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An Insight of Living Liver Donor Imaging

Mohamed Ibrahim Taema [1], Mohamed Mohsen Tolba Fawzi [2], Aya Mohamed Abd El-Rhim Ali [1], Mohamed Moataz Al-Fawal [1]

[1] Radiodiagnosis Department, Faculty of Medicine - Zagazig University

[2] National hepatology and tropical medicine research institute

Corresponding author: Aya Mohamed Abd El-Rhim Ali

E-mail: ayaboraey@yahoo.com

Abstract

Background: Several donor factors, including age and hepatic steatosis (> 30% on the basis of histologic findings), contribute to higher risk of graft loss at 1 year after transplant. Detection and accurate quantification of liver fat in potential donors is critical to minimize the risk of liver biopsy (complication rate, 5–6%) and for the recipient. steatosis detected on imaging confirmed by biopsy. the threshold for steatosis within a graft can vary based on preference of the institution, with the cutoff ranging from 20% to 30%. Several options for liver fat quantification exist and have varying degrees of accuracy and reproducibility. The most accurate, reliable, and clinically accessible method is the MRI-derived proton density fat fraction (PDFF). Computed tomography (CT) volumetry (CTV) has been widely used as a method for the preoperative volumetric assessment of the liver.

Keywords: Living Liver Donor, Computed tomography (CT) volumetry (CTV)

Introduction

The most important differences in candidate selection between Eastern and Western countries involve high-urgency patients, patients with hepatocellular carcinoma (HCC) and challenging surgical situations. **[1]**

High-Urgency Patients

Several studies in Asia have demonstrated excellent outcomes for LDLT in high-urgency situations. Coercion of donors and the possible increase of donor risks are among identified concerns with LDLT, especially in high urgency situations. **[1]**

The National Institutes of Health funded consortium showed that LDLT is beneficial even at lower Model for End-Stage Liver Disease score by preventing liver transplant candidates from developing renal failure and malnutrition, key determinants for mortality on the waitlist and posttransplant complications. Furthermore, data showed that the benefit of LDLT extends to late post-transplant outcomes, going beyond the benefit of earlier transplantation **[2]**

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Hepatocellular Carcinoma

It is an important cause of morbidity and mortality worldwide. It is the sixth most common cancer and the fourth leading cause of cancer death. In general, liver transplantation (LT) is the best treatment for early-stage HCC, since it simultaneously treats the tumor and the underlying liver disease, due to organ shortage, the careful selection and management of patients who may have a major survival benefit after grafting remains a fundamental question. **[3]**

Technical Challenges

Retransplantation, Budd-Chiari syndrome, and portal vein thrombosis especially with extension into the superior mesenteric vein had been regarded as contraindications for LDLT in most centers. However, the increased experience and improved techniques that have been demonstrated in some transplant centers in Asia show that these technical hurdles can be overcome and are not absolute contraindications for LDLT. **[1]**

Hemodynamic and Size Considerations

The size of the graft in LDLT is determined by the extent of hepatectomy and the relative size of the donor and recipient. A team in Kyoto initially led by Tanaka, rapidly accumulated a vast experience with LDLT and introduced an assessment of graft size related to the recipient weight. They defined the graft-recipient-weight-ratio (GRWR); this value equals graft size (kg) / recipient weight (kg) × 10. Based on their work, GRWR of 0.8 to 1.0 was established as a lower limit to prevent SFSS **[4]**.

The volume of liver graft is determined by either graft recipient weight ratio (GRWR), or the ratio of graft volume relative to standard liver volume of the recipient (GV/SLV); SFSG are those with a GRWR < 0.8% and/or those with a GV/SLV < 35% So, if GRWR < 0.8 % or a GV/SLV < 35%, the graft should be regarded as SFSG. **[5]**.

The use of grafts with some degree of steatosis is of concern for patients with SFSS, as these grafts will have a decreased tolerance to portal hyperperfusion. Acceptance for the presence of steatosis varies from one center to the another; however, it seems that the use of donor grafts with up to 30% steatosis does not affect outcomes **[6]**.

Intraoperative Doppler ultrasonography has been used in combination with hepatic portal inflow modulation to detect and offset hyperperfusion in a small-for-size graft. Importantly, numerous interventions that modulate the portal blood flow have been shown to prevent the development of the SFSS in experimental models, such as: the performance of a portocaval anastomosis, the ligation of the splenic artery banding of the portal vein. It is important to highlight that the role for inflow modulation at the time of major liver resection or as a salvage therapy in humans remains undefined **[7]**.

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Transplant Procedures

The three most commonly harvested grafts for LDLT are left lateral segment, left lobe, and right lobe grafts. The left lateral segment graft, which includes the Couinaud's segments II and III, is usually used for pediatric recipients or small size recipients.**[8]**

Right LDLT

Because of its size, right liver LDLT is the graft most commonly used in adult LDLT. Nonetheless, even a right liver graft can be subject to the catastrophic consequences of SFSS. **[2]**

As for the left lobe, optimal hepatic venous outflow is key for a successful outcome. The issue of whether or not to include the middle hepatic vein (MHV) in right lobe liver grafts remains controversial When the MHV is not included in the graft, it is advisable to preserve and reconstruct sizable (>5 mm) right inferior hepatic veins and segments 5 and 8 hepatic venous branches (V5, V8).**[1]**

Left Lobe LDLT

Most LDLT centers worldwide, except very limited centers, have used RL grafts for more than 90% of LDLT cases in adults because LL grafts are associated with a high risk of small-for-size syndrome (SFSS), which may cause graft loss **[9]**

Dual-Graft LDLT

Insufficient graft volume could result in small-for-size syndrome in recipients, whereas major liver donation predisposes the donor to a high risk of post-hepatectomy liver failure. Dual graft LDLT is therefore introduced to obtain combined graft sufficiency. Dual graft LDLT is indicated when: a single donation is unacceptable due to graft-to-recipient size mismatch, the future liver remnant is insufficient in the single donor after major resection, or there is a significant underlying disorder or anatomical variation within the donor liver. **[10]**

Post-transplant Care

Common early postoperative complications following LDLT include:bleeding and hepatic artery thrombosis .thrombectomy and revision of arterial anastomosis may also be successful in early HAT, especially if diagnosed via surveillance ultrasound. Primary nonfunction, an early postoperative complication which occurs in approximately 0.5-5 % of deceased donor liver transplantation (DDLT), is not commonly reported in LDLT, Rejection is reported at similar rates compared to whole liver transplantation, Late biliary strictures and infection rates are higher following LDLT, likely related to higher rates of biliary complications leading to biloma and intra-abdominal abscess. **[1]**

Several donor factors, including age and hepatic steatosis (> 30% on the basis of histologic findings), contribute to higher risk of graft loss at 1 year after transplant. Detection and accurate quantification of liver fat in potential donors is critical to minimize the risk of liver biopsy (complication rate, 5–6%) and for the recipient. steatosis detected on imaging confirmed by biopsy. the threshold for steatosis within a graft can vary based on preference of the institution, with the cutoff ranging from 20% to 30%. Several options for liver fat quantification exist and have varying degrees of accuracy and reproducibility. The most accurate, reliable, and clinically accessible method is the MRI-derived proton density fat fraction (PDFF). **[11]**

MDCT scan in essential to detect unexpected focal liver lesions. Although majority of these lesions are benign, like cysts or hemangiomas, presence of any large lesion or a malignant lesion is a contraindication for organ donation In addition, donor livers should be evaluated for the presence of fatty infiltration. It has been reported that with each 1% increase in hepatic fat content, functional mass of donor liver reduces by 1%. **[12]**

Unenhanced CT is a good method for hepatic fat estimation. On a non-contrast scan, normal liver has a higher attenuation than spleen. Fatty infiltration causes liver attenuation to be reduced and whenever liver attenuation is lower than that of spleen, on visual appearance alone, possibility of hepatic steatosis is high. A subjective five-point grading system for the degree of hepatic steatosis on the basis of hepatic attenuation and visualization of hepatic vessels. Whenever the hepatic vessels show a higher attenuation than the hepatic parenchyma on a non-contrast image (grade 5). **[12]**

Preoperative mapping of biliary anatomy is one of the critical assessments for donor selection and surgical planning. normal bifurcation of the donor liver requires only a single biliary reconstruction (choledochocholedochostomy or choledochojejunostomy) in the recipient. Other donor livers with aberrant drainage of the right ductal system, such as trifurcation and right posterior duct draining into left main duct, require two separate biliary anastomoses in order to prevent postoperative biliary leakage and long-term segmental atrophy in recipients. Although endoscopic retrograde cholangiopancreatography (ERCP) is well accepted as a gold standard for evaluation of biliary anatomy, it poses substantial risks (5.5% risk of pancreatitis, 3–5% risk of perforation) in otherwise healthy donors. Recently, MRCP has emerged as a non-invasive alternative imaging examination for evaluation of the biliary system and is performed with increasing frequency. **[13]**

There are many techniques that can be used for pre-oper- ative biliary mapping such as Magnetic Resonance Cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP) and (Computed tomogra- phy) CT cholangiography. ERCP is an invasive technique with known complications and hence not preferred in healthy subjects. CT cholangiography may also cause side effects due to the used contrast

media, and so is also relatively contrain- dicated in that group of subjects. MRCP is noninvasive, pre- cise and does not require contrast media making it the most appropriate investigation for preoperative biliary mapping. **[8]**

Liver volumetrics

Liver volumetrics is a key component of potential living liver donor evaluation because inadequate liver volume is the most common reason for donor exclusion based on imaging, and the decision to perform left versus right lobe harvesting largely depends on donor liver volume. For the donors, liver remnant volume [FLR] of 30%–40% of the total liver volume is required for donor survival. For the recipients, a graft-to-recipient weight ratio (GRWR) of at least 0.8% or a graft-to-standard liver volume ratio of at least 40% is needed for adequate graft function and to avoid small-for-size syndrome (SFSS) in the recipients. **[8]** Both CT and MRI can be used to obtain accurate liver volumes. Liver volume calculation should exclude large vessels, major fissures, and the gallbladder fossa. Reports should contain the volume of the left and right lobes (hemiliver), which is divided along the middle hepatic vein (MHV) and gallbladder fossa. Some centers use a virtual cut plane 1 cm to the right of the MHV, and others use the right margin of the MHV bounded anteriorly by the gallbladder fossa and posteriorly by the inferior vena cava (IVC), simulating the resection margin. The caudate lobe should be reported separately from the right and left lobes because the caudate lobe may or may not be included in the left lobe graft. The volume of the left lateral segment is specifically reported when donation is planned for pediatric and other small recipients. Most adult recipients need a left or right hemiliver graft. **[11]**

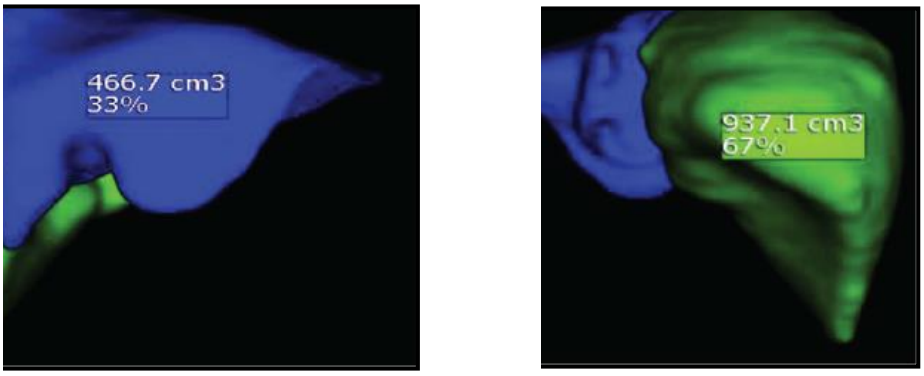

Fig. (1): Three-dimensional (3D) reconstructed CT images demonstrate liver volumetric measurements in cm3 and % of total liver volume. Depicted are the left (blue) and right lobes (green) of the liver divided by the hemihepatectomy plane, in the anterior **(a)**, and posterior **(b)** views.

In 1970, Heymsfield et al first described the liver volume measurement, and afterward, many manual and automated volume calculation programs have been implemented. Due to advances in technology, considering volumetric techniques as well, several generic

manual or computeraided segmentation protocols and commercially available institutions specialized in virtual software systems (such as our Liver Transplant Unit) have recently been advocated to simplify the volumetry calculation and provide more accurate and faster results of volumetry to the surgeons. **[14]**

Kwon et al found a 5% discrepancy between prospective (preoperative graft volume) and retrospective CT volumetry (postoperative graft volume). This error increases up to 10% when compared to actual graft weight measured at the time of operation. **[15]**

Factors affecting accuracy of CTV

Phase of contrast enhancement:

Volumetric assessment is dependent on the scan phase. There are significant differences in the total liver volume 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. The reason for this is because contrast-enhanced CT delineates s the vascular anatomy and the margins of any tumour better than unenhanced CT of the liver. **[15]**

Manual versus semi-automated versus automated methods of CTV

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 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. 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. **[16]**

Image section thickness

Recent advances in multi-detector row helical CT technology have enabled us to obtain isotropic three-dimensional (3D) image data, in which the slice thickness is typically 0.5–0.7 mm. With the use of 3D image data, partial volume effects are expected to decrease considerably, and the accuracy of CT liver volumetry can potentially be improved. On the other hand, the radiologists' or surgeons' workload (time) would be substantially more if they manually trace the liver contour on each image of 3D data instead of the usual two-

dimensional (2D) data, due to the considerable increase in number of images when using thinner slice sections. **[17]**

Software for calculation of liver volumes

Volumetric measurements of the liver have been described beyond the use of dedicated professional software. study was to compare ImageJ and OsiriX® when performing prospective CT volumetric analysis of the liver on a PC in patients undergoing major liver resection. The study also planned to compare the prospective measurements of ImageJ and OsiriX® to those of CT volumetry performed by a radiologist using classic radiology software (iNtuition®) linked to a CT scanner system. that study concluded that Prospective hepatic CT volumetry with ImageJ or OsiriX® is reliable and can be accurately used on a PC by nonradiologists. ImageJ and OsiriX® yield results comparable to the radiological software iNtuition®. **[18]**

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 and 40% in cirrhotic livers. **[19]**

Therefore, it is important to establish SLV criteria presented their formula for calculating liver size, at least 15 other formulas have been proposed for estimating SLV. However, as yet, no single formula is statistically. **[20]**

A number of body indices have been reported to impact liver volume, including sex, age, BH, BW, BMI and BSA. Of these factors, BSA is the most widely accepted parameter for determining SLV. BSA is widely used to normalize measurement of biological function with respect to variations in body size. Several formulas have been developed to calculate BSA. Due to the large variability in liver size based on race, sex, body shape and body size, the difference in actual liver volume and standard liver volume (SLV) is considered more sensitive than TLV alone. Therefore, it is important to establish SLV criteria for healthy individuals. **[20]**

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