# The Role of Liver Biopsy in the Potential Live Liver Donor

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## ISSUE

Does the potential live liver donor need to undergo a pre-donation liver biopsy?

## DATA

A common reason for excluding a potential deceased donor liver allograft for transplantation is the presence of significant hepatic steatosis on liver biopsy as this is associated with poor graft function.(1) Impaired or delayed graft function is also a risk when moderately steatotic (>20% macro-steatosis on biopsy) live donor liver allografts are used.(2) Increased steatosis with a small remnant may increase the risk of hepatectomy to the donor.

Potential live liver donors undergo a comprehensive evaluation that includes biochemical tests of liver function and cross-sectional liver imaging to exclude underlying liver disease. Elevated liver function tests (LFTs) (particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST)) are a contra-indication to live liver donation as they can indicate underlying liver disease and the potential donor should be advised to follow up with their primary care provider or hepatologist. In potential donors who have already undergone a recent liver biopsy, the finding of steatohepatitis is a contra-indication to donation. The commonest cause of elevated LFTs in the US population is non-alcoholic fatty liver disease (NAFLD) but hepatic steatosis or steatohepatitis can be present even with normal LFTs. Historically liver biopsy was the gold standard for assessing the degree of hepatic steatosis and was considered essential in the evaluation of the live liver donor.(3) Donors with greater than 20-30% macro-steatosis are typically excluded from donation (although this can vary based on center protocol). However, liver biopsy is an invasive test with a risk of bleeding and also sampling error as only a tiny fragment of liver tissue is obtained.

The last 10-15 years has seen a dramatic improvement in cross-sectional abdominal imaging techniques. Ultrasound (US) and computed tomography (CT) can accurately

detect significant hepatic steatosis (>10%) (4) but magnetic resonance imaging (MRI) appears to be the most accurate modality to measure hepatic fat content.(5) A retrospective comparison of 182 live liver donors who underwent liver biopsy and MRI with MR spectroscopy demonstrated a very high correlation with an area under the curve for detection of substantial macrovesicular steatosis of greater than 0.95/(5) Similar results have been obtained using MR elastography as a measure of liver stiffness which can very accurately detect hepatic steatosis that would preclude safe liver donation.(6) Perhaps the most accurate imaging test is MRI-proton density fat fraction that was nearly 100% effective in excluding donors with steatosis that would preclude donation, obviating the need for liver biopsy.(7)

Several other potential situations may arise rarely where a pre-donation liver biopsy might be considered to assess suitability for donation when laboratory studies or imaging may not be conclusive. These include donors with a history of prior significant alcohol use, evidence of prior hepatitis B exposure, heterozygous alpha-1-antitrypsin genotype and positive autoimmune serology. There is very limited data on whether liver biopsy in any of these situations is required and will depend on individual center policy on suitable donors. Most centers will evaluate donors with significant alcohol use (if not excluded on psychosocial grounds), donors with positive hepatitis B core antibody and positive autoimmune serology if LFTs and imaging are normal and a liver biopsy would not be required. If LFTs and/or imaging are abnormal donors usually would be excluded. Heterozygous alpha-1-antitrypsin genotype is typically not a contra-indication for liver donation with a recent study showing acceptable outcomes (8). In patients with a very low alpha-1-antitrypsin level the donor would be excluded without the need for a liver biopsy.

In deceased donor liver transplantation there is increasing use of positive hepatitis B (positive hepatitis B surface antigen) and hepatitis C donors due to the success of anti-viral therapy. Liver biopsy of the deceased donor allograft is routinely performed in these situations. Most centers have not expanded this practice to live donors but if this were to occur liver biopsy would presumably be required.

## RECOMMENDATONS

1. Liver biopsy does not need to be routinely performed on potential live liver donors when non-invasive imaging shows no steatosis.
2. Liver biopsy is not required in donors who are excluded because of significant steatosis (>20% or >30% depending on center protocol).
3. If non-invasive imaging shows >5% steatosis or clinically steatohepatitis is a concern, liver biopsy can be considered depending on the degree of steatosis and individual center protocol.

4. There are other situations where pre-donation liver biopsy may be considered but will depend on individual center policy on suitable donors.

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