Standardized Liver Volumetry for Portal Vein Embolization

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ABSTRACT

Major and extended hepatic resections are being performed with increasing frequency as morbidity and mortality rates after major hepatectomies have declined and definitions of resectability have expanded for primary and metastatic hepatic malignancies. Systematic assessment of the anticipated functional remnant liver is essential before major hepatic resection to avoid postoperative hepatic insufficiency and its attendant sequelae. The volume of the future liver remnant (FLR) correlates with FLR function and postoperative outcome. This article describes the rationale for FLR measurement, methods of measuring FLR volume, and standardization to the total estimated liver volume. The indications for portal vein embolization based on standardized liver volumetry are summarized.

KEYWORDS: Liver volumetry, future liver remnant, portal vein embolization

Objectives: On completion of this article, the reader should understand the rationale and methods of future liver remnant (FLR) volume measurement, as well as standardization of FLR volume to the total estimated liver volume to determine which patients should undergo portal vein embolization.

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Disclosure: Jean-Nicolas Vauthey, M.D. has disclosed that he receives Grant/Research Support from Sanofi-Aventis and is a member of the Speakers' Bureau for Genentech.

Complete surgical resection of primary and metastatic hepatic malignancies provides patients the best chance of long-term survival. With improvements in anesthetic monitoring, surgical techniques, and perioperative critical care, major and extended hepatic resections are being increasingly performed with low morbidity and mortality rates.^{1,2} This trend toward an aggressive surgical management results partly from an expansion of the traditional selection criteria for hepatic resection to include patients once deemed unresectable,

such as those with large and multiple tumors. Indeed, the definition of resectability has recently changed from one based on tumor characteristics, such as tumor number and size, to one based on whether the disease can be completely resected with negative margins. This paradigm shift implies that surgeons should focus on what will remain after resection, the future liver remnant (FLR), rather than concentrating on what is removed. These changes in criteria for resectability were formalized in a consensus conference on colorectal metastases

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Portal Vein Embolization; Guest Editors, David C. Madoff, M.D., and Thierry de Baere, M.D.

Semin Intervent Radiol 2008;25:104–109. Copyright © 2008 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

DOI 10.1055/s-2008-1076681. ISSN 0739-9529.

sponsored by the American Hepato-Pancreato-Biliary Association in 2006³ and in an international meeting on hepatocellular carcinoma.⁴

The objectives of this article are to review data supporting the need for meticulous FLR evaluation before hepatic resection and to discuss methodologies for FLR assessment. We advocate a standardized translatable approach to measuring FLR based on the association between liver and patient size.

RATIONALE FOR FUTURE LIVER REMNANT MEASUREMENT

Major or extended hepatectomy can be performed with near-to-zero mortality rates in patients without cirrhosis,⁵ yet significant morbidity, particularly postoperative hepatic insufficiency, remains a major concern.^{6–9} In a recent series of 1059 major hepatectomies performed in noncirrhotic patients, including 390 extended hepatectomies, Mullen et al⁸ reported that hepatic insufficiency complicated the postoperative course after 8% of the procedures. In such circumstances, patients often require prolonged intensive care unit stays, endure a protracted recovery, and can ultimately succumb to fatal hepatic failure. In the study by Mullen et al, the hepatic insufficiency-related mortality rate was 2.8%.⁸

Although the risk of postoperative hepatic insufficiency is influenced by multiple factors, a key determinant to ensuring adequate functional remnant liver is preoperative measurement of the FLR volume.^{10–13} Therefore, preoperative volumetric analysis of the anticipated FLR has become an essential component of surgical planning to ensure sufficient functional liver parenchyma remains and, consequently, to minimize the risks of postoperative hepatic insufficiency and mortality. Furthermore, the aim of volumetric analysis of the anticipated FLR is not simply to assess the volume of the FLR but rather to predict the function of the FLR. Studies have demonstrated that increased FLR volume is associated with improvements in biliary excretion, hepatic metabolic capacity, and postoperative liver function tests.^{14–16}

Precise FLR measurements are needed before extended right hepatectomy and in selected patients before right hepatectomy because of significant interpatient variation in hepatic volumes and variable contributions of hepatic segments to the total liver volume. Abdalla et al¹⁷ measured hepatic segment volumes in 102 Western patients without liver disease who underwent helical computed tomography (CT) for pathologies unrelated to the liver or biliary tree. The authors found that, on average, the right liver (segments V to VIII) contributes two thirds of the total liver volume (TLV), and the left liver (segments II to IV) represents a third of the TLV. The left lateral section (bisegment II/III) contributes approximately half the volume of the left

liver, or 16% of the TLV. However, a large degree of interpatient variability in liver volumes was observed, with the right and left liver contributions to the TLV ranging from 49 to 82% and 17 to 49%, respectively. Notably, bisegment II/III comprised 5 to 27% of the TLV, representing $\leq 20\%$ of the TLV in $> 75\%$ of patients (Fig. 1). The clinical implication of these findings is the need for a systematic preoperative evaluation of the FLR volume in patients without liver disease scheduled to undergo extended right hepatic resection; in addition, preoperative liver volumetry is warranted in all patients with chronic liver disease considered for right hepatectomy, as well as in those with normal underlying liver parenchyma when a small left liver is suspected.

METHODS FOR FUTURE LIVER REMNANT MEASUREMENTS

Several methods for liver volume determination have been proposed. Although ultrasonography is not accurate for volumetric measurement, 3D reconstruction of computed tomography (CT) images correlates closely with actual liver volume.^{11,18–20} Historically, CT measurements of liver volumes were inaccurate due to partial-volume effect, variability with respiratory phases, and interobserver variation.²¹ However, modern advances, including the development of helical and multidetector CT and the availability of software for 3D reconstruction, have reduced error rates for measuring liver volumes to $< 5\%$.²² CT volumetry entails tracing the hepatic segmental contours of each slice, measuring the enclosed area, and multiplying the surface area by slice thickness to calculate the volume (Fig. 2).²³ Intravenous contrast must be administered in several phases to delineate the vascular landmarks of the hepatic segments. Using modern techniques, CT measurements of preoperative FLR volume have been found to correlate linearly with actual volumes of the resected specimens.²² Because CT is routinely performed for both tumor staging and preoperative surgical planning, 3D CT volumetry has become the standard technique for measuring FLR.^{16,24,25}

The traditional method of measuring liver volumes focused on the liver to be resected, with CT measurements of the TLV and volume of liver to be resected. Volumes of each tumor were measured and subtracted from the calculation to yield a ratio of the estimated total nontumorous remnant liver as follows: $(\text{resected volume} - \text{tumor volume}) / (\text{TLV} - \text{tumor volume})$.^{11,19} However, this method is prone to errors in patients with multiple tumors because of the cumulative mathematical errors associated with multiple measurements of each tumor. In addition, in patients undergoing portal vein embolization (PVE), the atrophy of the embolized liver may significantly influence the CT-measured changes in TLV that follow the procedure.

Figure 1 Variability in volume contributions of the right liver, left liver, and bisegment II/III based on computed tomography volumetry in 102 patients. TLV, total liver volume. (Adapted with permission from Abdalla EK, Denys A, Chevalier P, Nemr RA, Vauthey JN. Total and segmental liver volume variations: implications for liver surgery. *Surgery* 2004;135:404–410. © Elsevier 2004.)

Moreover, this technique does not account for the actual functional liver volume in the presence of biliary dilation or when the liver parenchyma is compromised by prolonged cholangitis or vascular obstruction.^{16,26,27} Direct CT measurement of the TLV may be inaccurate in patients with large tumors or in cirrhotic patients with enlarged or shrunken livers. In such patients with chronic liver disease, some investigators have adopted algorithms incorporating functional tests, such as the indocyanine green retention at 15 minutes, in conjunction with the extent of planned resection.¹¹

To overcome the errors associated with traditional liver volumetry, Urata et al²⁴ introduced the concept of the total estimated liver volume (TELTV), based on the observation that in adults without chronic liver disease,

liver volume correlates linearly with body size and weight.²⁰ They compared CT volumetry to body size in 96 Japanese children and adults without liver disease to generate a formula to calculate TELTV based on body surface area (BSA). They also found that in subjects > 16 years, the TELTV correlated directly with body weight. For living donor liver transplantation, the recipient body weight is used to normalize the donor graft volume.^{28,29} Recently, a comparison of FLR measurements standardized to body weight and BSA showed that the two methods were highly correlated and yielded similar results in predicting postoperative hepatic dysfunction.³⁰

When applied in an autopsy study of Western patients, Urata's formula of TELTV based on BSA was

Figure 2 Standardized future liver remnant (sFLR) measurement before and after portal vein embolization (PVE). (A) The future liver remnant (FLR) volume, represented by bisegment II/III in this patient, is measured directly with computed tomography and standardized to the total estimated liver volume (TEL), which is calculated from the formula $-794 + 1267 \times \text{BSA}$ (body surface area). The FLR-to-TEL ratio is measured before (B) and after (C) PVE to assess the degree of hypertrophy. (Parts B and C adapted with permission from Vauthey JN, Madoff DC, Abdalla EK. Preoperative portal vein embolization: a Western perspective. In: Blumgart LH, ed. *Surgery of the Liver and Biliary Tract*. 4th ed. Vol. 2. Philadelphia: Elsevier; 2007:1461–1469.)

found to underestimate TELV by an average of 323 cm^3 .³¹ Hence a multicenter study of Western adult patients was undertaken to evaluate the correlation between TELV and body size.³² Liver volumes of 292 patients from major centers in Europe and United States were calculated from helical CT scans obtained for conditions unrelated to the hepatobiliary system. Pooled-sample regression analysis demonstrated that after adjusting for BSA, age and body mass index were not associated with TELV. A formula to estimate TELV based on BSA was determined, with $\text{TEL} = -794 + 1267 \times \text{BSA}$ (Fig. 3). The validity of this formula was corroborated by its close correlation with two independent equations derived from Western autopsy studies^{31,33} and by a meta-analysis that showed this formula to be the least biased of 12 different formulas and a precise method for TELV calculation.³⁴ The authors of the multicenter study found a consistently high degree of correlation between TELV and BSA at

Figure 3 Correlation between body surface area (BSA) and total liver volume (TLV) in 292 Western patients. (—) 95% confidence interval and (---) 95% predictive interval. (Reprinted with permission from Vauthey JN, Abdalla EK, Doherty DA, et al. Body surface area and body weight predict total liver volume in Western adults. *Liver Transpl* 2002;8:233–240.)

all participating centers, where different CT scanners and 3D reconstruction techniques were used. These findings reiterate the accuracy of CT volume measurement and show that reliable results can be obtained using different equipment and software.

The ratio of the CT-measured FLR volume to the TELV based on BSA yields the standardized FLR (sFLR) volume. The sFLR provides a determination of the percentage of the TELV that will remain after hepatic resection. Standardized liver volumetry represents a simple, accurate, and reproducible approach that overcomes the drawbacks of the traditional method for liver volumetry and permits a uniform comparison of FLR volume before hepatectomy, with or without PVE.

INDICATIONS FOR PORTAL VEIN EMBOLIZATION BASED ON STANDARDIZED LIVER VOLUMETRY

The minimum sFLR and indications for PVE should be tailored to each patient and depend on many factors, including the complexity of the anticipated resection, simultaneous procedures, patients' comorbidities, and underlying liver disease. Using standardized liver volumetry, guidelines have been proposed regarding the minimal amount of functional liver necessary for successful hepatic resection, based on multiple studies demonstrating a correlation between sFLR and postoperative outcome.^{5,16,35,36} In general, a sFLR of 20% is considered the minimum safe volume needed after extended hepatic resection in patients with normal underlying liver, whereas an sFLR of 40% is required in patients with cirrhosis or hepatitis. In patients who receive extensive chemotherapy before hepatic resection, a threshold volume for safe resection of 30% has been proposed (Fig. 4).³⁷ At our institution, patients with anticipated sFLR below the minimum threshold undergo CT volumetric analysis immediately before and 3 to 4 weeks after PVE to assess the degree of FLR hypertrophy. If the post-PVE sFLR remains below the threshold volume, then an additional 3 to 4 weeks

may be required, particularly in patients with impaired liver regeneration, such as diabetics and cirrhotics. However, in patients without liver disease, an early phase of hypertrophy occurs during the first 3 weeks after PVE, followed by a plateau phase in which the increase in FLR volume is minimal.³⁶ Thus, in patients with persistently small sFLR 3 weeks after PVE, rapid regeneration is unlikely to occur beyond this point.

In summary, knowledge of liver volumes is critical to avoid postoperative hepatic insufficiency after extended resection in patients without liver disease and after major resection in patients with liver disease. Standardized liver volumetry represents a simple straightforward method to estimate the FLR volume and postoperative function that overcomes the pitfalls associated with the traditional method of measuring liver volumes. Minimum sFLR thresholds for safe hepatectomy have been identified as 20% in patients with normal livers, 30% in those with chemotherapy-related liver injury, and 40% in those with chronic liver disease. Patients with anticipated remnant liver volumes below these cutoffs should be selected for preoperative PVE.

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Figure 4 Guidelines for minimum standardized future liver remnants before hepatic resection according to underlying liver condition. (Reprinted with permission from Zorzi D, Laurent A, Pawlik TM, Lauwers GY, Vauthey JN, Abdalla EK. Chemotherapy-associated hepatotoxicity and surgery for colorectal liver metastases. *Br J Surg* 2007;94:274–286. © British Journal of Surgery Society Ltd. Reproduced with permission. Permission is granted by John Wiley & Sons Ltd on behalf of the BJSS Ltd.)

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