years, no significant difference in DFS was observed between both groups (p = 0.572), and even found that patients in the PVE group had experienced recurrence of colorectal cancer liver metastasis earlier than the non-PVE group, although the rate of overall intrahepatic recurrence was not significantly different between the two groups (p = 0.749).

This is to say that PVE is a promising procedure that carries much benefit, but is not without its complications and drawbacks, and operators need to be well aware of both aspects of the procedure to effectively care for their patients.

2. Indications and Contraindications

The primary indication for pre-operative PVE is centered on the inability of the pre-embolization FLR to support whole liver function post-resection. With this in mind, several factors, such as the patient's baseline hepatic function, the size of the liver portion to be resected, complexity of the planned resection (i.e., extended right hepatectomy), age, and co-morbidities, are taken into account when determining patient eligibility. The adequacy of the FLR should be assessed using both the remnant volume and the remnant liver function. The FLR volume can be assessed with the FLR ratio, which can be calculated as FLR volume/TLV.

In patients with an otherwise normal underlying liver, PVE is indicated if there is an FLR < 20%, or an FLR to body weight ratio (FLR–BWR) ratio of < 0.5%, according to the Truant criterion [22]. In patients who have underlying liver dysfunction, including exposure to hepatotoxic chemotherapy or hepatic steatosis, PVE is considered for patients with an FLR < 30% or an FLR–BWR of <0.8% [23][24][25][26]. It should be noted here for transparency that there is literature suggesting that systemic chemotherapy did not impair liver hypertrophy in the setting of PVE [27][28][29]. Therefore, it remains up to the operator and the patients through their shared decision making whether to move forward with PVE. There remains a third demographic for which a different FLR cut-off applies for PVE consideration. Patients with Childs-Pugh class A cirrhosis require yet a higher expected FLR < 40% and an FLR - BWR ratio < 1.4% [30][31]. However, it needs to be noted here that in addition to Child-Pugh status, indocyanine green retention at 15 min (ICG-R15) is also often incorporated into the treatment algorithm, thereby changing the FLR percentage cutoff. MD Anderson Cancer Center utilizes the 40% FLR cutoff if the patient has Child A cirrhosis with a normal ICG-R15 (<10%), but will require a 50% FLR if the ICG-R15 is between 10–20% [32].

Contraindications to PVE are severe portal hypertension, uncontrollable intrahepatic portal-to-hepatic vein shunts, tumor thrombus in the portal vein, and occlusion of the portal vein in the FLR. Patients with extensive distant

metastatic disease or periportal lymphadenopathy cannot undergo resection, and therefore are not candidates for PVE.

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