INPLASY

INPLASY202590124

doi: 10.37766/inplasy2025.9.0124

Received: 30 September 2025

Published: 30 September 2025

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Quantitative ultrasound for hepatic steatosis: A systematic review highlighting the diagnostic performance of Ultrasound-Derived Fat Fraction

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ADMINISTRATIVE INFORMATION

Support - None received.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202590124

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 September 2025 and was last updated on 30 September 2025.

INTRODUCTION

Review question / Objective Research Question (PICO format) Population (P): Adult patients undergoing liver fat quantification with suspected or confirmed metabolic dysfunction-associated steatotic liver disease (MASLD). Intervention (I): Ultrasound-Derived Fat Fraction (UDFF). Comparator (C): MRI Proton Density Fat Fraction (MRI-PDFF) as the non-invasive reference standard; secondarily, comparisons with liver biopsy, Controlled Attenuation Parameter (CAP), and other quantitative ultrasound modalities. Outcomes (O): Diagnostic accuracy (sensitivity, specificity, AUC), reproducibility (inter- and intra-observer ICC), feasibility, and proposed threshold cut-off values for steatosis grading.

Rationale MASLD is the most common chronic liver disease, requiring accurate non-invasive diagnosis. MRI-PDFF is the gold standard but limited by cost and availability, while B-mode ultrasound lacks sensitivity. UDFF is a novel quantitative technique with potential for routine clinical use; this review evaluates its diagnostic accuracy, reproducibility, and optimal cut-offs.

Condition being studied Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as NAFLD/MAFLD, is the most prevalent chronic liver disease worldwide. It is characterized by excessive hepatic fat accumulation (≥5% of hepatocytes) and is strongly associated with obesity, type 2 diabetes, dyslipidemia, and cardiovascular risk. Accurate non-invasive quantification of liver steatosis is essential for diagnosis, risk stratification, and monitoring.

METHODS

Search strategy Databases: PubMed and Scopus, covering studies published from January 2014 to

April 2025. Keywords: “Ultrasound-Derived Fat Fraction (UDFF)” OR “Quantitative ultrasound” OR “attenuation coefficient” OR “backscatter coefficient” AND “Proton Density Fat Fraction” OR “MRI-PDFF” OR “MRI liver fat quantification” OR “magnetic resonance imaging PDFF”. Boolean operators (AND, OR) and MeSH terms were applied where applicable. PRISMA 2020 guidelines were followed.

Participant or population Adults (≥18 years) undergoing liver fat quantification with suspected or confirmed metabolic dysfunction-associated steatotic liver disease (MASLD) or at risk due to metabolic factors (e.g., obesity, type 2 diabetes, dyslipidemia, hypertension). Studies exclusively involving pediatric populations are excluded.

Intervention Ultrasound-Derived Fat Fraction (UDFF), a quantitative ultrasound technique that estimates hepatic fat content by combining the attenuation coefficient and backscatter coefficient, expressed as a percentage of liver fat fraction.

Comparator Magnetic Resonance Imaging Proton Density Fat Fraction (MRI-PDFF) as the primary non-invasive reference standard. Secondary comparators include liver biopsy, Controlled Attenuation Parameter (CAP), and other quantitative ultrasound techniques (e.g., UGAP, USFF).

Study designs to be included Prospective and retrospective observational studies directly assessing Ultrasound-Derived Fat Fraction (UDFF) for liver fat quantification. Priority is given to prospective studies using MRI-PDFF as the reference standard. Studies with liver biopsy, CAP, or other quantitative ultrasound techniques as comparators will also be considered. Randomized controlled trials are not expected in this field, and purely descriptive case reports, reviews, or conference abstracts without full data will be excluded.

Eligibility criteria Inclusion: Peer-reviewed full-text articles; studies involving adults (≥18 years); UDFF used for hepatic steatosis quantification; comparison with MRI-PDFF, liver biopsy, CAP, or other quantitative ultrasound techniques; reporting of quantitative outcomes (e.g., correlation, AUC, ICC, sensitivity/specificity, cut-off values).

Exclusion: Pediatric populations; case reports, reviews, editorials, letters, or conference abstracts without sufficient data; animal studies; studies not reporting UDFF-specific outcomes; duplicate publications of the same cohort.

Information sources Electronic databases PubMed and Scopus were systematically searched for relevant studies published between January 2014 and April 2025. Reference lists of included articles and related reviews were manually screened to identify additional eligible studies. No grey literature, conference abstracts without full data, or unpublished sources were included.

Main outcome(s) The primary outcome is the diagnostic performance of Ultrasound-Derived Fat Fraction (UDFF) compared with MRI-PDFF for detecting and grading hepatic steatosis. Effect measures include correlation coefficients (Pearson’s r, ICC), diagnostic accuracy metrics (AUC, sensitivity, specificity), and reproducibility (inter- and intra-observer agreement). Outcomes are assessed at the time of imaging, with no longitudinal follow-up.

Additional outcome(s) Proposed UDFF threshold cut-off values for mild, moderate, and severe steatosis.

Influence of cofactors such as BMI, waist circumference, visceral adipose tissue, dietary state, and probe/respiratory conditions on UDFF performance.

Comparison of UDFF with alternative modalities (CAP, UGAP, USFF, histology).

Technical feasibility, reproducibility, and inter-/intra-observer variability.

Data management Records identified from the database search were organized and screened for duplicates. Titles and abstracts were reviewed independently by two reviewers, followed by full-text assessment for eligibility. A standardized data extraction form was used to record study characteristics, imaging protocols, diagnostic performance metrics, reproducibility measures, and proposed cut-off values. Any discrepancies between reviewers were resolved through discussion, and if necessary, by consulting a third reviewer.

Quality assessment / Risk of bias analysis The methodological quality of the included studies was evaluated using the QUADAS-2 tool, covering four domains: patient selection, index test, reference standard, and flow/timing. Two reviewers performed the assessments independently, and disagreements were resolved by consensus.

Strategy of data synthesis Extracted data will be summarized in structured tables and narrative

form. Diagnostic performance metrics (AUC, sensitivity, specificity, correlation coefficients, ICC values) will be reported as provided by the original studies. Given the expected methodological heterogeneity, a formal meta-analysis will not be performed; instead, ranges and averages across studies will be presented. Subgroup synthesis will highlight differences in MRI-PDFF thresholds (≥5% vs ≥5.5%), study populations, and technical factors (e.g., ROI depth, patient positioning, probe pressure). Variability in proposed UDFF cut-off values will also be analyzed comparatively.

Subgroup analysis If data permit, subgroup analyses will be performed based on:

MRI-PDFF threshold used as reference (≥5% vs ≥5.5%).

Population characteristics (e.g., MASLD vs mixed populations; obese vs non-obese).

Technical factors (scanner manufacturer, ROI depth, body position, breath-hold technique).

Cofactors evaluated (BMI, waist circumference, visceral adipose tissue, metabolic markers).
These analyses aim to explore potential sources of heterogeneity in UDFF diagnostic performance and cut-off values.

Sensitivity analysis Sensitivity analyses will be conducted to assess the robustness of findings by:

Excluding studies not using MRI-PDFF as the reference standard.

Evaluating the impact of excluding studies with unclear or high risk of bias (based on QUADAS-2).

Comparing results when using different MRI-PDFF thresholds (≥5% vs ≥5.5%) for steatosis definition.

Language restriction No language restrictions were imposed during the initial search. However, only studies with available full texts in English were ultimately included in the review.

Country(ies) involved Greece.

Other relevant information This review followed the PRISMA 2020 guidelines for systematic reviews. No funding was received for this work. Conflicts of interest have been declared as none by all authors.

Date of searches: January 2014 – April 2025
Data extraction completed: April 2025.

Retrospective registration to inplasy

Keywords Ultrasound; UDFF; MRI-PDFF; Liver Steatosis; MASLD.

Dissemination plans The findings of this systematic review will be disseminated through publication in a peer-reviewed open access journal and presentation at relevant national and international scientific conferences in the fields of radiology, hepatology, and medical imaging. The results will also be shared with academic collaborators and, where appropriate, through institutional and professional society channels to support clinical adoption of quantitative ultrasound techniques.

Contributions of each author

Author 1 - Dimitrios Kavvadas - Conceptualization; Methodology; Formal analysis; Investigation; Data curation; Writing—original draft preparation; Project administration.
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