Remnant Growth Rate after Portal Vein Embolization Is a Good Early Predictor of Post-Hepatectomy Liver Failure

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BACKGROUND: After portal vein embolization (PVE), the future liver remnant (FLR) hypertrophies for several weeks. An early marker that predicts a low risk of post-hepatectomy liver failure can reduce the delay to surgery.

STUDY DESIGN: Liver volumes of 153 patients who underwent a major hepatectomy (>3 segments) after PVE for primary or secondary liver malignancy between September 1999 and November 2012 were retrospectively evaluated with computerized volumetry. Pre- and post-PVE FLR volume and functional liver volume were measured. Degree of hypertrophy (DH = post-FLR/post-functional liver volume − pre-FLR/pre-functional liver volume) and growth rate (GR = DH/weeks since PVE) were calculated. Postoperative complications and liver failure were correlated with DH, measured GR, and estimated GR derived from a formula based on body surface area.

RESULTS: Eligible patients underwent 93 right hepatectomies, 51 extended right hepatectomies, 4 left hepatectomies, and 5 extended left hepatectomies. Major complications occurred in 44 patients (28.7%) and liver failure in 6 patients (3.9%). Nonparametric regression showed that post-embolization FLR percent correlated poorly with liver failure. Receiver operating characteristic curves showed that DH and GR were good predictors of liver failure (area under the curve [AUC] = 0.80; p = 0.011 and AUC = 0.79; p = 0.015) and modest predictors of major complications (AUC = 0.66; p = 0.002 and AUC = 0.61; p = 0.032). No patient with GR >2.66% per week had liver failure develop. The predictive value of measured GR was superior to estimated GR for liver failure (AUC = 0.79 vs 0.58; p = 0.046).

CONCLUSIONS: Both DH and GR after PVE are strong predictors of post-hepatectomy liver failure. Growth rate might be a better guide for the optimum timing of liver resection than static volumetric measurements. Measured volumetrics correlated with outcomes better than estimated volumetrics. (J Am Coll Surg 2014;219:620−630. © 2014 by the American College of Surgeons)

In patients undergoing liver resection, the optimal future liver remnant (FLR) volume required for safe recovery is uncertain. For patients with normal liver parenchyma, 20% to 40% of the total liver volume has been suggested as the minimum,[1-7] and patients with underlying hepatic parenchymal disease (ie, steatosis, chemotherapy-associated liver injury, or cirrhosis) are believed to require larger percentage volumes.[8,9] Portal vein embolization

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Abbreviations and Acronyms
AUC = area under the curve
eGR = estimated growth rate
FLR = future liver remnant
FLV = functional liver volume
IQR = interquartile range
PVE = portal vein embolization
ROC = receiver operating characteristic
sFLR = standardized future liver remnant

(PVE) has become an important means to increase the FLR volume before major hepatectomy and thereby reduce postoperative liver failure. After an ill-defined period of time, usually 4 to 6 weeks, repeat imaging is used to determine if the minimum volume has been achieved and to decide if it is safe to proceed to surgery. However, the predictive value of these static measures is variable and not well studied in the post-PVE setting.

Typically, hepatectomy is performed several weeks after PVE to allow for adequate hypertrophy of the FLR. Correa and colleagues[10] showed that liver hypertrophy after PVE is more gradual than after hepatectomy, with only 25% of the eventual volume gained after 1 month. Continued growth has been observed for up to 1 year. A reliable early marker of adequate response after PVE is desirable, as it would not only predict successful perioperative outcomes, but would also support reduction of the delay between PVE and subsequent resection. Conversely, patients predicted to do poorly, even if their eventual post-hepatectomy volume gain appears sufficient, would be approached more cautiously or alternative nonresectional treatment would be sought. One such potential marker is the growth rate, which can be measured relatively early after PVE, before full hypertrophy has occurred. Shindoh and colleagues[11] recently reported the promising predictive value of growth rate for patients with colorectal liver metastases undergoing right hepatectomy.

The size of the FLR is typically expressed as a percentage of the functional liver volume (FLV). There is controversy about the optimum method of measuring FLR, which is traditionally done using computerized volumetry from CT or MRI,[5] although some advocate estimation of the FLV using a formula based on body surface area.[12] The ratio of the measured FLR to the estimated FLV has been termed *standardized FLR*, from which a rate of growth can be derived.

The current study examines the FLR growth rate in a broad population of patients submitted to PVE and correlates it to post-hepatectomy liver failure and overall morbidity. We also compared the measured growth rates and estimated growth rates (eGR) and assessed the ability of each to predict perioperative outcomes.

METHODS

The Institutional Review Board at Memorial Sloan Kettering Cancer Center granted a waiver of consent for this retrospective study. Two hundred and fourteen patients who underwent preoperative PVE followed by major hepatectomy (≥3 Couinaud segments) for malignant liver disease (primary and secondary) between September 1999 and November 2012 were identified from a prospectively maintained database. Patients were eligible if a CT or MRI scan was performed both before PVE and after PVE, but before hepatectomy. Thirty-three patients were excluded from the study because one or more required scans were missing, imaging coverage of the liver was incomplete, imaging quality was inadequate, or if one or more scans were from an external imaging source. An additional 28 patients were excluded if surgery was delayed for more than 3 months for any reason. A total of 153 patients were included in the analysis. Demographic, clinical, pathologic, and follow-up data were obtained from the database.

Embolization technique

The technique of PVE at our institution has been described previously.[13] In summary, an ipsilateral portal vein puncture was used to avoid injuring the FLR. Embolization was performed using polyvinyl alcohol particles. For right PVE, which represented the large majority of patients, the main right portal vein was embolized. When an extended right hepatectomy was planned, segment 4 portal inflow was not embolized in all except 4 patients, with the rationale being to avoid inadvertent reflux of embolic material into the remainder of the left portal system. Likewise, for a planned extended left hemihepatectomy, only the left portal vein was embolized.

Image processing

The pre- and post-PVE CT or MRI scans were processed using PC-based software (Scout Liver; Pathfinder Therapeutics). The liver was outlined on an axial scan in a semiautomated fashion; manual adjustment was usually needed to ensure that extrahepatic structures, such as the inferior vena cava, the base of the heart, and the abdominal wall, were excluded. Once designation of the liver extent was complete, a three-dimensional model of the organ was generated. The software computed the volume of the liver using a well-established technique.[14] The volume of tumors was calculated similarly. The 3-dimensional model was then manually divided into the embolized (resected) and nonembolized (remnant) sides along the principal plane of the liver defined by the middle hepatic vein and the gallbladder fossa.

The following volumetric data were obtained: total liver volume, total tumor volume, functional liver volume (FLV = total liver volume − total tumor volume),