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EDITORIAL – HEPATOBILIARY TUMORS

Portal Vein Embolization: Tailoring, Optimizing, and Quantifying an Invaluable Procedure in Hepatic Surgery

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In this issue, Yamashita et al.[1] present the experience of the University of Tokyo with portal vein embolization (PVE) in 338 patients from 1995 to 2013. The authors should be congratulated for presenting an extensive review of their indication, technique, and outcome of PVE. Over the past two decades, PVE has become an invaluable procedure in hepatic surgery. This editorial is an opportunity to revisit the indications for the procedure, the techniques to optimize the hypertrophy, and the methods to quantify its effects on regeneration.

In the study, Yamashita et al. used as indication for PVE a cut-off future liver remnant (FLR) volume of <40% in patients with normal liver function based on an indocyanine green retention rate at 15 min (ICGR15) of <10%. This cautious approach was associated with an excellent outcome following resection, with an hepatic insufficiency rate of 2% and 90-day mortality of 0.8%. Anatomically, the left liver, on average, accounts for 33% of the total liver volume (TLV), and a 40% cut-off implies that the majority of patients undergoing right hepatectomy should receive PVE, which seems unnecessary.[2] As such, the 40% cut-off value for PVE is higher than the 20–30% used in the West, and the study may include more PVEs than clinically indicated. In our own experience with 301 extended right hepatectomies in patients with normal liver function, we demonstrated that patients with 20–30% FLR had similar postoperative outcomes compared with patients with 30–40% FLR, and only the subset of patients with ≤20% FLR had increased hepatic insufficiency and perioperative mortality.[3] At MD Anderson Cancer Center, we recommend PVE for FLR of ≤20% in normal liver, ≤30% in injured liver, and ≤40% in fibrosis/cirrhosis.[4,5] Using appropriate indications for PVE, tailoring the procedure based on accurate volumetry and avoiding overutilization are important because PVE remains a procedure with a 7.8% risk of associated complications, as reported in the series of the University of Tokyo.

Yamashita et al. report an excellent degree of hypertrophy (median 10%) and kinetic growth rate (3.9–4.5% per week). In contrast, they report a median regeneration rate of 25% following PVE, which was lower than the regeneration rate of 62% following PVE in a recent series of 103 patients undergoing resection of colorectal liver metastases with small liver remnants.[6] The lower regeneration rate in the series from the University of Tokyo may be attributed to generous indications for PVE and the performance of PVE in patients with an already large FLR unlikely to undergo significant regeneration. The technique recently used at the University of Tokyo is alcohol injection, which has led to less recanalization of the portal vein. It would have been interesting for the authors to compare the hypertrophy rates between alcohol injection and Gelfoam plus coil particle previously used by the authors. An important aspect of the technique at the University of Tokyo is the minimal use of segment 4 embolization (6/319, 1.9%) in spite of a large number of extended right hepatectomies (116/256, 45.3%). A major issue of right PVE without segment 4 embolization prior to extended right hepatectomy is the undesirable segment 4 regeneration at the expense of lesser regeneration of the left lateral bisegment. To counter this undesirable effect, at Nagoya University and MD Anderson Cancer Center, right PVE with segment 4 embolization has been used with a significant increase in the hypertrophy of the left lateral bisegment, compared with right PVE without segment 4 embolization.[7,8]

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Yamashita et al. should be congratulated for presenting a detailed reporting of the volumetric outcome following PVE. The initial liver measurement includes the FLR before and after PVE and the TLV based on computed tomography. The FLR is expressed as a percentage of TLV. Alternatively, TLV can be derived from a formula based on body surface area, and the FLR is reported as the standardized FLR (sFLR).[9] This latter method of measurement avoids the mistakes associated with subtraction of multiple tumors, the inclusion of nonfunctional liver with dilated ducts in the measurements, and the use of a different denominator between pre- and post-PVE total liver volume. The second measurement is the degree of hypertrophy—the difference between the pre- and post-PVE measurement. This difference should be ≥5% to ensure a postoperative outcome with minimal postoperative hepatic dysfunction.[10] The third relevant measurement is the kinetic growth rate—the degree of hypertrophy divided by time (weeks) elapsed between the pre- and post-PVE measurements. Shindoh et al. reported that a kinetic growth rate ≥2% per week was associated with no liver failure-related deaths in a series of 103 patients with colorectal liver metastases.[11] The kinetic growth rate has become an invaluable functional tool to assess the FLR. A kinetic growth rate ≥2% per week predicts a favorable outcome even in patients sustaining complications, and appears to protect patients with infectious complications from progressing from hepatic dysfunction to liver failure.

Similar to other reports, Yamashita et al. indicated that 20% (63/319) of patients receiving PVE did not ultimately undergo resection, which was due to progression of disease in the majority of patients (76%) rather than the lack of regeneration (3%). This is a reflection of the patient population undergoing PVE. Patients typically have advanced cancer, often compounded by unfavorable tumor biology, and progress in the interval between PVE and resection.[12] Most patients undergoing PVE have adequate FLR hypertrophy, and only a minority do not have adequate liver regeneration after PVE. In such patients, we do not recommend Associating Liver Partition and Portal vein Ligation for Staged hepatectomy (ALPPS) because of its high morbidity rate. Alternative approaches in patients with inadequate hypertrophy after PVE are (i) preservation of segment 4 as part of the FLR and subsequent ablation of the liver metastases following right hepatectomy as completion ablation;[13] (ii) consideration of additional embolization of the right or middle hepatic vein;[14] or (iii) liver ablation using proton therapy.[15]

In conclusion, Yamashita et al. are commended for the third largest single-institutional series of PVE in the literature.[16,17] PVE has increased the number of patients who are candidates for major hepatectomy. In addition, PVE measurement can be used as a functional test to predict hepatic dysfunction, hepatic insufficiency, and liver-related liver failure. In spite of early fears regarding the risks of cancer growth associated with the release of hepatotrophic factors, the long-term outcome of patients undergoing PVE after resection of colorectal liver metastases or hepatocellular carcinoma is similar to the long-term outcome of matched patients not undergoing PVE prior to resection.[18,19]

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