Preoperative CT evaluation of potential donors in living donor liver transplantation

Sandeep Vohra, Neerav Goyal, Subash Gupta

Departments of Radiology, 1Surgical Gastroenterology and Liver Transplant and 2Surgical Gastroenterology and Liver Transplant, Center for Liver and Biliary Sciences, Indraprastha Apollo Hospital, New Delhi, India

Correspondence: Dr. Sandeep Vohra, Department of Radiology, Indraprastha Apollo Hospital, Sarita Vihar, Delhi Mathura Road, New Delhi - 110 076, India. E-mail: savohra@yahoo.com

Abstract

Living donor liver transplantation is an effective, life sustaining surgical treatment in patients with end-stage liver disease and a successful liver transplant requires a close working relationship between the radiologist and the transplant surgeon. There is extreme variability in hepatic vascular anatomy; therefore, preoperative imaging of potential liver donors is crucial not only in donor selection but also helps the surgeons in planning their surgical approach. In this article, we elaborate important aspects in evaluation of potential liver donors on multi-detector computed tomography (MDCT) and the utility of MDCT in presurgical assessment of the hepatic parenchyma, relevant hepatic vascular anatomy and segmental liver volumes.

Key words: CT angiography; fatty liver; hepatic vascular anatomy; liver volumetry; living donor liver transplantation

Introduction

Liver transplantation is being used as a definitive therapeutic option in management of patients with end-stage liver disease. Due to limited availability of deceased donor organ donations in India and most parts of the world, living donor liver transplantation (LDLT) is being increasingly used as a safe, viable, and efficacious surgical procedure in treatment of patients with liver failure (acute and chronic liver disease) and liver cancer. LDLT is the mainstay of liver transplants in India. Approximately 800-1000 liver transplant surgeries are performed in India annually.

LDLT is a complex, innovative surgical procedure, where a donor donates a part of his liver to the recipient, usually the right hemi-liver in adult liver transplants and the left lateral section or left hemi-liver in pediatric recipients. Role of imaging in preoperative evaluation of a potential donor is important as it helps in excluding focal or diffuse liver disease and also provides a detailed evaluation of the vascular and biliary anatomy along with assessment of liver volumes. This information is essential before taking up a major surgical task. With improving surgical techniques and immunosuppression, the long-term survival after LDLT has considerably improved.

In this article, we discuss the important aspects in preoperative donor evaluation on multi-detector computed tomography (MDCT), pertaining to assessment of fatty infiltration in donor liver parenchyma, identification of normal and variant hepatic vascular anatomy, and estimation of segmental liver volumes along with their utility in donor selection and surgical planning. More than 1500 living donor liver transplant surgeries have been performed at our institute over the last 8 years. Major indications and contra-indications of liver transplant have been summarized in Tables 1 and 2, respectively.
Portal and hepatic venous phase images were acquired at 20 and 60 s following the arterial imaging. No delay time was used and scanning was automatically triggered at a detection threshold of 180 Hounsfield units (HU) in lower thoracic aorta. CT angiographic images were obtained after intravenous administration of 100-120 ml of non-ionic contrast agent Iohexol 350 (Omnipaque, GE Healthcare, USA) at a flow rate of 5 ml/s. To ensure accuracy in the timing of arterial phase images, real-time bolus tracking was used and scanning was automatically triggered at a detection threshold of 180 Hounsfield units (HU) in lower thoracic aorta. Portal and hepatic venous phase images were acquired at 20 and 60 s following the arterial imaging. No positive or neutral oral contrast was given.

MDCT is an important tool in preoperative assessment of potential liver donors. It allows a faster, isotropic imaging of the liver parenchyma with excellent spatial resolution, in a single breath hold\(^\text{[11,12]}\). It provides an accurate, non-invasive angiographic detail of the complex hepatic vascular anatomy, and helps in evaluation of hepatic steatosis and segmental liver volumes\(^\text{[13]}\).

### Imaging Protocol

Imaging protocol on MDCT consists of obtaining non-contrast images through the liver parenchyma, followed by CT angiography in the arterial, portal, and hepatic venous phases. In our institution, we perform MDCT angiography as a part of donor work-up prior to surgery. Images that appear in this article have been obtained on a 64-row MDCT (Aquilion; Toshiba Medical Systems, Tokyo, Japan). CT angiographic images were obtained after intravenous administration of 100-120 ml of non-ionic contrast agent Iohexol 350 (Omnipaque, GE Healthcare, USA) at a flow rate of 5 ml/s. To ensure accuracy in the timing of arterial phase images, real-time bolus tracking was used and scanning was automatically triggered at a detection threshold of 180 Hounsfield units (HU) in lower thoracic aorta. Portal and hepatic venous phase images were acquired at 20 and 60 s following the arterial imaging. No positive or neutral oral contrast was given.

The setting of CT parameters was as follows: 120 kVp, variable mA exposure using the automated exposure control method to reduce patient radiation dose, 0.4 s as tube rotation time, and a pitch of 0.9. Post-contrast images were reconstructed with 1 mm slice thickness and a reconstruction interval of 0.8 mm. All the post-processed images have been created on a commercially available dedicated CT workstation (Vitrea; Vital Images Inc, Minn, USA).

Overlapping thin slab axial maximum intensity projection (MIP) and thick slab oblique coronal MIP images are best to depict the hepatic arterial anatomy as they provide excellent contrast between the enhanced vessels and liver parenchyma\(^\text{[7]}\). On the other hand, thin and thick slab axial and coronal MIP images and three-dimensional (3D) MIP and volume-rendered (VR) post-processed images should be used to delineate the porta-venous anatomy.
Evaluation of Liver Parenchyma

This is the first step in comprehensive preoperative evaluation of potential donors in LDLT. It is important to look for the presence of any 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, as increasing hepatic steatosis carries a high risk of postoperative liver dysfunction in donors and graft non-function in recipients. It has been reported that with each 1% increase in hepatic fat content, functional mass of donor liver reduces by 1%. Moderate to severe macrovesicular steatosis, i.e. ≥30% fat, as determined on liver biopsy, in the donor liver is considered unacceptably high for LDLT and such donors should be rejected.

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. Spleen is an appropriate organ for comparison, as overall splenic attenuation is not affected by diffuse pathological processes, is not likely to have fatty infiltration, is located in the same axial plane as liver on CT images. Lee et al. also proposed 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), the predicted hepatic fat content would be greater than 30% macrovesicular steatosis.

Other methods of hepatic fat estimation include measurement of hepatic attenuation in HU and calculation of the liver attenuation index (LAI). The LAI is the difference between mean hepatic attenuation and mean splenic attenuation (i.e. average density of liver – average density of spleen on non-contrast scan). Liver attenuation is calculated by placing the circular region of interest (ROI) of at least 1 cm² area at multiple places in the liver, covering all the hepatic segments. Care should be taken to avoid inclusion of macroscopic vessels and areas close to fissures during attenuation measurements. Splenic attenuation is measured by placing ROI at its upper, mid, and lower poles. Fatty infiltration in liver may be patchy in distribution. A large number of ROIs should be averaged in such cases to minimize the effect of heterogeneity.

Average attenuation of liver parenchyma on non-contrast CT images varies between 50 and 65 HU and is generally 8-10 HU greater than that of spleen. Limanond et al. found in their study that LAI > 5 HU correctly predicted the absence of significant macrovesicular steatosis. LAI values of -10 to 5 HU were suggestive of mild to moderate steatosis (6-30%), while LAI values of less than -10 HU were suggestive of moderate to severe hepatic steatosis (i.e. ≥30% fat) with a specificity of 100%.

Kodama et al. found that liver attenuation values alone also reflect the degree of fatty change and with average liver attenuation of 40 HU on a non-contrast scan, the predicted hepatic fat content is approximately 30%. Similarly, with
hepatic attenuation of 30 HU, the predicted hepatic fat content is approximately 50%.

If any of the CT attenuation values or indices show macrovesicular steatosis of 30% or greater, biopsy is not needed, as such donors will not be acceptable for liver transplant.\[18\]

Magnetic resonance (MR) imaging is another sensitive modality for detection and characterization of fatty infiltration in liver.\[16\] The degree of fatty infiltration can be determined by either using chemical shift imaging or MR spectroscopy, the latter being one of the most accurate methods for non-invasive assessment of fatty liver.\[16\] Details of MR technique are beyond the scope of this article.

At our institute, we evaluate the liver parenchyma for fatty infiltration using MR imaging including MR spectroscopy and on non-contrast CT images. Whenever MR spectroscopic fat fraction is ≥10% and/or the average density of liver is ≤50 HU with a CT LAI ≤0, liver biopsy is performed.

**Evaluation of Hepatic Vascular Anatomy**

Liver has a complex vascular anatomy with a high incidence of vascular variants. Preoperative knowledge of donor hepatic vascular anatomy is very important as transplant survival depends on the patency of all supplying and draining vessels in the graft.\[8\] Adequate arterial inflow to graft liver is necessary for avoidance of biliary necrosis.\[19\] Patency of the portal vein is crucial for graft survival and liver regeneration, while a patent hepatic vein outflow is needed to prevent hepatic congestion and graft dysfunction. MDCT is an excellent tool in providing a detailed road map of normal and variant hepatic vascular anatomy in the donor, and helps in guiding the surgical approach.

**Hepatic arterial anatomy and variants**

MDCT allows accurate delineation of the intrahepatic tertiary arterial branches as small as 1 mm in size.\[8\] In normal hepatic arterial anatomy, common hepatic artery (CHA) arises from the celiac axis. It divides into gastro-duodenal artery (GDA) and proper hepatic artery.\[7\] The latter ascends toward the liver hilum and divides into left hepatic artery (LHA) and right hepatic artery (RHA). LHA supplies the entire left hemi-liver, including segment IV. The RHA divides into anterior and posterior sectional branches which supply the anterior (VIII and V) and posterior sections (VI and VII) of right hemi-liver, respectively [Figure 5A].

It is important to measure the length of RHA (in right hemi-liver donation) or LHA (in left hemi-liver or lateral section donation) from their origin till the next bifurcation.\[7\] Artery with more than 1 cm length and diameter of more than 2 mm is preferable for anastomotic purposes.

In right posterior sectional grafts, a separate single artery to the posterior segments of right lobe (segments VI and VII) should be identified on imaging with an adequate extrahepatic length which will allow for safe anastomosis.

This normal hepatic arterial anatomy as described by Michel is seen approximately in 55% of the population, while the remaining have a variant arterial anatomy.\[20\]

Identification of the dominant arterial supply to segment IV is very important because its integrity is indispensable for the regeneration of remnant donor liver. Segment IV artery usually arises from the LHA; however, in approximately 11% of patients; it arises from the RHA and may traverse the transection plane to ascend into the left lobe. In such
cases, RHA is divided distal to the origin of segment IV artery. It is important to ensure preoperatively that the RHA segment distal to segment IV artery is of sufficient length to permit anastomosis [Figure 5B and C]. Uncommonly, segment IV artery may arise from the extrahepatic portion of segmental RHAs [Figure 5D].

Whenever RHA arises from the superior mesenteric artery (SMA) or LHA arises from the left gastric artery (LGA), they are termed as replaced/accessory hepatic arteries [Figure 5E]. Incidence of replaced hepatic arteries is 9-12%. A replaced hepatic artery usually has a longer length and allows a surgeon to perform safe anastomosis. Moreover, the origin of segment IV artery from a replaced RHA has never been observed, making it extremely safe for right hemihepatectomy.

Presence of multiple small vessels in a lobe precludes donation.

Other surgically important arterial variants include direct origin of hepatic artery from the aorta or entire hepatic artery from the SMA, and separate origin of all hepatic arterial branches from CHA.

Rarely, branches of RHA may arise from the distal portion of LHA and may traverse the left lobe liver parenchyma to enter the right lobe, making donor hepatectomy impossible [Figure 6].

Portal vein anatomy and variants
Classically, the main portal vein trunk branches into right and left portal veins at porta hepatis. The right portal vein (RPV) subsequently divides into anterior and posterior sectional branches at a variable length from the RPV origin. The right anterior portal vein (RAPV) supplies segments VIII and V, while the right posterior portal vein (RPPV) supplies segments VI and VII of the liver. The left portal vein (LPV), on the other hand, ascends along the falciform ligament and supplies the entire left hemi-liver (segments II, III, and IV) [Figure 7A].

This normal portal vein anatomy is most suitable for donation, as only one anastomosis is required between the donor and recipient portal veins. For right hemi-liver
donations, length of the RPV from the origin of LPV to its bifurcation should be measured, as this would be available to the transplant surgeon for anastomotic purposes. If this distance is small, vascular reconstruction in the back bench may be required, which could have an impact on surgical management.

Variations in the branching pattern of intrahepatic portal vein have been reported in 20-30% of cases and usually affect right hemi-liver donation. Nakamura and associates described a classification of portal vein branching patterns with five variations (A-E), where type A is the usual bifurcation type (normal branching pattern). Type B is a trifurcation pattern without the trunk of RPV. In type C, the right anterior sectional branch (RAPV) arises separately from the proximal or extra-parenchymal part of LPV. In type D, RAPV arises separately from a distal or intra-parenchymal portion of LPV, while in type E, branches of segment V and VIII originate separately from LPV.

In the trifurcation pattern (type B), RAPV and RPPV branches can still be harvested as a single stump, with surgical expertise. In the C pattern of portal branching in the donor results in two portal venous openings in the right lobe graft and would require separate reconstruction. If these two branches are close to each other, they can be joined to make a single orifice (venoplasty). If they are not, an interposed vein graft may be needed for reconstruction, making transplantation a challenging task. Therefore, the distance between the two branches must be carefully measured on imaging.

Intraparenchymal branching of RAPV from LPV (type D) and type E branching patterns are uncommon and are considered absolute contraindications for surgery.

In addition, accessory portal vein branches to right hemi-liver from LPV can also be seen rarely, and they need to be preserved for anastomotic purposes.

Hepatic venous anatomy and variants
There are three major hepatic veins which drain liver parenchyma into the inferior vena cava (IVC). Usually right hepatic vein (RHV) is the largest and drains a major part of right hemi-liver into IVC. The middle hepatic vein (MHV) drains central liver segments (i.e. IV, V, and VIII), while left hepatic vein (LHV) predominantly drains segments II and III. In 60-70% of cases, MHV and LHV join to form a common stump before entering IVC, while RHV opens directly into IVC. Even when MHV and LHV open separately into IVC, an intimate relationship exists between the two in 100% of cases. Diameter of hepatic veins should be measured close to their IVC insertion.

Hepatic venous anatomy is quite variable. Drainage pattern of the MHV should be thoroughly evaluated, since it is an important surgical landmark. In right hemi-liver donation, the hepatectomy plane lies just to the right of the MHV. Branches from the anterior segments of right lobe (V and VIII) draining into the MHV run along the parenchymal resection plane. These veins need to be preserved and re-anastomosed in the recipient to prevent congestion and risk of graft failure in the transplanted right hemi-liver. Typically, venous branches from segments V and VIII which are larger than 4 mm in diameter are anastomosed in the back bench to a portal vein graft harvested from the explanted liver. A neo MHV is thus reconstructed, which is then anastomosed with recipient’s IVC or the LHV and MHV stump on the IVC during implantation.
technique provides outflow to the anterior sector of right hemi-liver and preserves the MHV with donor remnant liver. As a result, donor recovery is hastened.

Occasionally dominant outflow of right hemi-liver may occur via the MHV, where the segment VI vein joins the segment V vein before draining into the MHV [Figure 9D]. Preservation of this anterior segment vein becomes very important so as to maintain adequate outflow of a large portion of the right hemi liver graft.

Another important variant that affects right lobe donation is presence of accessory or inferior RHVs [Figure 9E]. They are seen in 40-50% of patients and more than one inferior hepatic vein may be present. Majority of these veins drain segments VI and VII, and inferior RHVs measuring more than 4 mm in diameter should be preserved and anastomosed separately to recipient’s IVC. When such veins are identified, their distance to the RHV should be measured in the coronal plane.\textsuperscript{11,12,23}

During harvesting of left lateral segment (LLS), a single LHV draining into IVC is suitable. Variations where segment II and III veins open separately into IVC should be avoided for LLS hepatectomy.\textsuperscript{7}

**Biliary Assessment**

Evaluation of normal and variant biliary anatomy can be performed by CT or MR cholangiography. MDCT cholangiography is performed using 20 ml of the cholangiographic contrast agent iopamidol meglumine 52% (Cholografin, Bracco Diagnostics, Princeton, NJ), diluted in 80 ml of normal saline, administered as a 30-60 min intravenous infusion.\textsuperscript{11} CT imaging is performed 15 min after completion of the infusion. MDCT has shown to provide images with high spatial resolution and better delineation of smaller ducts, as compared to MR cholangiography.\textsuperscript{11} However, CT cholangiography is less commonly used, as the market for contrast medium is
limited to a few countries and is also not available in India. Moreover, some authors have observed higher incidence of adverse reactions to biliary contrast agents, raising concerns about their safety.[6,13] In routine clinical practice, preoperative assessment of biliary tree in potential liver donors is done using MR cholangiography.

Variant biliary anatomy has been observed in 30-35% patients.[5] With increasing surgical expertise, a bile duct variation rarely excludes a person from being a liver donor. However, it is very important to preoperatively evaluate unusual patterns of bile duct branching, in order to modify the cutting plane during graft retrieval and the pattern of ductal anastomosis in the recipient.[5] This helps in reducing postoperative biliary complications. Per-operative cholangiograms are also obtained in all donor hepatectomy surgeries before hepatic resection is performed.

**Liver Volumetry**

It is very important to calculate the graft and remnant liver volumes before hepatic resection, in order to ensure adequate hepatic function and liver regeneration after surgery, both in recipients and donors.

The minimum graft size required for LDLT to provide adequate functional hepatic mass in the recipient is defined as the graft-to-recipient body weight ratio (GRBWR) and should be greater than 0.8%. On the other hand, the donor liver remnant volume must be greater than 30% of the original liver volume to ensure donor safety and prevent postoperative hepatic insufficiency.[23] CT volumetry is considered a standard method for preoperative estimation of the hepatic graft and remnant weight.[24]

Hepatic venous phase is used for CT volumetric assessment, as in this phase, hepatic veins are delineated with maximum contrast. The 3D VR images of liver parenchyma are generated on a dedicated CT workstation, depicting the hepatic veins in detail.

Hepatic volumetry performed manually requires slice-to-slice manual contouring of the liver surface on axial images, using an electronic cursor tool, on at least one-fifth of all the native venous phase images in the data set, depending on the liver shape. Intermediate contours are calculated automatically by the workstations using shape-based interpolations.[27] To improve the accuracy in volumetric measurements, all the large vessels (IVC and the proximal portion of portal and hepatic veins) and major fissures should be excluded from the traced liver margins.

With automated CT volumetry software, liver margins can be outlined automatically on the basis of the difference in attenuation between the liver and surrounding tissues. The automated methods of CT volumetry significantly reduce the time required for volumetry.

A virtual hepatectomy plane is defined on the 3D hepatic vein models and axial MIP images, for segmental volume analysis, in a manner simulating the anticipated surgical resection plane during donor hepatectomy. This plane typically runs in a curved manner, just to the right of MHV, from its junction with the IVC superiorly to the gall bladder fossa inferiorly.[6] This relatively avascular plane corresponds well with the intraoperative ischemic line which is determined after clamping of the corresponding inflow vessels (hepatic artery and portal vein) [Figure 10]. Once all the liver margins have been traced along the hepatectomy plane, the right and left lobe liver volumes are calculated, along with graft weight/remnant volume.

Nakayama et al.[29] found in their study that both manual and automated CT volumetric methods yielded acceptable measurements when compared with the data obtained from resected liver, and there was no statistical difference in volume estimation between these two methods.

**Coincidental Findings**

It is important to look at other abdominal visceral organs, peritoneal cavity, lung parenchyma, or bones for the presence of any ancillary finding which may have a bearing on the donor making him unfit for organ donation. Left-sided gall bladder[28] should be looked for and if present, would make the donor unsuitable [Figure 11]. A summary of salient imaging findings to be evaluated on MDCT in preoperative assessment of potential donors in LDLT has been presented in Table 3.

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**Table 3: Check list of major CT findings in evaluation of potential liver donors**

<table>
<thead>
<tr>
<th>CT of the donor liver</th>
<th>Salient findings to be assessed</th>
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</thead>
<tbody>
<tr>
<td>Liver parenchyma</td>
<td>Presence of any benign or malignant liver lesion</td>
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<tr>
<td></td>
<td>Fatty infiltration</td>
</tr>
<tr>
<td>Hepatic vascular anatomy</td>
<td>Branching pattern</td>
</tr>
<tr>
<td>Arterial anatomy</td>
<td>Number of arteries supplying the lobe to be resected</td>
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<tr>
<td></td>
<td>Presence of accessory/replaced hepatic arteries</td>
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<td></td>
<td>Length of artery available for anastomosis</td>
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<tr>
<td></td>
<td>Dominant arterial supply to segment IV</td>
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<tr>
<td>Portal venous anatomy</td>
<td>Branching pattern</td>
</tr>
<tr>
<td></td>
<td>Available length of portal vein for anastomosis</td>
</tr>
<tr>
<td></td>
<td>Presence of any accessory portal vein branch</td>
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<tr>
<td>Hepatic venous anatomy</td>
<td>Drainage pattern of middle hepatic vein especially of segment V/VIII veins</td>
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<tr>
<td></td>
<td>Presence of any inferior hepatic veins</td>
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<tr>
<td>Segmental liver volumes</td>
<td>Remnant liver volume should be &gt;30%</td>
</tr>
<tr>
<td></td>
<td>Graft-to-recipient body weight ratio ≥0.8%</td>
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CT: Computed tomography
Conclusion

MDCT is an excellent non-invasive imaging tool in liver donor evaluation, as it provides a detailed vascular road map to the operating surgeon, gives an assessment of the hepatic parenchyma and segmental liver volumes, and allows better planning for a safe surgical approach. Thorough knowledge of normal and variant hepatic anatomy is required to prevent complications and transplant failures. More importantly, imaging helps a surgeon to select the right donor and prevents intraoperative surprises.

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