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The WCC Note™

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FATTY LIVER: The Epidemic Wolf in Sheep's Clothing, PART 2

Nonalcoholic fatty liver disease (NAFLD) has become the most prevalent liver disease in the United States, affecting all age groups. It encompasses a spectrum of disease, ranging from simple steatosis, steatohepatitis (NASH), fibrosis and cirrhosis, to hepatocellular carcinoma. (1) This issue of *The WCC Note* examines the imaging avenues available to diagnosis and quantify hepatic steatosis.

NAFLD and Ultrasound

What does recent literature report about ultrasound imaging of hepatic steatosis?

1. The gray scale findings include the following:
   a. The diagnosis of fatty liver can be made if:
      i. The liver is more echogenic than the renal cortex and spleen.
      ii. Ultrasound wave attenuation is present.
      iii. The diaphragm loses definition.
      iv. The intrahepatic architecture has poor delineation.
      v. There should be more than just one or two of the above present. (2)
   b. A 2008 review reported ultrasound sensitivity ranged 67-84% and specificity 77-100% for severe fatty liver (more than 30% fat by weight). It has been reported as poor at diagnosing lesser degrees of steatosis. (3)
   c. Subjective visual assessment of fatty liver at ultrasound has marked observer variability. (4)
   d. A 2009 study reported that a hepatorenal sonographic index of 1.49 (the ratio between the mean brightness levels in a region of interest in the liver and spleen) predicted steatosis of >5% with a sensitivity of 90%, specificity 90%. Steatosis of >60% was reported at an index of 2.23 (sensitivity 90%; specificity 93%). (5)

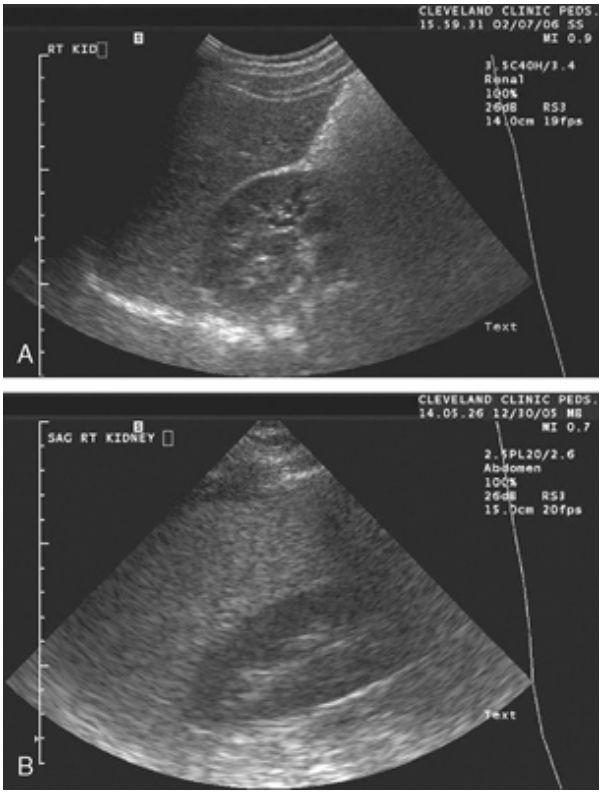

Figure 1: Sonographic features of normal liver (A) show same echogenicity as the kidney while fatty liver (B) shows increased echogenicity compared with the kidney. (34)

2. Elastography
   a. A significant positive correlation was reported between median acoustic radiation force impulse elastography (ARFI) and liver fibrosis in patients with NAFLD. (6)

NAFLD and CT

What are some updates on CT of hepatic steatosis?

1. Hepatic steatosis can be diagnosed on CT if:
    a. Noncontrast:
        i. Liver attenuation is at least 10 Hounsfield units (HU) less than the spleen.
        ii. The liver attenuation is <48 HU (7, 8, 9); or <40 HU when lipid is about 30%. (9,10)
    b. With contrast:
        i. The comparison of the liver and spleen HU is not as reliable. (2)
        ii. Fatty liver can be diagnosed if liver attenuation is less than 40 HU. (2)
2. Then if the liver is < 40 HU, is that specific for liver steatosis?
    a. No. Ischemic or mucinous metastases, or abscesses can have this attenuation. Clinical, laboratory, and other imaging features need consideration. (2)
3. Lipid quantification can be performed by the following methods:
    a. Hepatic attenuation measurement
        i. A value of 40 HU is reported to represent fatty change of approximately 30%. (9, 10)
    b. Hepatic attenuation index
        i. A ratio of hepatic HU to splenic HU less than 0.8 is reported as highly specific for moderate to severe (>30%) macrovesicular steatosis. (11, 9)
    c. Hepatic attenuation difference at dual-energy CT
        i. Ma *et al* note, in review, that while there is a paucity of literature to validate its use, an increase in fatty content associates with decreased HU at low energy; when the energy level increases, the fat attenuation increases. (9)
4. Unenhanced CT studies have reported:
    a. Visual grading and liver attenuation index were shown reliable and similarly accurate for diagnosis of 30% or higher macrovesicular steatosis in living hepatic donor candidates. (12)
    b. Moderate to severe macrovesicular steatosis (i.e. >30%) can be accurately diagnosed in the living hepatic donor, avoiding biopsy, but biopsy is still needed if the CT calculates <30% fat. Coexistent fatty liver and hemosiderin or occult liver disease would be possible. (13, 14, 15)
    c. Low dose unenhanced CT detected hepatic steatosis in asymptomatic patients, while clinical risk factor profiles proved unreliable. (16)

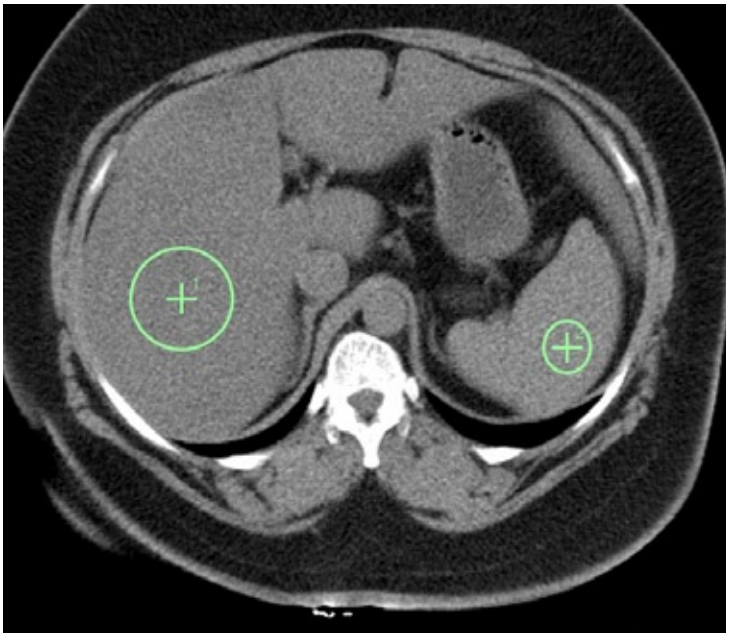

Figure 2: CT without contrast demonstrates liver 41 HU, spleen 56 HU.

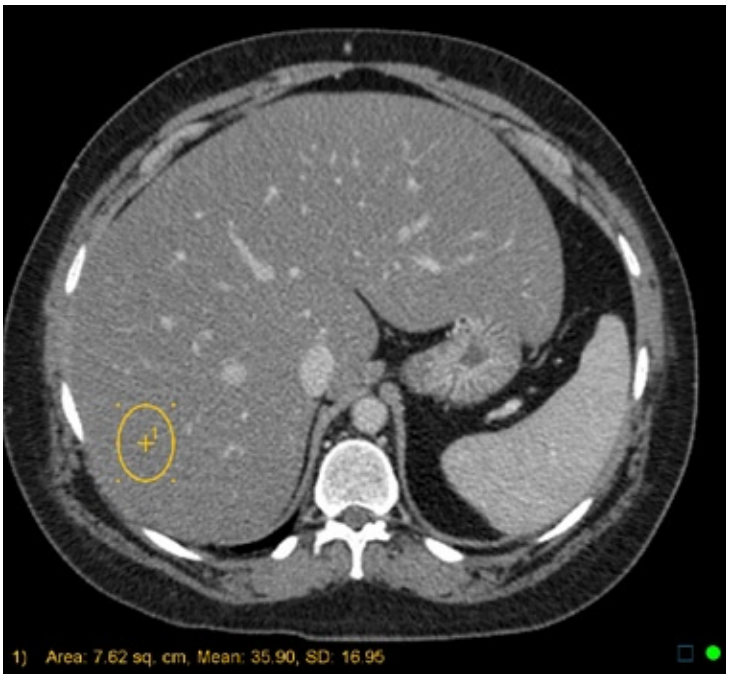

Figure 3: Liver CT with contrast in 33-year-old female demonstrates liver attenuation 36 HU.

NAFLD and MRI

What MRI methods are used to evaluate hepatic steatosis?

1. Spectroscopy
    a. This technique uses the frequency position along the x-axis to separate and characterize chemicals within voxels. (17)
    b. Localized or single-voxel MRI. Sequences include:
        i. Point-resolved spectroscopy (PRESS)
        ii. Stimulated echo acquisition mode (STEAM)
        iii. A reconfigured STEAM sequence has been reported with breath-hold acquisition of T2-corrected lipid measurement. (18)
        iv. A disadvantage is that a large, single voxel is studied. (19)
    c. Spectroscopy shows good correlation to hepatic lipid content, sensitive to as little as 0.5% lipid change, and potentially useful for therapy assessment, as reviewed by Lall *et al.* (3)
    d. The summation of individual lipid peaks calculates the total liver triglyceride content. (9)
2. Chemical shift imaging: Fat and water protons precess at different frequencies in a magnetic field. Exploiting this allows for detection and quantification of fatty infiltration. Multiple sequences have been developed on this basis. These are:
    a. Two-point Dixon MRI
        i. This technique offsets the rephrasing pulse in a spin echo (SE) sequence to create out-of-phase images, with the unmodified SE images used as in-phase. Summation and subtraction of these images yields water-only and fat-only images to quantify fat, but magnetic field inhomogeneity and longer scan times limit its use (9)
        ii. A recent study at 3T reported a 2D decomposition technique to identify distinct in-phase/opposed-phase and fat/water ratios for in vitro steatosis, iron overload, and combined disease. (20)
    b. Three-point Dixon MRI
        i. Developed to overcome the field inhomogeneity, it uses a third image with phase correction but increases scan time. (9)
    c. Modified Dixon
        i. When fast gradient echo (GRE) was developed, this method used shorter TEs and TRs to decrease scan time and allow breath hold images.
        ii. As reviewed by Ma *et al*, it can detect mild hepatic fat of 10% or more. (9)
    d. Triple-echo chemical shift GRE
        i. This breath-hold low flip angle technique with correction for T2* was reported to accurately quantify hepatic fat. (21)

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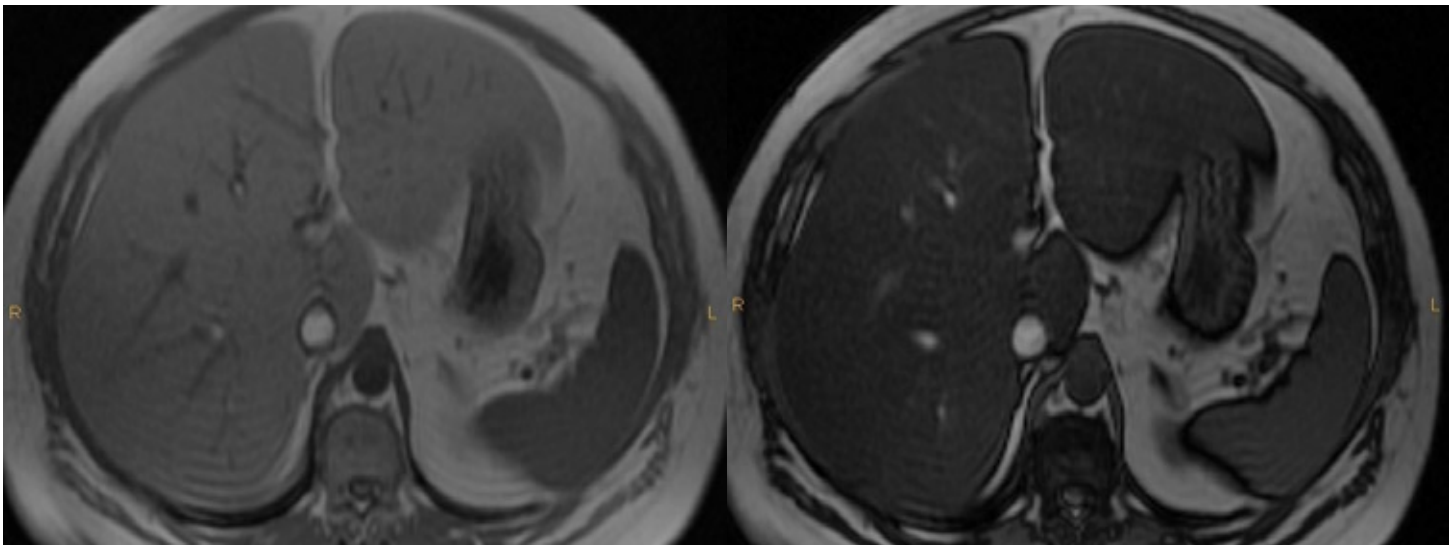

Figure 4: T1 in-phase MRI (left) and T1 out-of-phase MRI (right) shows liver signal loss on out-of-phase image (same patient as figure 3).

e. Opposed-phase T1
    i. When fat and water proton magnetization are in phase, their signal is additive. When out-of-phase, signal intensity decreases.
    ii. Dual echo fast GRE sequences decrease scan time, allow breath hold imaging, and minimize T2* when shorter TEs are used.
    iii. Opposed-phase T1-weighted images showed signal intensity loss that could be used to grade the severity of liver steatosis. (22)
    iv. A relative signal decrease of less than 20% allowed correct prediction of liver donation appropriateness in 53 of 57 patients. (23)
    v. Using MR spectroscopy as the reference standard, in- and out-of-phase imaging rapidly estimated liver fat content. A cutoff value of 5.1% discriminated between normal and elevated liver fat. (24)
    vi. Potential pitfalls include:
        1. The presence of liver iron, which can cause signal intensity loss on in-phase images. (25)
        2. Fat fractions >50%, which cannot be reliably assessed (26)
        3. Fat is spectrally complex. (26)

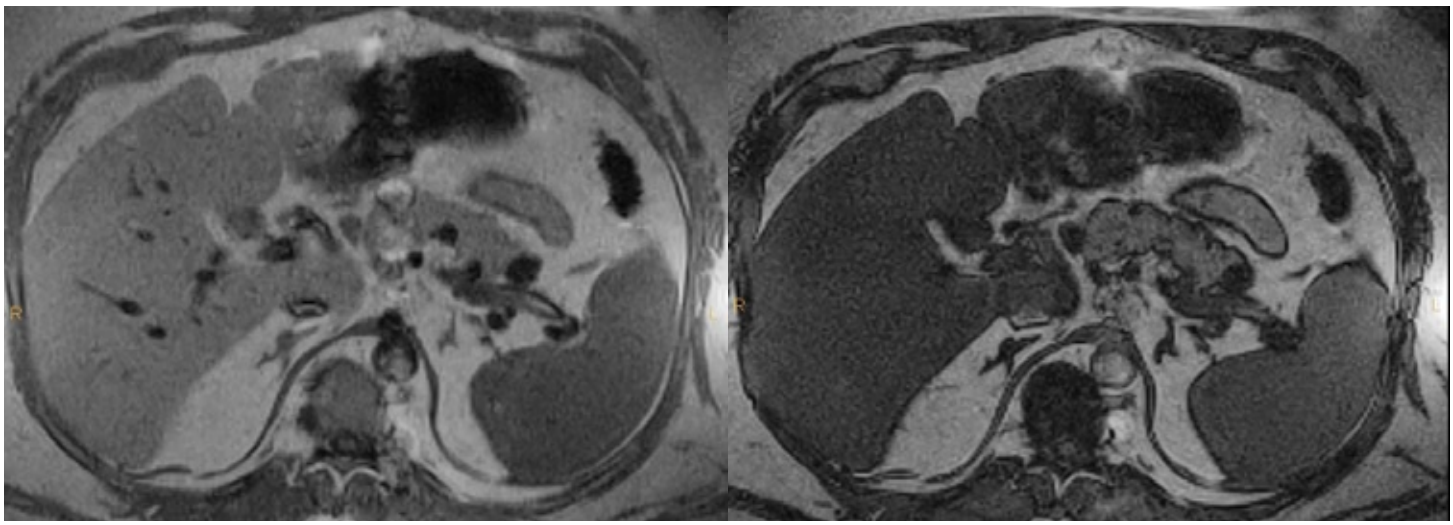

Figure 5: T1 in-phase MRI (left) and T1 out-of-phase MRI (right) of 55-year-old male shows diffuse liver signal loss on out-of-phase image.

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3. MR elastography
    a. This technique employs three phases. Mechanical waves are generated in tissue. The micron-level displacements are imaged using motion-sensitizing gradients. Wave images are processed to generate quantitative maps. (26)
    b. MR 7T elastography detected early steatohepatitis in rats by showing increased elasticity. (27, 28)
4. Low-flip-angle multiecho GRE
    a. This is reported to provide high diagnostic and fat-grading accuracy in NAFLD. (29)
    b. According to O'Regan *et al.*, it can provide fat measurement without acquiring a separate T2* map (unlike dual echo) and correlates highly with T2-corrected proton MR spectroscopy. (30)
5. Fast spin echo (FSE)
    a. T2-weighted fat saturated FSE images are compared to T2-weighted non-fat- saturated FSE images. A decrease in signal intensity on the fat-saturated images suggests fatty infiltration.
    b. This method avoids the T2* effect signal loss of liver iron in the cirrhotic patient, which can be problematic in GRE sequences. (31, 9)

Hepatic Fat Deposition

What are the patterns of hepatic fat deposition?

1. Diffuse fatty infiltration is most common. (2)
2. Focal deposition or diffuse fatty infiltration with focal sparing shows:
    a. No mass effect,
    b. Geographic shape,
    c. Poorly defined margins,
    d. Positioning adjacent to the porta hepatis, gallbladder fossa, ligamentum venosum, or falciform ligament (perhaps because of variant venous circulation), and
    e. Contrast enhancement similar to or less than normal liver. (2)
3. Multifocal deposition:
    a. Is an uncommon pattern with multiple fat foci in atypical locations,
    b. May be round or oval,
    c. Is a difficult diagnosis,
    d. Must have microscopic fat,
    e. Chemical shift GRE may be helpful, and
    f. May be seen with regenerative nodules in cirrhosis. (2)
4. Perivascular:
    a. Has fat halos around hepatic and/or portal veins;
    b. Has an unknown pathogenesis. (2)
5. Subcapsular:
    a. This distribution occurs in insulin-dependent diabetics on peritoneal dialysis who get insulin added to the peritoneal dialysate.
    b. The etiology is thought to be due to direct exposure of that region to a higher concentration of insulin. (2)
6. Patients with fatty liver and concomitant focal liver lesions may display peritumoral sparing of the fat, leading to atypical imaging appearances. (32)

TUMORS and Microscopic Fat

What tumors are pitfalls and can contain microscopic fat?

1. Hepatic adenomas may contain microscopic fat.
2. Hepatocellular carcinomas, angiomyolipoma, and focal nodular hyperplasia may contain microscopic fat and soft tissue. (2, 33)

CONCLUSION

Conclusion: **Noncontrast CT can accurately diagnose moderate to severe hepatic steatosis (>30%) but is not accurate at lower levels. MRI techniques to detect and quantify hepatic steatosis currently emphasize chemical shift imaging, with spectroscopy as the gold standard. Ultrasound suffers from subjectivity and inability to diagnose lesser degrees of hepatic fat, though a recent study of the hepatorenal index was encouraging.** ■

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