Review

CT volumetry of the liver: Where does it stand in clinical practice?

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Imaging-based volumetry has been increasingly utilised in current clinical practice to obtain accurate measurements of the liver volume. This is particularly useful prior to major hepatic resection and living donor liver transplantation where the size of the remnant liver and liver graft, respectively, affects procedural success and postoperative mortality and morbidity. The use of imaging-based volumetry, with emphasis on computed tomography, will be reviewed. We will explore the various technical factors that contribute to accurate volumetric measurements, and demonstrate how the accuracies of these techniques are influenced by their methodologies. The strengths and limitations of using anatomical imaging to estimate liver volume will be discussed, in relation to laboratory and functional imaging methods of assessment.

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Introduction

Liver volume estimation is undertaken in the preoperative assessment of patients undergoing liver resection or liver transplantation. In the assessment of suitability for surgery, key considerations include preoperative baseline liver function, patient size, standardized liver volume (SLV), and postoperative residual liver volume (future liver remnant or FLR). These factors are also applicable, in the appropriate context, for a subset of patients who may require portal vein embolization (PVE) to increase FLR volume. Volumetry may also be important for post-therapy assessment, such as following liver transplant to assess graft regeneration and treatment response assessment of liver malignancies.

Volumetric determination should be a multidisciplinary approach. The need for close communication between the surgeon and the radiologist is vital in the determination of the choice of surgical plane (such as hemi-hepatectomy versus extended hemi-hepatectomy), assessment of resectability and the visualization of tumour extent. Prior careful assessment of the liver function is also vital, as a diseased liver (e.g., steatosis and cirrhosis) requires significantly more residual volume as compared to a normal healthy liver.

Computed tomography (CT) volumetry (CTV) has been widely used as a method for the preoperative volumetric assessment of the liver, for the indications as described above. The use of other imaging methods, such as magnetic resonance imaging (MRI) and ultrasound, have also been explored and have shown reliable organ volume measurements when the appropriate scanning protocols are
employed. The strengths and limitations of the various imaging modalities for liver volume estimation are discussed subsequently.

**Clinical applications of CTV**

**Liver resection**

It is imperative to achieve accurate determination of the liver volume, especially in patients with chronic liver disease or cirrhosis where the size of the remnant liver becomes even more important as a prognostic factor. As the presence of underlying liver disease can potentially influence the surgical resectability of a lesion, accurate determination of any hepatic parenchymal disease (particularly cirrhosis) is therefore vital. There are many non-invasive methods available in the evaluation of liver cirrhosis, such as ultrasonic transient elastography (Fibroscan). However, histological diagnosis via liver biopsy remains the reference standard for the diagnosis of liver cirrhosis, and should be considered in the subset of patients with equivocal laboratory and imaging findings.

The FLR-to-SLV ratio is used as an indicator in predicting the likelihood of postoperative liver failure after major hepatic resection, particularly in patients with pre-existing chronic liver disease. The SLV is based upon the regression analysis of normal population (typically transplant donors), and in which a formula can be calculated either from a patient’s body weight (BW) or body surface area (BSA). A study of 301 extended right hepatectomies demonstrated an inverse correlation amongst small (<20%), intermediate (20–30%), large (>30%) FLR volumes and increasing risk for postoperative deaths. In patients with normal livers, an SLV <20% following major surgical resection has been found to be associated with higher postoperative morbidity and liver insufficiency, including the length of stay in the intensive care unit. The exact FLR can be patient-specific and a range of cut-off percentages have been proposed in various publications. For example, in a prospective study, Ferrero and colleagues found that an FLR of approximately 26.5% is required for patients with a healthy liver. However, for patients with underlying liver disease, it is generally accepted that the FLR required is considerably larger than those with a normal liver given the impaired baseline function of the hepatocytes. In order to ensure surgical success and to reduce significant morbidity and mortality, a patient with cirrhosis will require an FLR of >50% whereas the requirement is >40% in patients with high-grade steatosis. To overcome the potentially low FLR after liver resection, PVE can be performed preoperatively to induce contralateral hypertrophy and, therefore, reduce the loss of liver mass following surgery.

Postoperative infection is also a major cause of mortality. Increased risk of severe infection is inversely correlated with FLR. In the study of Schindl et al. on 104 patients who underwent liver resection, analysis of the subgroup of patients with smaller relative residual liver volume showed a significant relation between severe hepatic dysfunction and infection, suggesting that there may be a relationship between liver function, innate immunity, and susceptibility to infections.

**Living donor liver transplantation**

The liver volume is also a key factor in the selection of the appropriate individual for living donor liver transplantation (LDLT). Imaging of the recipient should be carried out as close to the time of planned transplantation as possible so as to obtain an accurate reflection of the recipient’s disease state, particularly if there is underlying malignancy as tumour can rapidly progress. Any vascular invasion or thrombosis should be readily identified, as this influences the plausibility of transplantation. Additionally, proximity of the tumour to the main hepatic and portal vasculature as well as the central bile ducts should be highlighted. In patients with end-stage cirrhosis, imaging should actively seek to exclude hepatocellular carcinoma (HCC). CT of the thorax and abdomen should be acquired at the same sitting to rule out metastatic disease or concomitant extra-hepatic primary malignancy, should a hepatic tumour be present.

Although the imaging findings of the recipient have no significant impact on donor selection, precise assessment of the donor liver volume is crucial in determining whether the donor is suitable for LDLT to ensure safety for both donor and recipient. Preoperative imaging is required to ensure there is no underlying focal or diffuse liver disease that may make transplantation unsuitable, such as steatosis, cirrhosis, and focal benign or malignant neoplasms. For accurate liver volume estimation, a good understanding of intrahepatic vascular and biliary anatomy is important. Sound knowledge of the surgical procedure is required for accurate evaluation of the donor liver volume. The key anatomical variants that may potentially influence the surgical techniques should be highlighted. For example, typical anatomy of the hepatic arterial is only seen in 55–61% of the population. Common variants include replaced left hepatic artery from the left gastric artery and replaced right hepatic artery from the superior mesenteric artery as well as accessory right or left hepatic arteries. Precise details of the vascular anatomy and its associated territories can be obtained via angiography or through the use of personalized computer analysis software, such as the LiverAnalyzer (MeVis Distant Services, MeVis Medical Solutions, Bremen, Germany; Fig 1).

Using CTV there is generally good correlation of the estimated volume with graft weight obtained. A study by Nakayama et al. showed that the mean weight of an adult liver was 881.1 ± 249.8 g, whereas the mean measured volume of the liver was 956.99 ± 280.1 cm³. For an adult donor, a remnant liver volume of 30% for the donor is considered to be the minimum threshold for transplantation to proceed, providing that there is no steatosis or other underlying liver disease. Small-for-size syndrome occurs when the graft size is too small for the
recipient, and may manifest in the form of postoperative cholestasis, poor bile production, refractory ascites, and prolonged prothrombin time. A minimum graft-to-recipient weight ratio of 0.8 has been recommended by some authors to prevent small-for-size syndrome, and the use of volumetry calculator will help to determine the adequacy of the potential liver graft.13

However, it is important to note that graft function and survival are not only influenced by graft size, but can also be affected by pre-existing disease in the donor’s liver prior to transplantation. Specifically, hepatic steatosis is a common finding in developed countries and can have significant impact on surgical outcome in the transplant. In the study of D’Alessandro et al.14 involving 124 donor livers for transplantation, there was a significantly higher rate of primary non-function and initial poor function in patients who were shown to have received livers with severe hepatic steatosis on donor liver biopsy, compared to those who received livers with none or lesser degrees of hepatic steatosis.14 Upon identification of a potentially steatotic liver in the donor, MRI of the liver can help to further quantify the degree of steatosis.

Pre-operative increase of remnant liver volume

Transarterial chemoembolization (TACE) involves the administration of a chemotherapeutic agent into the hepatic artery followed by hepatic artery embolization (HAE). TACE has been shown to be effective in downsizing HCCs as these tumours preferentially obtain their blood supply from the hepatic artery. Occlusion of the hepatic artery results in selective ischaemia of the tumour and enhances the cytotoxic effect of the chemotherapeutic agent. TACE is frequently performed before PVE in patients with HCCs to prevent tumour growth during the time interval of PVE and scheduled resection (Fig 2).15 In addition, TACE blocks the arterio-portal shunts that are commonly encountered in HCC whose presence could potentially attenuate the effects of PVE.

PVE causes reduction in the size of the embolized hepatic lobe and hence induces compensatory hypertrophy of the remnant portion of the liver (Fig 3). PVE has been widely regarded as an effective means to increase the FLR volume, particularly in patients with inadequate remnant liver volume who require major or extended hepatectomy.16,17 This implies that a higher proportion of patients with previously unresectable disease can now benefit from surgery following a successful PVE procedure.18 Other than just increasing the FLR volume, PVE performed prior to resection has been shown to decrease the peri-operative mortality.19,20 The increase in FLR after PVE may also be used for prognostication. An increase of >5% in FLR may indicate low risk for liver failure after major resection.21
Emerging techniques

The use of HAE after PVE has also been recently reported as a method to accelerate the hypertrophy of the remnant liver in patients with an inadequate increase of the remnant liver volume following unsuccessful PVE. The effects of such arterial embolization on liver regeneration were, however, inconsistent and this procedure runs the risk of severe liver ischaemia predisposing to hepatic abscess formation.

In view of the variable results and risk of hepatic infection following HAE, hepatic vein embolization (HVE) has also been performed in patients with inadequate remnant liver volume after PVE. In a paper by Hwang et al., the use of HVE following PVE has shown favourable results. However, limited literature is available on this emerging technique, and more studies will be required to accurately assess the efficacy of this procedure.

Factors affecting accuracy of CTV: technical considerations

Phase of contrast enhancement: does it matter?

Volumetric assessment is dependent on the scan phase. There are significant differences in the total liver volume...
and graft-liver volume calculations between the largest (venous) and smallest (without contrast medium administration, also known as plain) CT phases. CTV based on the “largest” (venous) CT phase is associated with considerable overestimation, whereas volumetry based on the “smallest” (plain) CT phase yields the least significant overestimation. However, even though CTV based on the “smallest” (plain) CT phase most accurately matches the actual intraoperative findings, the venous phase is typically preferred in practice.25 The reason for this is because contrast-enhanced CT delineates the vascular anatomy and the margins of any tumour better than unenhanced CT of the liver.

**Manual versus semi-automated versus automated methods of CTV: which is better?**

CTV has traditionally been performed by manual contour tracing of the hepatic contours and summation of the liver area on each axial section, usually by a radiologist (Fig 4). Contour tracing is typically carried out using the standard optical mouse. Novel ways of tracing the liver margins have been devised, including the use of a freehand electromagnetic pen tablet.26 There is comparable accuracy and precision in these two methods. The mean segmentation time per patient is significantly shorter with the use of the freehand electromagnetic pen contour-tracing method. However, such manual methods are operator-dependent and require considerable time and attention. To further speed up the process and avoid tedious operations, automated and semi-automated ways of volumetric measurements have been proposed.11,27-29

Various techniques and algorithms have been described for the automated methods of volumetry, including three-dimensional (3D) active contour segmentation and geodesic active contour segmentation coupled with level set algorithms.31 One such technique involves the estimation of the mean CT attenuation value of the liver and selection of the initial candidate regions of the liver on each section using the estimated CT value of the liver. The liver is then separated from other adjacent organs via the analysis of edge information inside the initially estimated liver. A 3D image of the liver is subsequently reproduced for the calculation of liver volume.29

Automatic segmentation often fails for certain CT images that are low in contrast or have missing edges due to similar intensity of adjacent organs or machine noise. Thus, semi-automated methods are proposed to include the user in the processing loop to guide automated segmentation, which provides more flexibility and control over the volumetric determination. An example using the “random-walk” technique is shown in Fig 5.30 Semi-automatic segmentation introduced by Wimmer et al.31 received the highest average performance score of 84.6 as stated in the 2007 proceedings of the Medical Image Computing and Computer-Assisted Intervention workshop regarding segmentation of the liver. Basically, their algorithm can be divided into three steps. The first step is manual delineation. Manual delineation works on two-dimensional (2D) multiplanar reconstruction views. It captures the cross-section of the liver by user input control points or live wire.32 Experiments show that typically six to eight contours can achieve good results. The second step is 3D surface reconstruction, which works by using radial basis function based on the manual delineation.33 The last step is surface evolution, which evolves the reconstructed 3D surface using a level set framework comprising both image and shape information.34 In general, semi-automatic methods have been show to outperform automatic methods.

In terms of duration of examination, the average user time for automated volumetry is around 0.57 ± 0.06 min/case, whereas those for semi-automated and manual volumetry are around 27.3 ± 4.6 and 39.4 ± 5.5 min/case, respectively.26 This implies a highly effective time-saving measure of >30 min/case if one switched from manual to automated means of volumetric assessment.

**Image section thickness**

As accurate liver volume estimation relies on precise segmentation of the liver, one can expect more accurate results when using CT images that have smaller section thicknesses. Furthermore, there is an inverse relationship between the section thickness and the calculated liver volumes, that is, liver volumes obtained from analysis of submillimetre thick CT sections are typically larger than volume calculated from thicker images.35 A maximum error of 5% in the calculated graft volume should be expected if 6 mm thick sections are used.

However, the use of thinner sections translates to a greater number of axial sections needed for segmentation, hence more time required for volumetric analysis. This is

![Figure 4](image-url) **Figure 4** Selected axial sections through the liver demonstrate manual contour tracing of the left hepatic lobe using syngo MultiModality Workplace (MMW). The MMW then generates a volumetric measurement of the area of interest.
most time consuming when a manual method of contour tracing is utilized. Supposing that a typical adult liver span is 12 cm, the use of 6 mm and 0.625 mm sections requires segmentation of approximately 20 images and 192 images, respectively. The balance between accuracy of volume estimation and time required for image analysis should be carefully weighed.

With regard to the use of volumetry in MRI, the source data are derived from dynamic 3D imaging, such as volumetric interpolated breath-hold examination (VIBE) and liver acquisition with volume acquisition (LAVA). Reiner et al. suggested the use of 6 mm and 8 mm section thicknesses for CT and MRI, respectively, for a good balance between accuracy of calculated volume and time efficiency.

Software for calculation of liver volumes

Volumetric measurements of the liver have been described beyond the use of dedicated professional software. Various authors have used more accessible, generic image processing software such as OsiriX® (Apple Mac OS), Photoshop®, ImageJ®, to measure hepatic volumes, and these have been found to correlate well with conventional CTV (performed in institutions) as well as with intra-operative graft volume. The use of these software packages on a personal computer has also been explored. A study showed small interobserver variability (up to 5%) in the determination of total liver volumes, resection volumes, and tumour volumes using OsiriX software by surgical trainees when compared to CT scanner-linked Aquarius (iNtuition®, by Terra Recon) software by a radiologist. The average time to complete volumetric determination with OsiriX® is 19 ± 3 min using a 5 mm section thickness.

Which formula to use to calculate liver volumes?

Formulas to estimate the SLV have been established using logistical regression statistical techniques. A patient with a non-diseased liver requires a FLR-to-BW ratio of ≥0.4 or FLR-to-TLV ratio of ≥20% in order to ensure safe and appropriate hepatic resection. A number of papers have been published based on different ethnic groups. There is currently no consensus as to which formula is better, that is, whether a BW-derived or BSA-derived formula is more accurate in predicting the SLV. Chun et al. compared patient’s BW and BSA as an indicator in the

<table>
<thead>
<tr>
<th>Reference</th>
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<tr>
<td>DeLand, 1968</td>
<td>SLV = 1020 × BSA – 220</td>
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<tr>
<td>Heinemann, 1999</td>
<td>SLV = BSA × 1072.8 – 345.7</td>
</tr>
<tr>
<td>Vauthey, 2002</td>
<td>SLV = BW × 18.51 + 191.80</td>
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<tr>
<td>Urata, 2002</td>
<td>SLV = (BSA)² × 1267.28 – 794.41</td>
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<tr>
<td>Yoshizumi, 2003</td>
<td>SLV = (706.2 × BSA) + 2.4</td>
</tr>
<tr>
<td>Hashimoto, 2006</td>
<td>SLV = (BSA)² × 772</td>
</tr>
<tr>
<td>Fu-Gui, 2009</td>
<td>SLV = BSA × 961.3 – 404.8</td>
</tr>
<tr>
<td></td>
<td>SLV = BW × 11.508 + 334.024</td>
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Note: BSA (DuBois formula) = 0.007184 × (weight in kg)⁰.⁴²⁵ × (height in cm)⁰.⁷₂⁵; BSA (Mosteller formula) = (weight in kg × height in cm)⁰.⁶/60.
Other methods of liver function assessment

Clinical and laboratory assessment

The most common assessment of hepatic functional reserve is based on a detailed clinical examination with laboratory results (including liver function tests, coagulation profile, and platelet count). Several scoring systems could be formulated based on clinical and laboratory findings. The Child–Pugh classification is frequently used to assess the severity of cirrhosis as well as to extrapolate mortality. It is also used to guide management and to determinate the suitability of resection or transplant. It is derived from five indices (serum albumin level, serum bilirubin level, extent of coagulopathy, presence of ascites, and encephalopathy). Similarly, the Model for End-Stage Liver Disease is also used in the assessment of patients for liver transplantation. The score is derived from a linear regression model based on the international normalized ratio as well as serum bilirubin and creatinine levels.

Conclusion

Imaging-based volumetry of the liver is vital in the pre-operative planning for major hepatic resection or liver
transplantation as well as in the determination of future remnant liver volume. CTV is currently the preferred means of imaging-based volumetry. As the techniques evolve and become more user-friendly, clinicians managing patients who require preoperative assessment of liver function should be aware of its strengths and limitations, in order to utilize CTV appropriately. In future, morphological volumetric assessment of the liver should be combined with the use of functional imaging in order to more accurately reflect functional liver volume, to better predict postoperative liver dysfunction in patients with impaired liver function.

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References