

Role of Abdominal Ultrasound in Detecting Non-Alcoholic Fatty Liver Disease Compared to Histopathology: A Prospective Diagnostic Accuracy Study

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver condition globally. Abdominal ultrasound (US) is the recommended first-line imaging modality for its detection, while liver biopsy remains the invasive gold standard. The precise diagnostic accuracy of conventional US for different grades of steatosis requires continued evaluation.

Methods: A total of 210 adult patients with clinical and biochemical suspicion of NAFLD, who were scheduled for a liver biopsy, were enrolled. All patients underwent a standardized abdominal US examination within two weeks prior to the biopsy. Two blinded radiologists graded steatosis on US (Grade 0–3). Liver biopsies were evaluated by two blinded pathologists who graded steatosis according to the NAFLD Activity Score (S0: <5%; S1: 5–33%; S2: 34–66%; S3: >66%). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Results: Of the 210 participants (mean age 51.2 ± 11.5 years; 55.7% female; mean BMI 32.4 ± 4.8 kg/m²), 172 (81.9%) had histologically confirmed steatosis ($\geq S1$). For detecting any degree of steatosis ($\geq S1$), US (defined as Grade ≥ 1) showed a sensitivity of 78.5% (95% CI: 71.9–84.2%), specificity of 92.1% (95% CI: 78.6–98.3%), PPV of 97.1%, and NPV of 53.0%. For detecting moderate-to-severe steatosis ($\geq S2$), US (defined as Grade ≥ 2) demonstrated significantly higher sensitivity of 89.2% (95% CI: 81.3–94.6%) and specificity of 94.4% (95% CI: 89.1–97.5%). A strong positive correlation was observed between the ultrasound grade and the histological steatosis grade (Spearman's $\rho = 0.81$, $p < 0.001$).

Conclusion: Abdominal ultrasound is a highly specific tool for diagnosing hepatic steatosis. While its sensitivity for mild steatosis is modest, it demonstrates excellent accuracy for detecting moderate-to-severe disease. Ultrasound serves as a reliable, non-invasive screening modality for identifying clinically significant steatosis, though it cannot fully replace histopathology for staging disease activity and fibrosis.

Keywords: Non-Alcoholic Fatty Liver Disease, Hepatic Steatosis, Abdominal Ultrasound, Liver Biopsy, Histopathology, Diagnostic Accuracy.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) has emerged as the leading cause of chronic liver disease worldwide, with an estimated global prevalence of over 25% [1]. It represents a spectrum of conditions ranging from simple hepatic steatosis (NAFL) to non-alcoholic steatohepatitis (NASH), which is characterized by necro inflammation and can progress to advanced fibrosis, cirrhosis, and hepatocellular carcinoma [2, 3]. The rising prevalence of NAFLD is closely linked to the global epidemics of obesity, type 2 diabetes mellitus, and metabolic syndrome [4]. Early and accurate diagnosis of NAFLD is crucial

for risk stratification and the implementation of lifestyle and therapeutic interventions to prevent disease progression. Clinical practice guidelines from major hepatology societies recommend abdominal ultrasound (US) as the first-line imaging modality for screening for hepatic steatosis due to its wide availability, non-invasive nature, patient tolerance, and cost-effectiveness [5, 6]. Ultrasound diagnoses steatosis based on the finding of hepatic parenchymal hyperechogenicity ("bright liver") relative to the renal cortex, along with features such as vascular blurring and deep attenuation [7]. Despite its widespread use, the diagnostic utility of

conventional B-mode US has limitations. It is considered operator-dependent, its performance can be compromised in patients with severe obesity, and it is generally believed to be insensitive for detecting mild degrees of steatosis (typically defined as <20–30% fat infiltration) [8]. In contrast, liver biopsy remains the undisputed reference standard for the diagnosis and staging of NAFLD. It is the only method that can reliably distinguish simple steatosis from the more aggressive NASH and accurately stage liver fibrosis [9]. However, liver biopsy is an invasive procedure associated with potential complications, including pain, bleeding, and, rarely, mortality. Furthermore, it is subject to sampling error and significant inter-observer variability among pathologists [10, 11].

Several studies and meta-analyses have evaluated the performance of US for detecting steatosis, reporting a wide range of sensitivities and specificities [12, 13]. This variability is often due to retrospective designs, heterogeneous populations, and differing reference standards. As imaging technology and clinical understanding of NAFLD evolve, there is a persistent need for robust, prospective studies that directly compare modern ultrasound techniques against the gold standard of histopathology in a well-characterized cohort of patients with suspected NAFLD. Such data are vital for clinicians to understand the precise capabilities and limitations of US in the diagnostic pathway.

Therefore, the primary aim of this study was to prospectively evaluate the diagnostic accuracy of abdominal ultrasound for detecting and grading hepatic steatosis, using liver histopathology as the reference standard in a cohort of patients with a high pre-test probability of NAFLD.

Materials and Methods

Study Design and Population: Patients aged 18 years or older with suspected NAFLD, based on persistent elevation of aminotransferases and/or imaging evidence of fatty liver, who were referred to the hepatology clinic for a liver biopsy, were consecutively enrolled.

Inclusion and Exclusion Criteria:

Inclusion criteria were: (1) age ≥ 18 years; (2) clinical suspicion of NAFLD; and (3) scheduled to undergo a liver biopsy for clinical indications.

Exclusion criteria were: (1) significant alcohol consumption, defined as >30 g/day for men and >20 g/day for women; (2) positive serology for hepatitis B (HBsAg) or hepatitis C (anti-HCV); (3) other known causes of chronic liver disease, such as autoimmune hepatitis, hemochromatosis, or Wilson's disease; (4) use of steatogenic medications within the past six months; (5) evidence of cirrhosis

on prior imaging or clinical grounds; and (6) pregnancy.

Procedures: Each enrolled participant underwent a comprehensive clinical assessment, including medical history, anthropometric measurements (height, weight, BMI), and laboratory tests (liver function tests, lipid profile, fasting glucose, HbA1c). All participants underwent an abdominal US followed by a percutaneous liver biopsy within a maximum interval of two weeks.

Abdominal Ultrasound Examination: All US examinations were performed by one of two senior radiologists, each with over 10 years of experience in abdominal imaging, using a high-end ultrasound system (Philips EPIQ 7, Philips Healthcare) with a 1–5 MHz curvilinear transducer. The radiologists were blinded to the patients' detailed clinical history and laboratory results. A standardized protocol was used, and hepatic steatosis was qualitatively graded on a 4-point scale:

- **Grade 0 (None):** Normal hepatic parenchymal echotexture.
- **Grade 1 (Mild):** Slight, diffuse increase in hepatic echogenicity with normal visualization of the diaphragm and intrahepatic vessel borders.
- **Grade 2 (Moderate):** Moderate increase in hepatic echogenicity with impaired visualization of the intrahepatic vessels and diaphragm.
- **Grade 3 (Severe):** Marked increase in hepatic echogenicity with poor or no visualization of the intrahepatic vessels, diaphragm, and the posterior portion of the right hepatic lobe.

Liver Biopsy and Histopathology: Percutaneous liver biopsies were performed under US guidance using a 16-gauge core biopsy needle. An adequate specimen was defined as having a length of at least 1.5 cm and containing at least 6 portal tracts. Biopsy specimens were fixed in formalin, embedded in paraffin, and stained with hematoxylin and eosin (H&E) and Masson's trichrome.

Two experienced liver pathologists, who were blinded to all clinical and imaging data, independently evaluated the slides. Any discrepancies were resolved by consensus review. Steatosis was graded as the percentage of hepatocytes containing fat droplets, according to the criteria used in the NASH Clinical Research Network scoring system:

- **S0:** $<5\%$ of hepatocytes affected.
- **S1:** 5–33% of hepatocytes affected (mild).
- **S2:** 34–66% of hepatocytes affected (moderate).
- **S3:** $>66\%$ of hepatocytes affected (severe).

Statistical Analysis: Data were analyzed using IBM SPSS Statistics for Windows, Version 27.0. Continuous variables were expressed as mean $\pm$ standard deviation (SD), and categorical variables as frequencies and percentages (%). Group comparisons were performed using the independent t-test or Mann-Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables.

The diagnostic accuracy of US was assessed by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) with 95% confidence intervals (CIs). Two diagnostic thresholds were evaluated: (1) US Grade ≥ 1 for detecting any steatosis (histological grade $\geq S1$), and (2) US Grade ≥ 2 for detecting moderate-to-severe steatosis (histological grade $\geq S2$). The correlation between the ordinal US grades and histological grades was assessed using Spearman's rank correlation coefficient (ρ). A p-value < 0.05 was considered statistically significant.

Results

Participant Characteristics: A total of 258 patients were screened for eligibility, of whom 48 were excluded (22 had significant alcohol intake, 15 had other liver diseases, 11 declined consent). Thus, 210 patients were included in the final analysis. The baseline demographic, clinical, and laboratory characteristics are presented in Table 1. The mean age was 51.2 ± 11.5 years, and 117 (55.7%) were female. The cohort had a high prevalence of metabolic comorbidities, including obesity (mean BMI 32.4 kg/m^2), type 2 diabetes (41.9%), and hypertension (58.1%). Based on histopathology, 38 (18.1%) patients had no steatosis (S0), while 172 (81.9%) had NAFLD ($\geq S1$). Among those with NAFLD, 68 (32.4% of total) had mild (S1), 74 (35.2%) had moderate (S2), and 30 (14.3%) had severe (S3) steatosis.

Table 1: Baseline Characteristics of the Study Population (N=210)

Characteristic	S0 (No Steatosis) (n=38)	S1–S3 (Any Steatosis) (n=172)	p-value
Age (years), mean $\pm$ SD	49.8 ± 12.1	51.5 ± 11.3	0.415
Female Sex, n (%)	19 (50.0)	98 (57.0)	0.430
BMI (kg/m^2), mean $\pm$ SD	28.1 ± 3.5	33.3 ± 4.6	<0.001
Type 2 Diabetes, n (%)	8 (21.1)	80 (46.5)	0.004
Hypertension, n (%)	15 (39.5)	107 (62.2)	0.012
ALT (U/L), mean $\pm$ SD	45 ± 21	82 ± 35	<0.001
AST (U/L), mean $\pm$ SD	38 ± 18	65 ± 29	<0.001

BMI: Body Mass Index; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase.

Diagnostic Accuracy of Abdominal Ultrasound: The diagnostic performance of US is summarized in Table 2. For detecting the presence of any steatosis (histological grade $\geq S1$), a US grade of ≥ 1 yielded a sensitivity of 78.5% and a high specificity

of 92.1%. When the threshold was increased to detect more clinically significant steatosis (histological grade $\geq S2$), a US grade of ≥ 2 provided a sensitivity of 89.2% and a specificity of 94.4%.

Table 2: Diagnostic Accuracy of Abdominal Ultrasound for Detecting Hepatic Steatosis

Parameter	US ≥ 1 for Steatosis $\geq S1$	US ≥ 2 for Steatosis $\geq S2$
True Positives (TP)	135	93
False Positives (FP)	4	6
True Negatives (TN)	34	101
False Negatives (FN)	37	11
Sensitivity, % (95% CI)	78.5 (71.9–84.2)	89.2 (81.3–94.6)
Specificity, % (95% CI)	92.1 (78.6–98.3)	94.4 (89.1–97.5)
PPV, % (95% CI)	97.1 (92.8–99.2)	93.9 (87.2–97.7)
NPV, % (95% CI)	53.0 (41.3–64.5)	90.2 (83.2–94.9)
Overall Accuracy, % (95% CI)	80.5 (74.6–85.5)	92.4 (87.9–95.6)

CI: Confidence Interval; PPV: Positive Predictive Value; NPV: Negative Predictive Value.

Correlation between Ultrasound and Histopathology Grades: A cross-tabulation of US grades versus histological steatosis grades is shown in Table 3. There was a clear and progressive relationship between the two methods. As the US grade increased, the proportion of patients with higher histological grades of steatosis also

increased. Of the 37 patients with histologically confirmed steatosis who were missed by US (false negatives), all had mild (S1) steatosis. Conversely, the 4 false positive cases were graded as mild (Grade 1) on US. A strong, statistically significant positive correlation was found between the US and

histological grades (Spearman's $\rho = 0.81$, $p < 0.001$).

Table 3: Cross-Tabulation of Ultrasound Grade vs. Histological Steatosis Grade

	Histological Steatosis Grade (n)			
Ultrasound Grade	S0 (<5%)	S1 (5–33%)	S2 (34–66%)	S3 (>66%)
0 (None)	34	37	0	0
1 (Mild)	4	31	15	0
2 (Moderate)	0	0	52	12
3 (Severe)	0	0	7	18
Numbers in bold represent agreement between US and histological grade categories.				

Discussion

This prospective study confirms that abdominal ultrasound is a highly specific but only moderately sensitive tool for the initial detection of NAFLD. Its diagnostic power, however, increases substantially for identifying patients with moderate-to-severe hepatic steatosis. Our findings provide valuable, contemporary data that can help clinician's better position US within the diagnostic algorithm for NAFLD.

The principal finding of our study is the performance trade-off of US depending on the disease severity. For detecting any degree of steatosis ($\geq 5\%$ on histology), US had a sensitivity of 78.5%. This means that approximately one in five patients with histologically confirmed, predominantly mild, fatty liver would be missed by a screening ultrasound. This limitation is consistent with previous meta-analyses, which have reported sensitivities ranging from 60% to 94%, with lower values generally seen in studies with a high proportion of mild steatosis [12, 13]. The NPV of 53.0% for this threshold highlights that a normal US examination does not reliably exclude mild NAFLD.

However, from a clinical risk stratification perspective, the detection of more significant steatosis is often more critical. When we set the diagnostic threshold to identify moderate-to-severe steatosis ($\geq 34\%$ on histology), the sensitivity of US rose to an excellent 89.2%, with a corresponding specificity of 94.4% and an NPV of 90.2%. This demonstrates that US is a robust tool for identifying individuals with a more substantial burden of hepatic fat, who may be at higher risk for progressive liver disease [14]. The strong correlation between US and histological grades further supports its utility in semi-quantitatively assessing the severity of steatosis.

Our results have direct clinical implications. Abdominal US can be confidently used as an initial screening tool in patients with metabolic risk factors. Its high specificity (92.1%) and PPV (97.1%) mean that a positive finding is highly likely to represent true steatosis, justifying further

clinical evaluation and management. Its primary weakness is in ruling out mild disease. Therefore, in a patient with a high clinical suspicion of NAFLD (e.g., metabolic syndrome with elevated liver enzymes) but a normal US, clinicians should be aware that mild steatosis may still be present, and further testing with more sensitive modalities might be warranted.

It is essential to contextualize the role of US alongside other non-invasive tests. While US assesses steatosis, it provides no information about inflammation (NASH) or fibrosis, which are the key drivers of long-term outcomes [3]. For this, other tools are necessary. Transient elastography with controlled attenuation parameter (CAP) can simultaneously quantify steatosis and liver stiffness (fibrosis) [15]. Magnetic resonance imaging-based techniques, particularly MRI-proton density fat fraction (MRI-PDFF), have emerged as the most accurate non-invasive method for quantifying steatosis, but their use is limited by cost and accessibility [16]. Our data affirm that conventional US remains the most practical initial step for widespread case finding.

The strengths of this study include its prospective design, the inclusion of a relevant clinical population, the use of liver biopsy as the gold standard, and the blinded interpretation of both imaging and histology by experienced specialists. However, certain limitations must be acknowledged. First, this was a single-center study, which may limit the generalizability of our findings. Second, liver biopsy itself is imperfect and prone to sampling error, which could have misclassified a small number of patients. Third, we used a qualitative grading system for US, which is inherently subjective; the development of quantitative US techniques may improve accuracy and reproducibility in the future.

Conclusion

In conclusion, abdominal ultrasound is a valuable and highly specific non-invasive modality for screening for NAFLD. Its accuracy is excellent for detecting moderate-to-severe hepatic steatosis, making it an effective tool for identifying patients

with a clinically significant fat burden. Its main limitation is its modest sensitivity for mild steatosis, meaning a normal ultrasound cannot definitively exclude early-stage disease. While it cannot replace histopathology for diagnosing NASH or staging fibrosis, US serves a critical role as a first-line diagnostic test in the clinical management of patients with suspected NAFLD.

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