Supplementary Data 1. Details of imaging examinations.

Computed tomography Protocol and Liver Fat Measurement

The routine four-phase liver computed tomography (CT) protocol of our institution was obtained using the following parameters: slice thickness of 2.5–3.0 mm; reconstruction interval of 2.0–3.0 mm; rotation time of 0.5–0.75 seconds; peak voltage of 100–120 kVp; and tube current of 150–250 mAs. Before the injection of contrast media, unenhanced images were obtained. For the assessment of hepatic steatosis (HS), three 1.5 cm square regions of interest (ROIs) were manually placed in the liver on the unenhanced CT images by a board-certified radiologist (J.S.B.) to measure the hepatic attenuation. Three ROIs were placed at different sites avoiding large vessels in the right lobe of the liver between hepatic segments V, VI, VII, and VIII that were defined according to the Couinaud classification system (Fig. 2A). The measured Hounsfield units of three ROIs were averaged to yield the hepatic attenuation. Splenic attenuation was measured by averaging the three Hounsfield units measured by placing three ROIs at three different sections. Thereafter, the CT index of HS was calculated as hepatic attenuation minus splenic attenuation.

Magnetic resonance imaging Protocol and Liver Fat Measurement

All patients underwent chemical shift 3-D spoiled gradient-recalled echo sequences for proton density fat fraction (PDFF) measurements using 3.0-T magnetic resonance systems from various manufacturers. PDFF is calculated as the ratio of MRI-visible fat protons to the sum of MRI-visible fat and bulk (free) water protons [1]. For PDFF measurements, a complex-based chemical shift-encoded water-fat reconstruction technique was used. The magnetic resonance imaging (MRI)-PDFF sequences used six echoes, T2* correction calculated from signal decay, a low flip angle to minimize the T1 bias between fat and water and a multipeak fat model [2]. PDFF maps were generated from corrected water and fat images as fat signal intensities/(fat signal intensities+water signal intensities) [1]. PDFF and T2* maps were automatically generated by each vendor's algorithm, and the PDFF map was used for measurement.

The radiologist (J.S.B.) manually placed a 1 cm circular ROIs in each of the nine Couinaud liver segments on the water-only images that lacks quantitative information to avoid potential information bias. Each ROI was placed near the center of each segment, while taking care to exclude major vessels, the liver edge and artifacts. Thereafter, the ROIs were pasted onto the identical locations on the PDFF maps (Fig. 2B). The PDFF in each of the nine ROIs was averaged to yield a single hepatic PDFF value for each patient. There was no substantial artifact that disturbed ROI placement.

Controlled Attenuation Parameter Examination

The controlled attenuation parameter (CAP) was measured by using a transient elastography (TE) device (Fibroscan, Echosens, Paris, France). After fasting for at least three hours, TE was performed while the patient was lying with maximum abduction of his/her right arm. A 3.5-MHz M probe or a 2.5-MHz XL probe depending on the skin thickness was placed at the ninth to 10th intercostal spaces over the right lobe of the liver at the level of the mid-axillary line [3]. TE examinations were performed by one of several experienced operators who had experience with more than 100 TE scans. TE examinations were performed until a minimum of 10 valid liver stiffnesses were obtained. CAP was obtained only when the liver stiffness measurement was valid. A TE examination was considered reliable if the interquartile range to median ratio of liver stiffness <0.3 [4]. The median CAP value (dB/m) obtained from reliable TE examinations was used for analysis.

Grayscale Ultrasound Examination

After optimizing technical parameters such as gain adjustment, placement of focal zone and the optimum location of the transducer for each patient, the echogenicity of hepatic parenchyma was assessed and compared to the renal cortex at the mid-axillary line (Fig. 2D). Increased hepatorenal index indicated mild steatosis, whereas isoechogenicity of hepatic parenchyma to that of right kidney was considered no HS. If there was blurring of portal vein wall, it was regarded as moderate steatosis. Marked attenuation of US beam that resulted in poor visualization of the diaphragm deep to the liver was considered severe steatosis.

Attenuation Imaging Examination

The sampling box was carefully positioned on the center of the image to avoid the rib shadow. Structures such as large vessels, ducts, cysts, calcifications, etc. were automatically excluded on the sampling box by the removal filtering technique because of significant errors in the attenuation calculation. The degree of attenuation was color-coded and demonstrated in the sampling box. Attenuation imaging (ATI) mapping was also used in the uniform attenuation for a high-quality B-mode signal intensity. Thereafter, a 2×4 cm or more sized fan-shaped regions of interest (ROI) for measurement was placed within the sampling box. The measurement ROI box was carefully placed in the middle portion of the sampling box, generally 4–9 cm from skin line, avoiding the orange-colored area on the upper part of the ROI (subcapsular area) and the dark blue colored or the vacant area at the bottom of the ROI (weak signal and high noise level with significant errors). The attenuation coefficient (AC) can be obtained by removing the influence of the gain profile and beam profile on the observed B-mode signal

intensity. The remaining pure signal intensity change within the ROI is displayed as a line profile in the upper right corner. The sample points on the line profile are acquired by averaging the signal intensity within the ROI along the same depth. The slope of the line profile corresponds to the AC, which is dB/cm/MHz and displayed on the lower left corner (Fig. 2E). Additionally, the goodness of fit of the line profile was displayed as an R^2 value next to the AC, which indicates the reliability of the result. The R^2 values were categorized into poor (R^2<0.80), good (0.80≤R^2<0.90), and excellent (R^2>0.90), which were displayed in red, yellow, and white, respectively. ACs with R^2 ≥0.90 were regarded as valid measurements in our study.

Comparison of Imaging Tools for Detecting HS ≥10%

For the detection of HS ≥10%, the results were similar to those for the detection of HS ≥5%. The area under the curve (AUC) of MRI-PDFF (0.945; 95% confidence interval [CI], 0.887 to 0.978) was significantly higher than that of CT (0.829; 95% CI, 0.750 to 0.892), CAP (0.856; 95% CI, 0.781 to 0.914), and grayscale ultrasonography (0.807; 95% CI, 0.725 to 0.873) (P<0.05) (Supplementary Table 2, Supplementary Fig. 1). The AUC of ATI (0.905; 95% CI, 0.838 to 0.951) tended to be inferior to that of MRI-PDFF (P=0.199) but tended to be superior to that of CT (P=0.058) and was not significantly different from the value of CAP (P=0.284). Compared with grayscale US, ATI was significantly more accurate (P=0.013). The sensitivity of MRI-PDFF was the highest (97.7%). In terms of specificity, the value of grayscale US was the lowest (72.4%), while the values of the other tools were similar (85.5%–86.8%). The detailed results of the pairwise comparisons among the imaging tools for sensitivity and specificity for detecting HS ≥10% are presented in Supplementary Table 5.

References

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