Efficacy and Safety of Portal Vein Embolization for Two-Stage Hepatectomy in Patients with Colorectal Liver Metastasis

Steven Y. Huang, MD, Thomas A. Aloia, MD, Junichi Shindoh, MD, PhD, Joe Ensor, PhD, Colette M. Shaw, MD, Evelyne M. Loyer, MD, Jean-Nicolas Vauthey, MD, and Michael J. Wallace, MD

ABSTRACT

Purpose: To examine the efficacy and safety of portal vein embolization (PVE) when used during two-stage hepatectomy for bilobar colorectal liver metastases (CLM).

Materials and Methods: PVE was performed as an adjunct to two-stage hepatectomy in 56 patients with CLM. Absolute future liver remnant (FLR) volumes, standardized FLR ratios, degree of hypertrophy (DH), and complications were analyzed. Segment II and III volumes and DH were also measured separately. All volumetric measurements were compared with a cohort of 96 patients (n = 37 right portal vein embolization [RPVE], n = 59 right portal vein embolization extended to segment IV portal veins [RPVE+4]) in whom PVE was performed before single-stage hepatectomy.

Results: For patients who completed RPVE during two-stage hepatectomy (n = 17 of 17), mean absolute FLR volume increased from 272.1 cm^3 to 427.0 cm^3 ($P < .0001$), mean standardized FLR ratio increased from 0.17 to 0.26 ($P < .0001$), and mean DH was 0.094. For patients who completed RPVE+4 during two-stage hepatectomy (n = 38 of 39), mean FLR volume increased from 288.7 cm^3 to 424.8 cm^3 ($P < .0001$), mean standardized FLR increased from 0.18 to 0.26 ($P < .0001$), and mean DH was 0.083. DH of the FLR was not significantly different between two-stage hepatectomy and single-stage hepatectomy. Complications after PVE occurred in five (8.9%) patients undergoing two-stage hepatectomy.

Conclusions: PVE effectively and safely induced a significant DH in the FLR during two-stage hepatectomy in patients with CLM.

ABBREVIATIONS

CLM = colorectal liver metastasis, DH = degree of hypertrophy, FLR = future liver remnant, PVE = portal vein embolization, RPVE = right portal vein embolization, RPVE+4 = right portal vein embolization extended to segment IV portal veins, RV = resection volume, S2+3 = segments II and III, S4 = segment IV, TLV = total liver volume

Surgical resection of metastatic disease is regarded as the most effective strategy for long-term survival in patients with colorectal liver metastasis (CLM), with reported 5-year survival rates of 58% (1–3). However, only 10%–20% of patients with CLM are deemed surgical candidates (4). Two key reasons why CLM is considered unresectable are the risk of major morbidity and mortality related to an insufficient future liver remnant (FLR) (5) and the presence of bilobar hepatic metastases involving any portion of FLR. Preoperative portal vein embolization (PVE) was developed to induce hypertrophy in FLR to address the issue of postoperative hepatic insufficiency (6–8). Now that PVE has gained acceptance as a reliable tool to improve FLR adequacy, attention is focused on addressing disease within FLR by performing a two-stage hepatectomy with PVE performed between the two stages. Disease in FLR is resected in a limited single-stage hepatectomy, and then PVE is performed to induce hypertrophy of FLR to an

From the Departments of Diagnostic Radiology (S.Y.H., E.M.L., M.J.W.), Surgical Oncology (T.A.A., J.S., J.-N.V.), and Biostatistics (J.E.), The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030; and Department of Radiology (C.M.S.), Jefferson University Hospitals, Philadelphia, Pennsylvania. Received May 16, 2013; final revision received October 8, 2013; accepted October 11, 2013. **Address correspondence to** S.Y.H.; E-mail: syhuang@mdanderson.org

From the SIR 2013 Annual Meeting.

None of the authors have identified a conflict of interest.

J Vasc Interv Radiol 2014; 25:608–617

http://dx.doi.org/10.1016/j.jvir.2013.10.028

adequate volume. Finally, resection of the remaining metastatic disease is performed during the final stage (9).

Two-stage hepatectomy is safe and effective in patients with bilobar CLM (9–12). Although hypertrophy of FLR does occur in response to PVE in the setting of two-stage hepatectomy (5,9,13,14), it is unclear whether the insult caused by first-stage liver resection impairs the magnitude of FLR hypertrophy induced by PVE. Prior studies have been limited by small numbers of patients undergoing two-stage hepatectomy and PVE (5,14), lack of an appropriate control cohort of patients undergoing PVE in the setting of single-stage hepatectomy (9,13), and differences in PVE technique limiting generalizability of results (5,14). A recent retrospective study from our institution analyzing the efficacy of PVE in patients with very low FLR volume found that adequate regeneration was observed in nearly all of these patients (96.5%) (13). Of 144 patients undergoing percutaneous right portal vein embolization extended to segment IV portal veins (RPVE+4), 32 (22%) procedures were performed after a first-stage partial left hepatectomy as part of a two-stage hepatectomy approach.

Our current work builds on this earlier analysis and is unique in many ways. First, our analysis includes an additional 23 patients who underwent PVE as an adjunct to two-stage hepatectomy (total n = 55 patients; n = 38 patients undergoing RPVE+4, n = 17 undergoing right portal vein embolization [RPVE]). Second, in our earlier work, all 144 patients (n = 32 RPVE+4 two-stage hepatectomy and n = 112 RPVE+4 single-stage hepatectomy) were grouped to calculate percentage of hypertrophy, making it difficult to determine if RPVE+4 in the setting of two-stage hepatectomy is efficacious compared with a control cohort of patients who underwent RPVE+4 in the setting of single-stage hepatectomy. Third, the focus of our previous work was to describe the operative morbidity and mortality after the second-stage operation of two-stage hepatectomy; specific morbidity data related to PVE was limited. The main purpose of our study was to examine the efficacy and safety of PVE on FLR hypertrophy when used in conjunction with two-stage hepatectomy in patients with CLM compared with a control cohort of patients in whom PVE was performed as an adjunct to single-stage hepatectomy.

An additional issue that is controversial is the utility of performing RPVE+4 (15). Prior studies of patients undergoing single-stage hepatectomy compared the changes in volume for segments II and III (S2+3) after RPVE and RPVE+4 (15–17), but results have differed with two groups finding an increase in S2+3 volumes after RPVE+4 (15,16) and one group finding no significant increase in S2+3 volumes (17). The efficacy of RPVE+4 in patients undergoing two-stage hepatectomy has yet to be described, and so a secondary purpose of our study was to evaluate the effect RPVE+4 had on S2+3 hypertrophy for patients undergoing two-stage hepatectomy.

MATERIALS AND METHODS

We retrospectively reviewed 168 consecutive patients with CLM who underwent PVE between May 1998 and January 2011 for this study, which was compliant with the Health Insurance Portability and Accountability Act and approved by our institutional review board. PVE was performed as a component of two-stage hepatectomy in 65 patients; the remaining 103 patients underwent PVE before single-stage hepatectomy and were used as a comparison cohort. Both the two-stage hepatectomy group and the single-stage hepatectomy group were divided into subgroups based on whether RPVE+4 was performed. There were 16 patients excluded because of missing computed tomography (CT) volumetric data (n = 9), staged PVE (ie, performing PVE in separate procedures; n = 4), and percutaneous intraoperative radiofrequency ablation performed in lieu of surgical resection during first-stage hepatectomy (n = 3). Our study population comprised the remaining 152 patients (**Fig 1**).

Two-stage hepatectomy was performed in 56 patients (n = 17 for RPVE and n = 39 for RPVE+4), and single-stage hepatectomy was performed in 96 patients (n = 37 for RPVE and n = 59 for RPVE+4). No patients underwent transarterial chemoembolization or radioembolization, and no patients had evidence of cirrhosis. Data were retrospectively collected on age, sex, diabetes status, body mass index, and use or nonuse of neoadjuvant chemotherapy within 3 months of PVE. Clinical characteristics for the four subgroups of patients in this study (RPVE single-stage hepatectomy, RPVE two-stage hepatectomy, RPVE+4 single-stage hepatectomy, and RPVE+4 two-stage hepatectomy) are shown in **Table 1**.

During the study period, patients underwent PVE if the volume of FLR was $\leq$ 20% of the standardized total liver volume (TLV) for normal liver (18), $\leq$ 30% in patients with fibrosis or severe liver injury (19), and $\leq$ 40% in patients with cirrhosis (20,21). Standardized TLV was calculated using a formula for body surface area in square meters: standardized TLV = $-794.41 + 1{,}267.28 \times$ body surface area (22). All patients generally underwent abdominal CT with volumetry 2–8 weeks after PVE.

At our institution, PVE was performed via a transhepatic ipsilateral (ie, on the side of the liver being resected) approach, which has been described previously (23–25). We use a combination of trisacryl particles and coils to occlude the branches of the right portal vein with or without segment IV (S4) portal veins. Although we realize there are alternative occlusive agents, we prefer to use particles and coils because our technique results in