

Preoperative Portal Vein Embolization

A method to improve the safety of major hepatic resection.

BY DAVID C. MADOFF, MD

Advances in hepatobiliary surgical techniques have led to improved perioperative outcomes in patients selected for major hepatic resection. Although fatal liver failure after resection is rare, complications associated with cholestasis, impaired synthetic function, and fluid retention still contribute to prolonged recovery time and extended hospital stay.^{1,2} Factors contributing to the risk of perioperative liver failure are multiple, but one of the most important factors associated with this complication is the volume of the remnant liver. Patients considered high-risk are those with normal underlying liver in whom more than 75% of the functional liver mass will be removed, or those with chronic liver disease who undergo resection of more than 60% of their functional liver mass.^{2,3}

One strategy used to improve the safety of extensive liver surgery in patients with anticipated marginal remnant livers is preoperative portal vein (PV) embolization (PVE). PVE redirects blood flow to the future liver remnant (FLR) to initiate hypertrophy of the nonembolized segments and has been shown to improve functional reserve of the FLR before surgery. In appropriately selected patients, PVE can reduce postoperative morbidity and enable safe, potentially curative hepatectomy for patients not previously considered candidates for resection based on small anticipated liver remnants.³⁻¹³

For this reason, PVE prior to major hepatectomy is now considered the standard of care in many comprehensive hepatobiliary centers worldwide.³⁻¹³ To understand the benefits of PVE, this article reviews the importance of understanding liver regeneration, the rationale and technical considerations for PVE, the indications and contraindications for its use, and outcomes after PVE and resection.

MECHANISMS AND RATES OF LIVER REGENERATION

The liver's ability to regenerate after injury or resection is the basis for performing PVE in patients with anticipated small remnant livers after major hepatectomy. Despite its substantial metabolic load, the liver is quiescent in terms of hepatocyte replication, with up to 0.01% of hepatocytes undergoing mitosis at any time.¹⁴⁻¹⁶ However, this low cell turnover in healthy liver can be altered by toxic injury or surgical resection, which stimulates sudden, massive hepatocyte proliferation resulting in recovery of the functional liver mass within 2 weeks after the loss of up to two thirds of the liver. The regenerative response is mediated by the proliferation of surviving hepatocytes within the acinar architecture of the remnant liver.

The cellular events during liver regeneration result from growth-factor stimulation in response to injury. In the regenerating liver, hepatocyte growth factor, transforming growth factor- α , and epidermal growth factor are important stimuli for hepatocyte replication. HGF is the most potent mitogen for hepatocyte replication, and in combination with other mitogenic growth factors, can induce the production of cytokines, including tumor necrosis factor- α and interleukin-6, and activate immediate response genes that ready the hepatocytes for cell-cycle progression and regeneration. Insulin is synergistic with HGF, which explains the slower regeneration rates seen in patients with diabetes.^{17,18} Importantly, extrahepatic factors are transported primarily from the gut via the PV and not by the hepatic artery.^{7,19-21}

The amount of hepatocyte proliferation is directly proportional to the stimulus (ie, a minor liver stimulus will result in only a localized mitotic reaction), but any injury greater than 10% will result in proliferation of

cells throughout the liver.²² However, when compared to replication after resection, the peak replication after PVE is delayed approximately 3 to 4 days, suggesting that the hypertrophy stimulus generated by hepatocyte removal is stronger than that produced by apoptosis seen after PVE.²³

Also important to this discussion is that the chronically diseased liver has a lower capacity to regenerate than healthy liver.²³ This may result from a diminished capacity of hepatocytes to respond to hepatotropic factors or from parenchymal damage such as fibrosis that may lead to slower portal blood flow rates.²⁴ Noncirrhotic livers regenerate fastest, at rates of 12 cm³/day to 21 cm³/day at 2 weeks, 11 cm³/day at 4 weeks, and 6 cm³/day at 32 days after PVE.^{18,25} However, regeneration rates are slower (9 cm³/day at 2 weeks) in cirrhotic patients, with comparable rates found in diabetic patients.^{18,26}

CLINICAL RATIONALE FOR PVE PRIOR TO MAJOR LIVER RESECTION

The clinical use of PVE is based on experiments first reported in 1920 by Rous and Larimore, who studied the consequences of segmental PV occlusion in rabbits and found progressive atrophy of hepatic segments with ligated PVs and hypertrophy of hepatic segments with patent PVs.²⁷ Subsequent investigators reported in clinical studies that PV or bile-duct occlusion secondary to tumor invasion or ligation leads to atrophy of the ipsilateral lobe (ie, liver to be resected) and hypertrophy of the contralateral liver (ie, liver to remain in situ after resection).²⁸⁻³⁰ In 1986, Kinoshita et al first reported the use of PVE to limit extension of portal tumor thrombi from hepatocellular carcinoma (HCC) for which transarterial embolization (TAE) was ineffective.³¹

In 1990, Makuuchi et al reported the initial experience using PVE solely to induce left liver hypertrophy prior to right hepatectomy.⁸ Their rationale was three-fold: (1) to minimize the abrupt rise in portal pressure at resection that can lead to hepatocellular damage to the FLR; (2) to dissociate portal–pressure-induced hepatocellular damage from the direct trauma to the FLR during physical manipulation of the liver at the time of surgery; and (3) to improve overall tolerance to major resection by increasing hepatic mass prior to resection in order to reduce the risk of postresection metabolic changes.

Following PVE, alterations of liver function tests are usually minor and transient with many experiencing no changes. When transaminase levels rise, they generally peak at levels less than three times baseline 1 to 3 days after PVE and return to baseline within 7 to 10 days.^{8,9,18,32-35} Slight changes in white blood cell count and total serum bilirubin level may be seen. Synthetic functions of the liver are almost never affected.

When compared to TAE, PVE is much less toxic.⁷ The “postembolization syndrome” seen after TAE is not a typical feature after PVE because there is no distortion of the hepatic anatomy, only minimal inflammation, except immediately around the embolized vein, and little, if any, parenchymal or tumor necrosis.^{8,36} Animal studies reveal that hepatocytes undergo apoptosis and not necrosis after PV occlusion,^{37,38} which explains the absence of significant systemic symptoms following PVE.

MEASUREMENT OF FLR VOLUME AND PREDICTING FUNCTION AFTER PVE

Computed tomography (CT) with volumetry is essential for planning hepatic resection.^{12,39,40} Three-dimensional CT volumetric measurements are acquired by outlining the hepatic segmental contours and calculating the volumes from the surface measurements from each slice. Contrast-enhanced CT scans must be performed to demarcate the vascular landmarks of the hepatic segments.

Two techniques of CT volumetry are commonly used. The first method measures the volume of the entire liver plus tumors and then the volumes of each measurable tumor. Total “normal liver” volumes are then estimated by subtracting tumor volume from total volume and calculated as: (resected volume – tumor volume)/(total liver volume – tumor volume).^{5,41} This method can be challenging when multiple tumors are present, and the error of each volume calculation is additive. Furthermore, this approach does not account for the actual functional liver volume when there is vascular obstruction, chronic liver disease, or biliary dilatation in the liver to be resected.

The second, more accurate method standardizes liver remnant size to individual patient size to account for the reality that larger patients need larger liver remnants than do smaller patients. CT is used to directly measure the FLR, which is by definition disease-free. The total liver volume is then estimated by a formula (total estimated liver volume (TEL) = $-794.41 + 1,267.28 \times \text{BSA}$, $r^2 = .454$, $P < .001$) derived from the close association between liver size and patient size based on body weight and body surface area (Figure 1).¹² The FLR/TEL ratio is calculated to provide a volumetric estimate of function of the FLR. From this method of calculation, a correlation between the anticipated liver remnant and operative outcome has been established.⁴² At our institution, CT scans are performed immediately before PVE and approximately 3 to 4 weeks after PVE to assess the degree of FLR hypertrophy. Similarly, Shirabe et al recognized the importance of standardizing liver volume to patient size and found that no patient with underlying liver disease who had a standardized liver volume greater than 285 mL/m² body surface area died of liver failure following resection.²

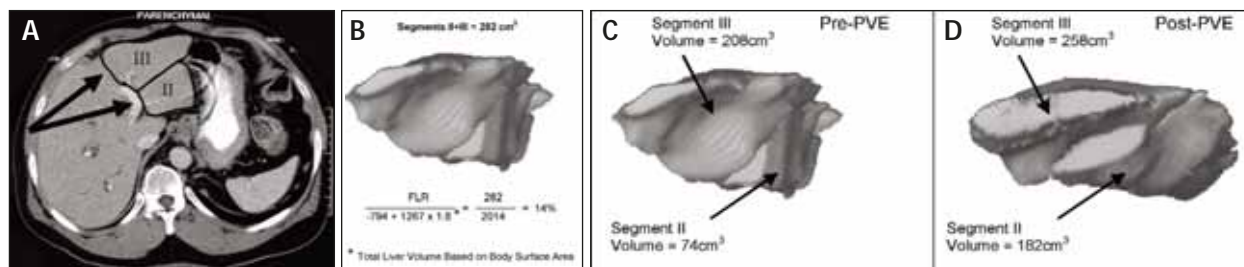


Figure 1. Hypertrophy of the future liver remnant after PVE as determined by three-dimensional reconstruction of computed tomography images (Reprinted with permission from Madoff DC, et al. *J Vasc Interv Radiol.* 2005;16:779-790.) (A). Three-dimensional volumetric measurements are determined by outlining the hepatic segmental contours and then calculating the volumes from the surface measurements of each slice (B). Formula for calculating total liver volume is based on patient's body surface area (Modified and reprinted with permission from Vauthey JN, et al. *Liver Transpl.* 2002; 8:233-240.) (C). Before embolization, the volume of segments II and III is 283 cm³, or 14% of the total liver volume (2,036 cm³). After embolization, the volume of segments II and III is 440 cm³, or 21% of the total liver volume (an increase of 7%) (Modified and reprinted with permission from Vauthey JN, et al. *Surgery.* 2000;127:512-519.) (D).

For patients with cirrhosis, some groups advocate tests to assess liver function, with the most common test being indocyanine green retention (ICGR). Makuuchi et al use ICGR as part of their clinical algorithm to determine the extent of safe resection in a cirrhotic patient based on this measurement and extent of planned resection.^{43,44}

PVE APPROACHES

PVE redirects portal flow toward the hepatic segments that will remain after surgery. To ensure adequate hypertrophy, embolization of portal branches must be complete so that recanalization of the occluded portal system does not occur.⁴⁵

PVE is performed by three standard approaches: the transhepatic contralateral (ie, via the FLR), transhepatic ipsilateral (ie, via the liver to be resected), and intraoperative cannulation of the ileocolic vein (will not be discussed herein). These approaches are chosen on the basis of operator preference, type of hepatic resection planned, extent of embolization, and type of embolic agent used.

The contralateral approach, the most widely used for right PVE,³¹ is performed via a peripheral left PV branch (usually segment III). A catheter is advanced through an introducer into the right PV for PVE (Figure 2).

The advantage of this approach is that catheterization of the desired right PVs is more direct. However, the disadvantage is potential FLR injury. Recently, a large multicenter study of 188 patients who underwent contralateral PVE reported 24 (12.8%) adverse events including migration of embolic material to the FLR in 10 patients, occlusion of a major portal branch requiring intervention in three patients, bleeding in five patients, and transient liver failure in six patients.⁴⁶ Adverse events associated with the migration of embolic material using the contralateral approach may compromise the integrity of the FLR and may make

the planned resection more difficult or impossible. Also, segment IV embolization, if needed, may prove technically difficult.

The ipsilateral approach, first described by Nagino et al, is performed from a peripheral right PV access (Figure 3).⁴⁷ A balloon occlusion catheter is advanced through a sheath into the right portal tree. Embolization with fibrin glue or ethanol can be performed in right PV (and segment IV) branches. Unfortunately, these catheters are not available outside of Japan, so additional techniques were needed.

Our group at M.D. Anderson Cancer Center has advocated the ipsilateral approach for PVE using standard angiographic catheters and readily available embolic agents (eg, particles and coils) (Figure 4).^{48,49} This technique may allow more widespread use of this approach, especially if segment IV embolization is needed. We perform PVE through a 6-F sheath placed into a distal right PV branch. Because of tech-

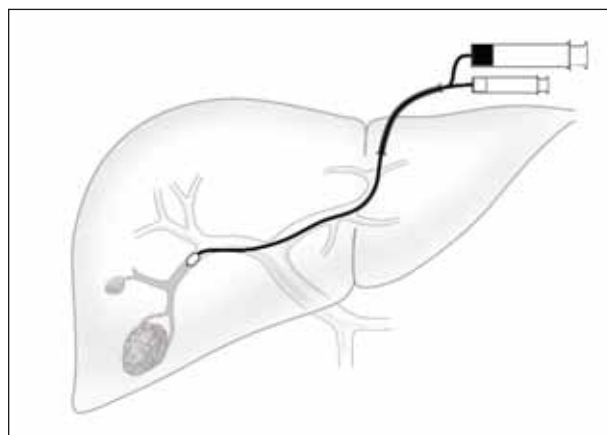


Figure 2. Schematic representation of the contralateral approach as described by Kinoshita et al.³¹ An occlusion balloon catheter is placed into the right portal branch with delivery of embolic agent in antegrade direction.

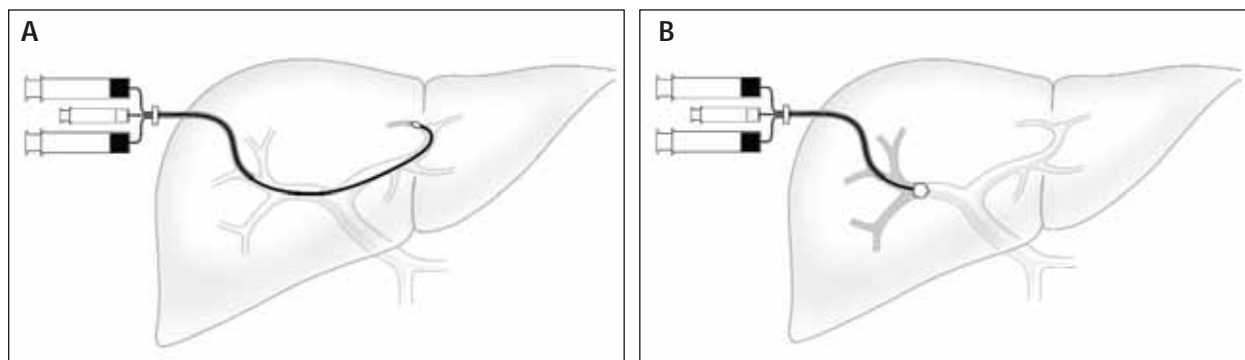


Figure 3. Schematic representation of the ipsilateral approach for right PVE and segment IV as described by Nagino et al. Different portions of the balloon catheter are used for antegrade embolization of the segment IV veins (A) and for retrograde delivery of embolic agent into the right portal system (B).

nical factors when right PVE needs to be extended to segment IV (eg, difficulty exchanging catheters through an embolized right portal system with nontarget embolization risk), segment IV embolization is performed first. A 3-F microcatheter is advanced coaxially through a 5-F catheter into the segment IV portal branches so the embolic agents can be delivered. Once segment IV PVE is completed, a 5-F reverse-curved catheter is used for right PVE. After PVE, embolization of the access tract is performed with coils or gelfoam to reduce the risk of perihepatic hemorrhage at the puncture site.

The major benefit of the ipsilateral approach is that the FLR is not instrumented. However, catheterization of the right portal branches may be more difficult because of severe angulations between right portal branches necessitating the use of reverse-curve catheters. Another potential disadvantage of this approach is that some embolic material could be displaced upon catheter removal, leading to nontarget embolization, although this has not occurred in our experience of more than 100 ipsilateral PVE procedures. In addition, ipsilateral access has not been a problem, even in patients with large liver tumors.

Embolic Material

Many embolic materials have been used for PVE without significant differences in degrees or rates of hypertrophy.⁷ In their initial report, Makuuchi et al used gelatin sponge but frequent recanalization was observed within 2 weeks after PVE.⁸ In comparison with other embolic agents, gelatin sponge appears to induce less hypertrophy at 4 weeks. Kaneko et al proposed a combination of gelatin sponge with the sclerosing agent polidocanol that produced portal occlusion for up to 8 weeks after PVE in canines.⁵⁰

Others prefer N-butyl-2-cyanoacrylate (NBCA) mixed with ethiodized oil because the mixture leads to fast, reliable hypertrophy and minimizes the delay between PVE and

resection.⁵¹ NBCA ensures PV occlusion, which persists beyond 4 weeks and has led to a 90% increase in FLR volume after 30 days while the combination of gelatin sponge and thrombin resulted in only a 53% volume increase after 43 days.⁹ There are two potential drawbacks of NBCA for PVE: (1) it induces an inflammatory process (peribiliary fibrosis or casting of the PV) that may increase the difficulty of the subsequent resection, and (2) it is difficult to use clinically, especially in patients with reduced hepatopetal portal flow as is often seen in cirrhotics.^{33,34} These altered flow dynamics can lead to nontarget embolization within other segments.³³

Ethanol has been useful for PVE owing to its strong coagulation effect. Shimamura et al reported that 20 mL of ethanol was adequate to produce complete right PV occlusion with a massive increase in FLR size.²⁶ Ogasawara et al demonstrated near doubling of the left liver volume within 4 weeks for patients with chronic liver disease and HCC who had PVE with ethanol.⁵² Unfortunately, ethanol produces the greatest changes in liver function tests, and thus poor patient tolerance may be found.⁵³ However, although ethanol causes considerable periportal fibrosis, endothelial destruction, and necrosis, recanalization is rare.

Fibrin glue mixed with ethiodized oil is another commonly used agent for PVE that usually induces less than 75% portal occlusion at 2 weeks and less than 25% portal occlusion at 4 weeks.⁵³ However, Nagino et al report increases in FLR volume of 10% to 20% after a mean of 18 days following PVE with this mixture.^{10,18,54}

Recently, particles such as polyvinyl alcohol (PVA) particles for PVE have been used.^{37,39,48,55} PVA particles are safe, cause little periportal reaction, and generate durable PV occlusion, especially when used in combination with coils.³⁷ Theoretically, the particles occlude the small "outflow" vessels (ie, third-order PVs and smaller), while the coils occlude the larger "inflow" vessels (ie, second-order PVs). In the ini-

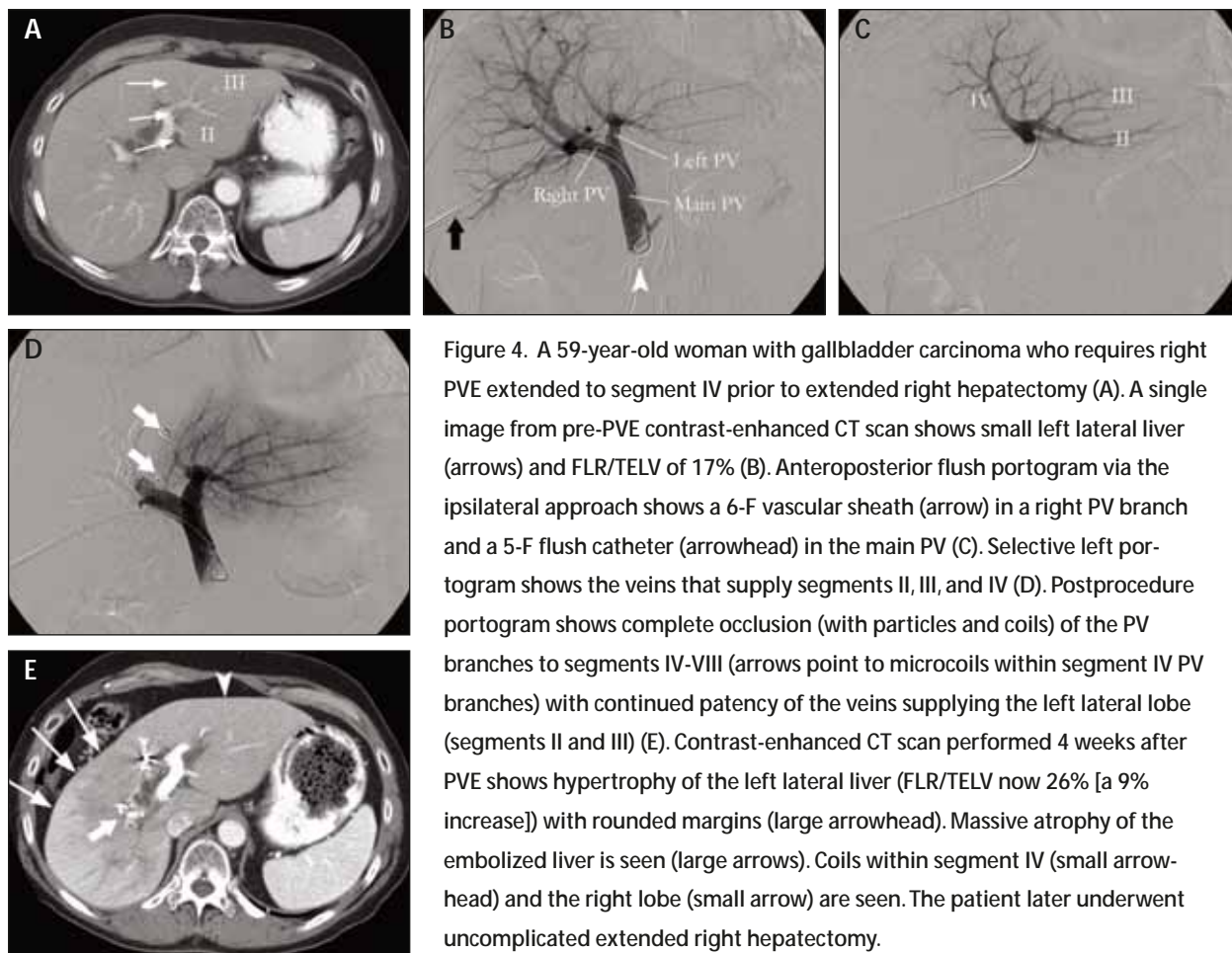


Figure 4. A 59-year-old woman with gallbladder carcinoma who requires right PVE extended to segment IV prior to extended right hepatectomy (A). A single image from pre-PVE contrast-enhanced CT scan shows small left lateral liver (arrows) and FLR/TEL of 17% (B). Anteroposterior flush portogram via the ipsilateral approach shows a 6-F vascular sheath (arrow) in a right PV branch and a 5-F flush catheter (arrowhead) in the main PV (C). Selective left portogram shows the veins that supply segments II, III, and IV (D). Postprocedure portogram shows complete occlusion (with particles and coils) of the PV branches to segments IV-VIII (arrows point to microcoils within segment IV PV branches) with continued patency of the veins supplying the left lateral lobe (segments II and III) (E). Contrast-enhanced CT scan performed 4 weeks after PVE shows hypertrophy of the left lateral liver (FLR/TEL now 26% [a 9% increase]) with rounded margins (large arrowhead). Massive atrophy of the embolized liver is seen (large arrows). Coils within segment IV (small arrowhead) and the right lobe (small arrow) are seen. The patient later underwent uncomplicated extended right hepatectomy.

tial clinical report in a single patient, no recanalization of the right PV was observed 5 weeks after PVE with PVA particles alone.⁵⁵ In our study of 26 patients who had PVE with PVA particles and coils, the mean FLR/TELV increase was 8% (pre-PVE FLR/TELV, 17.6%; post-PVE FLR/TELV, 25.4%), and the mean absolute FLR volume increased 47%.⁴⁸ More recently, both FLR hypertrophy and overall resection rates were further improved using small spherical particles and coils for right PVE extended to segment IV in patients with an otherwise normal liver when compared with PVA particles and coils.⁴⁹

Newer agents continue to be developed that may provide more complete and permanent occlusions in an attempt to reduce recanalization and ultimately provide better and faster hypertrophy.

Complications

As with all transhepatic procedures, complications can occur from PVE. These include subcapsular hematoma, hemoperitoneum, hemobilia, pseudoaneurysm, arteriovenous fistula, arterioportal shunts, PV thrombosis, transient

liver failure, pneumothorax, and sepsis.^{46,56} In 2002, Kodama et al reported that seven (15%) of 47 patients had complications after PVE: two pneumothoraces, two subcapsular hematomas, one arterial puncture, one pseudoaneurysm, one hemobilia, and one PV thrombosis.⁵⁶ As most technical complications occurred in the punctured lobe, Kodama et al recommended that the ipsilateral approach be attempted first.

More recently, studies from other investigators have been published that reiterate the low procedural complication rates (range, 9.1%-12.8%) for right PVE, whether or not segment IV is embolized.^{46,49}

INDICATIONS AND CONTRAINDICATIONS FOR PVE

Indications

To determine whether a patient will benefit from PVE, many factors must be considered by the surgeon treating the patient.¹³ First, the presence or absence of underlying liver disease will impact on the liver remnant volume needed for adequate function. Second, patient size must be con-

sidered such that larger patients require larger liver remnants than smaller patients require. Third, the extent and complexity of the planned resection and the probability that associated nonhepatic surgery will be performed at the time of liver resection must be kept in mind. These factors must be considered in the setting of the patient's age and comorbidities that may impact hypertrophy, such as diabetes.

The first factor considered in determining whether PVE is indicated is the presence or absence of underlying liver disease. As previously described, a normal liver has greater regenerative capacity than cirrhotic liver, functions more efficiently, and tolerates injury better. Patients can survive resection of up to 90% of healthy liver, but survival after resection beyond 60% of the functional parenchyma in cirrhotic patients is unlikely.³ Lethal hepatic failure is more common after resection in cirrhotic patients, and other complications of the poorly functioning liver remnant (eg, ascites, fluid retention, and wound breakdown from poor protein synthesis) occur with greater frequency after resection in cirrhotic patients. Retrospective data suggest an increased risk of surgical complications in patients after preoperative systemic or regional chemotherapy such that some investigators have recommended a minimal FLR volume of 40% in patients treated extensively with preoperative systemic chemotherapy.^{57,58}

With regard to liver volume, there is clearly a limit to how small a liver remnant can remain after resection. If too little liver remains, immediate postresection hepatic failure leads to multisystem organ failure and death. If a marginal volume of liver remains, cirrhotic or not, the lack of reserve often leads to a cascade of complications, prolonged hospital and intensive care unit stays, and slow recovery or slowly progressive liver failure over weeks to months with eventual death. Therefore, guidelines have evolved from recognition of the importance of the presence or absence of liver disease and proper attention to liver volume and patient size. Standardizing FLR size to patient size is critical to appropriate determination of the need for PVE. A recent prospective randomized study confirmed the benefit of PVE in cirrhotic patients before right hepatectomy, and Kubota et al suggested an FLR of <40% should prompt PVE prior to major hepatectomy.^{5,59} This guideline has been extended to patients in whom the liver is compromised by chronic liver disease, high-dose chemotherapy, or severe fibrosis.^{7,23,26,42}

In patients with an otherwise normal liver, the indications for PVE have evolved with greater imaging accuracy and the use of standardized liver volumes. Although extended resections (ie, five or more liver segments) are performed with a low likelihood of death from liver failure, small-for-patient-size normal liver remnants are associated with increased complications and slower recovery from surgery.³ An

FLR/TELV ratio >20% is associated with four-fold fewer complications than an FLR/TELV ratio of 20% or less.³ This finding was validated in a retrospective study that revealed that residual liver volume, not resected volume, predicts the posthepatectomy course.⁶⁰ Failure to follow these well-established guidelines may result in PVE overutilization.⁵⁹

It is important to recognize and individualize the indication for PVE by using a standardized 20% cutoff for liver volume because of intrahepatic segmental variability. Liver volume analysis has revealed that the lateral left liver (segments II and III) contributes less than 20% of the total liver volume in over 75% of patients in the absence of compensatory hypertrophy. Further, the left liver (segments II, III, and IV) contributes 20% or less of the total liver volume in more than 10% of patients.⁶¹ Thus, a FLR/TELV ratio <20% can be expected in most patients who do not develop compensatory hypertrophy from tumor growth and require an extended right hepatectomy. In this subset of patients, the use of right PVE with extension to segment IV is indicated.^{13,49} However, left PVE is rarely necessary, as Nagino et al showed that a left trisegmentectomy with caudate lobectomy results in resection of only 67% of the liver, leaving a FLR of 33%—the same residual volume after right hepatectomy in a normal liver.¹⁰ Volumetric analysis of normal livers also confirms the consistently large volume of the posterior right liver (segments VI and VII).⁶²

Contraindications

With the exception of overt clinical portal hypertension in patients who are not candidates for major hepatic resection, there are no absolute contraindications to PVE; in cases of tumor invasion of the PV, PVE is not appropriate as portal flow is already diverted.¹³ Relative contraindications to PVE include (1) tumor extension to the FLR or extrahepatic metastatic disease (including periportal lymphadenopathy), (2) uncorrectable coagulopathy, (3) tumor precluding safe transhepatic access, (4) biliary dilatation in the FLR (if the biliary tree is obstructed, drainage is recommended), (5) mild portal hypertension, and (6) renal failure. The presence of an ipsilateral tumor may preclude safe transhepatic access if the tumor burden is great, but this is unlikely in our experience. However, if access to an adequate PV branch is not possible, the contralateral approach can always be considered.

OUTCOMES FOLLOWING PVE AND HEPATECTOMY

Chronic Liver Disease

In patients with chronic liver disease, increases in non-embolized liver volumes after PVE vary (range, 28%-46%), and hypertrophy after PVE may take longer because of slower regeneration rates.^{18,32} The degree of fibrosis may

limit regeneration, possibly resulting from reduced portal flow.⁵⁸ Complication rates after PVE are higher in patients with chronic liver disease because of the increased risk of secondary PV thrombosis, presumably from slow flow in the main PV after PVE.⁴⁶ The combination of TACE of the tumor followed by PVE within 2 weeks may optimize outcome for some patients who have HCC in the presence of chronic liver disease and require major resection.⁶³ Patients with overt portal hypertension are not candidates for major hepatectomy and therefore are not candidates for PVE. However, mild portal hypertension is not a contraindication to PVE followed by hepatectomy provided liver function test results are otherwise normal.

In patients with chronic liver disease, the number and severity of complications after major hepatectomy are decreased by PVE compared to patients without PVE.^{18,32,58,63,64} A recent prospective study showed significant benefit of PVE in cirrhotics prior to right hepatectomy.⁵⁹ PVE was performed when the estimated FLR volume was predicted to be <40% with significant increases in the FLR volume in all embolized patients. No patient suffered liver failure or death following resection in the PVE group (0 of 10 patients), whereas 3 of 19 patients in the non-PVE group suffered liver failure and one patient died. Overall and disease-free survival rates were similar with or without PVE. Tanaka et al reported several benefits of PVE in a larger study of patients with cirrhosis and HCC.⁶⁵ Disease-free survival rates were similar, but cumulative survival rates were significantly higher in the PVE group than in the non-PVE group. In addition, patients with recurrence following PVE plus resection were more often candidates for further treatment, an additional benefit of PVE in the long term.

No Chronic Liver Disease

The outcome from PVE and subsequent resection may be even more closely linked to PVE in patients with otherwise normal livers. In cirrhotics, right PVE extended to segment IV is not used because extended hepatectomy is rarely indicated or possible in a cirrhotic patient. In patients without cirrhosis who have hilar cholangiocarcinoma or liver metastases, PVE is frequently needed prior to extended right hepatectomy owing to the high incidence of small volume left lateral bisegment (II + III) in the absence of compensatory hypertrophy.⁶¹ The rationale for complete embolization of the liver to be resected, including right portal branches and segment IV branches, stems from the concept that hypertrophy requires complete diversion of portal flow to the intended liver remnant. Nagino et al were the first to emphasize the benefit of "trisegment" PVE prior to extended hepatectomy for hilar cholangiocarcinoma and noted that hypertrophy of a portion of the liver to be resected (segment IV) would

increase the difficulty of resection.¹⁰ Later, they showed that PVE of the right liver + segment IV was not only safe, it provided a statistically significant FLR volume gain (mean, $122 \pm 39 \text{ cm}^3$) compared to right PVE alone (mean, $66 \pm 35 \text{ cm}^3$).¹¹

Several studies have validated residual volume as the key to prediction of postoperative course. Vauthey et al reported 127 consecutive extended hepatectomies using standardized liver volume calculations to select patients for PVE and extended hepatectomy.⁴ In this series, only six patients (5%) experienced significant postoperative liver insufficiency; the postoperative complication rate was 31%, and only one patient (0.7%) died after hepatectomy. The median survival was 41.9 months, and the overall 5-year survival rate was 26% for the entire group. Similarly, Shoup et al found that FLR volume 25% or less was an independent predictor of postoperative complications and increased length of hospital stay and recommended FLR volume assessment prior to consideration of PVE.⁶⁰ Elias et al demonstrated that patients considered to have unresectable tumors owing to inadequate liver volume at presentation could undergo complete resection after treatment with PVE, with an associated 5-year overall survival rate of 29%.⁶⁶ Lastly, Azoulay et al found that the 5-year overall survival rate after resection in patients who required PVE was similar to that in patients who did not require PVE (40% vs 38%, respectively).⁶

FUTURE DIRECTIONS

The prediction of liver function based on gross estimates, such as liver volumes standardized to patient size, and increase in volume and function of liver remnant based solely on diversion of portal flow leaves large opportunities for improvement in the treatment of liver tumors. More accurate functional tests that can quantify and predict liver function are needed. Furthermore, an improved understanding of liver regeneration physiology might further lead to agents or methods to regenerate healthy liver selectively. Limits of potentially curative therapy for liver tumors continue to expand because of critical evaluation of existing data, prospective study and multidisciplinary evaluation of and treatment of patients with the complex combination of liver tumors and liver disease. ■

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