Radiology

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Diagnostic Accuracy of CT for the Detection of Hepatic Steatosis: A Systematic Review and Meta-Analysis

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Background: CT plays an important role in the opportunistic identification of hepatic steatosis. CT performance for steatosis detection has been inconsistent across various studies, and no clear guidelines on optimum thresholds have been established.

Purpose: To conduct a systematic review and meta-analysis to assess CT diagnostic accuracy in hepatic steatosis detection and to determine reliable cutoffs for the commonly mentioned measures in the literature.

Materials and Methods: A systematic search of the PubMed, Embase, and Scopus databases (English-language studies published from September 1977 to January 2024) was performed. Studies evaluating the diagnostic accuracy of noncontrast CT (NCCT), contrast-enhanced (CECT), and dual-energy CT (DECT) for hepatic steatosis detection were included. Reference standards included biopsy, MRI proton density fat fraction (PDFF), or NCCT. In several CECT and DECT studies, NCCT was used as the reference standard, necessitating subgroup analysis. Statistical analysis included a random-effects meta-analysis, assessment of heterogeneity with use of the I^2 statistic, and meta-regression to explore potential sources of heterogeneity. When available, mean liver attenuation, liver-spleen attenuation difference, liver to spleen attenuation ratio, and the DECT-derived fat fraction for hepatic steatosis diagnosis were assessed.

Results: Forty-two studies (14 186 participants) were included. NCCT had a sensitivity and specificity of 72% and 88%, respectively, for steatosis (>5% fat at biopsy) detection and 82% and 94% for at least moderate steatosis (over 20%–33% fat at biopsy) detection. CECT had a sensitivity and specificity of 66% and 90% for steatosis detection and 68% and 93% for at least moderate steatosis detection. DECT had a sensitivity and specificity of 85% and 88% for steatosis detection. In the subgroup analysis, the sensitivity and specificity for detecting steatosis were 80% and 99% for CECT and 84% and 93% for DECT. There was heterogeneity among studies focusing on CECT and DECT. Liver attenuation less than 40–45 HU, liver-spleen attenuation difference less than −5 to 0 HU, and liver to spleen attenuation ratio less than 0.9–1 achieved high specificity for detection of at least moderate steatosis.

Conclusion: NCCT showed high performance for detection of at least moderate steatosis.

Supplemental material is available for this article.

Hepatic steatosis is the result of the abnormal accumulation of triglycerides in hepatocytes, which can initiate a cascade of inflammatory responses, referred to as steatotic liver disease (SLD) (1,2). Metabolic dysfunction–associated SLD is the most common form of SLD in the United States and worldwide and is rapidly becoming the most common cause of chronic liver disease (3–7). It is a significant risk factor for cardiovascular disease, fibrosis, cirrhosis, liver cancer, liver failure, and death (8–16). Early detection of this condition is critical to allow early intervention and prevent complications.

Liver biopsy has traditionally been the reference standard for the diagnosis and grading of hepatic steatosis (17). More recently, MRI-based fat quantification techniques have been introduced as alternatives to biopsy (18). Specifically, the MRI proton density fat fraction (PDFF) technique has high accuracy and is strongly correlated with biopsy (19). The high cost of these methods and limited accessibility make them unsuitable as screening tools. US is considered the first-line imaging–based screening tool, given its lower cost and easier access (20). Although CT is not currently considered a screening tool for hepatic steatosis, it has an important role in opportunistic identification of hepatic steatosis because of its widespread use. A considerable number of patients with hepatic steatosis are diagnosed serendipitously during CT examinations performed for other indications (10,21).

Liver attenuation has an inverse linear relationship with the degree of steatosis (22). In noncontrast CT (NCCT), liver attenuation is dictated by the fat, water, and protein content of the liver parenchyma. In contrast-enhanced CT (CECT), the relationship is more complex because of confounding factors and the variable contribution of contrast agents to liver attenuation (23). Absolute liver attenuation, liver-spleen attenuation difference, and liver to spleen attenuation ratio have been proposed as markers of steatosis at NCCT and CECT, with variable reported performances (24). More recently, a dual-energy (DECT)–derived fat map was introduced as a novel marker of steatosis (25). CT performance for hepatic steatosis detection has been inconsistent

Abbreviations

CECT = contrast-enhanced CT, DECT = dual-energy CT, NCCT = noncontrast CT, PDFF = proton density fat fraction, SLD = steatotic liver disease

Summary

Noncontrast CT was a reliable method for detection of at least moderate hepatic steatosis (over 20%–33% fat at biopsy), with a pooled sensitivity and specificity of 82% and 94%, respectively.

Key Results

- A systematic review and meta-analysis of 15 scientific articles and 5983 patients revealed 82% sensitivity and 94% specificity of noncontrast CT for the detection of at least moderate hepatic steatosis (over 20%–33% fat at biopsy).
- Studies on the value of contrast-enhanced CT and dual-energy CT for the detection of steatosis were less common, which made it difficult to draw conclusions on the true performance of these methods.

across various studies, and no clear guidelines on optimum thresholds have been established.

The primary objective of this study was to conduct a systematic review and meta-analysis of the current literature to assess the accuracy of NCCT, CECT, and DECT in identifying at least moderate steatosis. The secondary objective was to determine reliable cutoffs for the commonly mentioned parameters in the literature.

Materials and Methods

This systematic review and meta-analysis study was exempt from the requirement for local institutional review board approval and was compliant with the Health Insurance Portability and Accountability Act. Best practices in diagnostic test accuracy systematic reviews were applied (26–28). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Individual Patient Data and of Diagnostic Test Accuracy statements were used to inform reporting (29–32).

Study Design

Multiple databases, including PubMed, Embase, and Scopus, were searched on January 1, 2024, to identify published studies evaluating the accuracy of CT for identifying hepatic steatosis. A variety of free-text and keyword combinations of *CT* and *fatty liver* or *steatosis* were used as search terms (Appendix S1). The electronic search covered the time frame from September 1977 to January 2024. In addition, a manual search of reference lists from previously identified review articles and extracted articles was performed to identify further relevant literature.

The inclusion criteria were published and indexed literature in the English language that reported either of the following: *(a)* parameters of diagnostic accuracy, including sensitivity, specificity, or cross-tabulations of NCCT, CECT, or DECT for the detection of hepatic steatosis with use of biopsy or PDFF as the reference standard or *(b)* diagnostic accuracy of CECT or DECT with use of NCCT or CECT, respectively, as the reference standard. Studies that did not provide original data, such as comments, editorials, news, guidelines, and reviews, were excluded from the analysis. Conference abstracts were also excluded.

Data Extraction

Two researchers (M.H., postdoctoral researcher with 7 years of research experience, and D.A., radiologist with 5 years of experience) independently reviewed the search outcomes to determine which articles to include for data extraction. Any inconsistencies were resolved by consensus. In cases where articles did not directly present measures of accuracy, the sensitivity and specificity were approximated on the basis of the reported data and graphs.

Quality Assessment

The quality of each article was assessed using the modified Quality Assessment of Diagnostic Accuracy Studies, or QUADAS, criteria (31). The QUADAS-2 risk-of-bias domains (patient selection, index test, reference test, and flow and timing) and applicability domains were rated as low risk, high risk, or unclear risk.

Diagnostic Performance Measures

The end point of the studies was the presence or absence of hepatic steatosis, which was measured differently in each study on the basis of the specific criteria and definitions. Different liver fat content cutoffs were used in different studies. For this meta-analysis, two different definitions (based on biopsy or PDFF) were used for any degree of steatosis and for at least moderate steatosis. Any degree of steatosis was defined as having at least 5% fat at biopsy or at least 6% fat at PDFF, whereas at least moderate steatosis was defined as having over 20%–33% fat deposition at biopsy or at least 17% fat at PDFF (33–37).

In studies where relevant data were accessible, the accuracy for diagnosing hepatic steatosis with use of the *(a)* mean liver attenuation (in Hounsfield units), *(b)* mean liver-spleen attenuation difference, *(c)* mean liver to spleen attenuation ratio, and *(d)* DECT-derived fat fraction was assessed.

Statistical Analysis

Pooled sensitivity and specificity were computed using the data on the numbers of true-positive, false-negative, true-negative, and false-positive findings. Bivariate random-effects model was used for meta-analysis of diagnostic test accuracy, and forest plots were calculated. Reverse logit transformation was used to determine the effect of sample size using proportion-based data. The Clopper-Pearson method was used to calculate the CI. $P < .05$ was used to determine statistically significant difference.

To determine the existence of heterogeneity between studies, the I^2 statistic was used, which represents the proportion of total variation across studies that is due to heterogeneity rather than chance. A value of 50%–75% suggests substantial heterogeneity, and 75%–100% indicates considerable heterogeneity (38,39). Tau^2 and χ^2 statistics, reported in the forest plots, were calculated to assess between-study variance and heterogeneity, respectively (40). The analysis was completed with the "Meta" package in R (R Foundation, version 4.1.3). Logit transformations of sensitivity and specificity were generated, and the Pearson correlation coefficient (r) was calculated. A positive correlation between sensitivity and specificity (coefficient >0) was also considered a marker of heterogeneity (38,40). Potential sources of heterogeneity (grade [any degree of steatosis or at least moderate steatosis], time frame, and cutoff definition) were investigated using meta-regression, as planned. Sensitivity analyses were

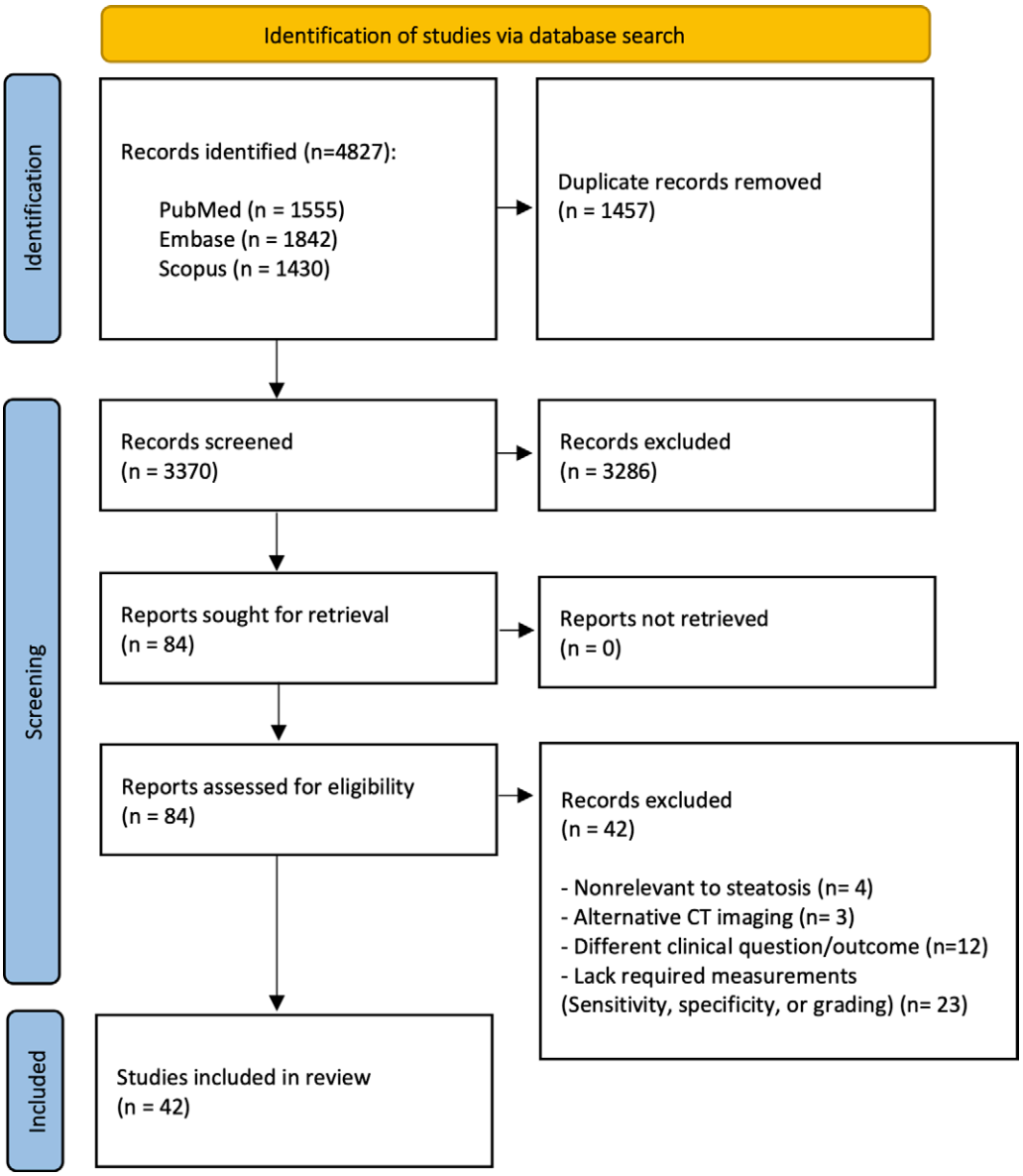


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses, or PRISMA, flow diagram.

performed to assess the robustness of the findings. These analyses were performed with a leave-one-out method.

The diagnostic test accuracy summary line (summary receiver operating characteristic curve) was obtained with the 'Restima' function of the 'Mada' package in R, which is a bivariable model used to compute the summary statistics for diagnostic test accuracy. Visual examination of the symmetry of the summary receiver operating characteristic curve was used to further evaluate heterogeneity (41).

All statistical analyses were conducted by an author (M.H.).

Results

Search Outcomes

A total of 4827 records were found, which, after the removal of duplicates, resulted in 3370 unique records for which the title and abstract were screened. Of those, 3286 articles were excluded without full-text assessment, leaving a total of 84 articles for full-text assessment of eligibility. After application of the inclusion and exclusion criteria, 42 studies were included in this systematic review and meta-analysis. The reasons for exclusion of the 42 studies included concerning another disorder other than SLD (n = 4), using alternative CT (n = 3), different clinical question or outcome (n = 12), and lack of required measurements (sensitivity, specificity, or steatosis grading) (n = 23). The PRISMA diagram provides information on the number of studies that did not meet the criteria (Fig 1).

The systematic review included 23 studies (36,37,42–62) of diagnostic accuracy that compared NCCT with biopsy or PDFF (Table 1), four studies (51,57,63,64) that compared CECT with biopsy or PDFF, five studies (65–69) that compared CECT with NCCT (Table 2), seven studies (18,70–75) that compared DECT with biopsy or PDFF, two studies (76,77) that compared DECT with NCCT, and one study that compared DECT with CECT (78) (Table 3).

Table 1: Summary of Noncontrast CT Studies

Study	Country	No. and F/M	Age*	Mean BMI	Reference Standard	Time Frame	Technique	Liver Disease	Steatosis Threshold	Diagnosis Threshold	Sensitivity (%)	Specificity (%)	Cutoff Basis
Limanond et al, 2004 (43)	USA	42 13/29	31 ± 9.66	27	Biopsy	<4 weeks	NA	Donors	HS ≥5	L-S <5	87	93	Predefined
Park et al, 2006 (46)	Korea	154 50/104	31 ± 10.5	NA	Biopsy	Same day	120 kVp	Donors	HS ≥30	L <58 L <42 L-S < −7 L-S < −9 L/S <0.9 L/S <0.8	100 73 91 82 91 81	95 100 99 100 97 100	Optimum cutoff and cutoff for 100% specificity
Cho et al, 2008 (57)	USA	26 NA	62 ± 12.6	28	Biopsy	<5 months	NA	Mixed	HS ≥30	L-S < −10	11	100	Predefined
Lee et al, 2010 (45)	Korea	161 58/103	32 ± 9.6	23	Biopsy	Same day	NA	Donors	HS ≥5 HS ≥30	L-S <6.5 L-S <3.2	50 73	77 91	Optimum cutoff
van Werven et al, 2010 (50)	Netherlands	43 21/22	62	27	Biopsy	<3 weeks	120 kVp	Mixed	HS ≥5	L <54.2	70	74	Optimum cutoff
Marsman et al, 2011 (53)	Netherlands	32 12/20	58 ± 8.8	25	Biopsy	<4 months	NA	Colorectal liver metastases	HS ≥5 HS ≥33	L <60.4 L <54.2	84 70	64 87	Optimum cutoff
Pickhardt et al, 2012 (49)	USA	315 108/207	31 ± 10.1	23	Biopsy	Same day	120 kVp	Donors	HS ≥30	L <50 L-S <−1	54 59	100 100	Cutoff for 100% specificity
Kan et al, 2014 (55)	Japan	67 26/41	52 ± 14	28	Biopsy	NA	NA	MASH	HS ≥5	L/S <1.1	83	93	Optimum cutoff
Kuzu et al, 2015 (52)	Turkey	27 12/15	40 ± 9.6	27	Biopsy	<1 month	NA	Donors	HS ≥5 HS ≥20	L <42.5 L-S < −0.5 L/S <0.98 L <42.5 L-S <5 L/S <0.98	80 93 93 89 89 89	75 83 83 61 56 56	Optimum cutoff
Rogier et al, 2015 (47)	France	109 40/69	55 ± 16	27	Biopsy	Same day	NA	Donors	HS ≥30	L/S <0.90 L <34.67	79 79	98 97	Optimum cutoff
Saba et al, 2015 (48)	Italy	51 15/36	57 ± 9.9	NA	Biopsy	Same day	NA	Mixed	Mild moderate	L <50 L <35	70 63	86 93	Predefined
Byun et al, 2018 (62)	Korea	4413 1474/2939	31 ± 9.4	…	Biopsy	<3 days	120 and 100 kVp	Donors	HS ≥5 HS >33	L-S ≤14 L-S ≤2 L-S ≤5 L-S ≤ −3	95 34 95 66	17 95 54 96	Cutoff for 95% specificity or 95% sensitivity
Pickhardt et al, 2018 (59)	USA	72 NA	54 ± 12	NA	PDFF	<1 month	120 kVp	NA	PDFF ≥14	L <45	100	98	Cutoff for 100% sensitivity
Adalı et al, 2019 (44)	Turkey	264 107/157	35 ± 8.6	28	Biopsy	<30 days	NA	Donors	HS >5 HS ≥15	L-S <6 L-S <0	77 94	77 76	Predefined
Haberal et al, 2019 (42)	Turkey	181 87/94	36 ± 9.3	NA	Biopsy	NA	120 kVp	Donors	HS >5	Visual grading system based on vessel visibility	85	100	NA
Şeker et al, 2019 (51)	Turkey	55 18/37	37 ± 9	NA	Biopsy	<1 week	120 kVp	Donors	HS ≥5 HS ≥20	L <55.5 L-S < −4 L/S <1.12 L <55.5 L-S < −4 L/S <1.12	74 71 81 81 75 75	88 88 79 90 92 92	Optimum cutoff
Ahn and Yun et al, 2020 (60)	Korea	2218 779/1439	31 ± 9	23	Biopsy	<3 days	120 and 100 kVp	Donors	HS ≥5	L-S <12.5 L-S <3.9	90 46	27 90	Cutoff for 90% sensitivity and 90% specificity
Jirapatnakul et al, 2020 (58)	USA	21 NA	65 (54–69)†	NA	Biopsy	<3 months	120 and 100 kVp	Mixed	At least moderate	L <40	100	88	Predefined
Chaudhary et al, 2021 (56)	India	273 121/152	32 ± 9.1	25	Biopsy	<1 month	NA	Donors	HS >10	L-S <5	100	71	Predefined
Bae et al, 2022 (54)	Korea	120 39/81	61 ± 10.5	24	Biopsy	< 3 months	120 kVp	Mixed	HS ≥5 HS >33	L-S ≤6 L-S ≤1	71 87	85 87	Predefined

Table 1 (*continues*)

Table 1 *(continued)*: Summary of Noncontrast CT Studies

Choi et al, 2022 (36)	Korea	165 51/114	36 ± 12	NA	MRS fat fraction	<1 week	100 kVp	Donors	PDFF ≥4.14 PDFF ≥15.72	L-S < −6.9 L/S <0.89 L-S < −6.9 L/S <0.89 L-S < −0.5 L/S <0.99	29 31 71 76 100 100	98 98 91 91 84 84	Optimum cutoff
Atef et al, 2023 (61)	Egypt	53 NA	26 ± 4	24	Biopsy	NA	120 kVp	Donors	HS ≥5	L <55.4 L-S <8.7 L/S <1.17	80 80 73	71 66 74	Optimum cutoff
Kim and Jeon et al, 2023 (37)	Korea	142 86/56	55 ± 13.85	24	Biopsy	<3 months	NA	NA	HS ≥5	L-S <3 L <47	70 54	82 89	Optimum cutoff

Note.—Body mass index was calculated as weight in kilograms divided by height in meters squared. *Donors* indicates CT performed for organ donor suitability. Hepatic steatosis (HS) thresholds and proton density fat fraction (PDFF) are percentage fat. Liver attenuation (L) and liver-spleen attenuation difference (L-S) are expressed in Hounsfield units. L/S = liver to spleen attenuation ratio, MASH = metabolic dysfunction–associated steatohepatitis, MRS = MR spectroscopy, NA = not available.

* Unless otherwise specified, data are means ± SDs.

† Value is median age (y), with the IQR in parentheses.

Table 2: Summary of Contrast-enhanced CT Studies

Study	Country	No. and F/M	Age*	Mean BMI	Reference Standard	Time Frame	Technique	Liver Disease	Steatosis Threshold	Diagnosis Threshold	Sensitivity (%)	Specificity (%)	Cutoff Basis
Panicek et al, 1997 (69)	USA	96 NA	NA	NA	NCCT	Same study	150 mL ICM (300 mg I/mL); 75–90-sec delay	Colorectal cancer	L-S <0	Radiologist visual assessment	88	99	Predefined
Jacobs et al, 1998 (65)	Switzerland	76 30/46	55	NA	NCCT	Same study	120 kVp; 150 mL ICM (300 mg I/mL); 80–90-sec delay	Mixed	L <40 L-S <10	Qualitative five-point scale	55	95	Predefined
Cho et al, 2008 (57)	USA	74 NA	62 ± 12.6	28	Biopsy	<5 months	NA	Mixed	HS ≥30	L-S < −43	27	85	Predefined
Kim et al, 2010 (63)	Korea	179 64/115	32 ± 9	23	Biopsy	Same day	120 kVp; 140 mL ICM (370 mg I/mL); portal venous phase	Donors	HS ≥10 HS ≥30	L-S < −6 L-S < −19	51 69	88 96	Optimum cutoff
Lawrence et al, 2011 (66)	USA	500 248/252	58 ± 14.4	NA	NCCT	Same study	120 kVp; 100 mL ICM (300 mg I/mL); portal venous phase	Mixed; most common, HCC	L-S <10	L-S <10	60	100	Predefined
da Fonseca Monjardim et al, 2013 (67)	Brazil	150 75/75	55 ± 14	NA	NCCT	Same study	120 kVp; 1.5–2 mL/kg, maximum volume of 150 mL; portal venous phase	NA	L-S <0	L <104	100	36	Predefined
Sagir Kahraman et al, 2017 (64)	Turkey	51 19/32	34 ± 10.2	NA	Biopsy	NA	120 kVp; 100 mL ICM (400 mg I/mL); phase, NA	Donors	HS ≥5	L-S <9.1	73	86	Optimum cutoff
Şeker et al, 2019 (51)	Turkey	55 18/37	37 ± 9	NA	Biopsy	<1 week	120 kVp; 1.5 mL/kg ICM (350 mg I/mL); hepatic venous phase	Donors	HS ≥5 HS ≥20	L-S < −1.5 L/S <0.98 L-S < −5.5 L-S < −11 L/S <0.94 L/S <0.87	77 77 94 56 94 56	100 100 92 100 90 100	Optimum cutoff
Pickhardt et al, 2023 (68)	USA	2777 1477/1300	57	NA	NCCT	Same study	120 kVp; portal venous phase	NA	L <40	L <65 L <85 L <110 L-S < −35 L-S < −20 L-S <0	41 86 99 40 71 96	100 88 35 93 79 35	Predefined

Note.—Body mass index was calculated as weight in kilograms divided by height in meters squared. *Donors* indicates CT performed for organ donor suitability. Hepatic steatosis (HS) thresholds are percentage fat. Liver attenuation (L) and liver-spleen attenuation difference (L-S) are expressed in Hounsfield units. HCC = hepatocellular carcinoma, ICM = intravenous contrast medium, L/S = liver to spleen attenuation ratio, NA = not available, NCCT = noncontrast CT.

* Data are means ± SDs.

Table 3: Summary of DECT Studies

Study	Country	No. and M/F	Age*	Mean BMI	Reference Standard	Time Frame	Technique	Liver Disease	Image Reconstruction	Steatosis Threshold	Diagnosis Threshold	Sensitivity (%)	Specificity (%)	Cutoff Basis
Hyodo et al, 2017 (18)	Japan	33 21/12	55 ± 9	27	Biopsy	<30 days	Fast kV switching 80/140 kVp	Mixed	Fat maps	HS >5	FVF ≥4.61	82	100	Optimum cutoff
Choi et al, 2021 (72)	Korea	49 16/33	63 ± 11.9	NA	PDFF	<90 days	Dual-source; 90/150 kVp	Mixed	VNC	PDFF >5	L <47.3 L-S <4.6 L/S <1.3	67 67 100	91 86 56	Optimum cutoff
Corrias et al, 2021 (74)	USA	39 19/20	59	NA	PDFF	<2 weeks	Fast kV switching 80/140 kVp	Oncologic patients	Fat maps	PDFF >6.5	FVF ≥6.5	93	89	Predefined
Kang et al, 2021 (71)	Korea	131 66/65	35 ± 11.2	23	Biopsy	<1 month	Dual-source DECT; 80/150 kVp	Donors	VNC	HS >10	L-S ≤10.1	83	78	Optimum cutoff
Beck et al, 2022 (78)	Germany	251 117/134	60 ± 16	NA	CECT	Same day	Dual-layer; 120 kVp; bolus of 80 mL iopromide	NA	Iodine maps	L-S <19	I_{pv-n} of 1.661	89	85	Optimum cutoff
Hong et al, 2022 (73)	Korea	33 16/17	46 ±13.2	NA	PDFF	Same day	Fast kV switching 80/140 kVp	NA	Fat maps	PDFF >5	FVF ≥4.61	90	100	Optimum cutoff
Niehoff et al, 2022 (76)	Germany	140 70/70	68	NA	NCCT	Same day	Photon-counting detector; 120 kVp	NA	VNC	L ≤40 L-S ≤ −10 L/S ≤0.8	L ≤38.5 L-S ≤ −1.5 L/S ≤0.96	94 96 95	92 90 100	Optimum cutoff
Zhang et al, 2022 (70)	USA	128 69/59	52 ± 17	NA	PDFF	<30 days	Split-beam, 120 kVp Au/Sn, 120 kVp; or dual-source 100/140 kVp	Mixed	VNC	PDFF >6	L <52.5	68	90	Predefined
Demondion et al, 2023 (75)	France	104 40/64	62 (50–69)†	25	PDFF	<31 days	Dual-layer; 120 kVp	NA	Fat maps	PDFF >5	FVF ≥5	90	80	Predefined
Catania et al, 2024 (77)	USA	316 166/150	59	28	NCCT	Same session	Dual-source; 80–140 kVp	NA	VNC	L <40	L <40 L <46	46 71	100 96	Predefined

Note.—Body mass index was calculated as weight in kilograms divided by height in meters squared. *Donors* indicates CT performed for organ donor suitability. Hepatic steatosis (HS) thresholds, proton density fat fraction (PDFF), and fat volume fraction (FVF) are given as percentages. Liver attenuation (L) and liver-spleen attenuation difference (L-S) are expressed in Hounsfield units. CECT = contrast-enhanced CT, DECT = dual-energy CT, I_{pv-n} = portal vein normalized iodine concentration, L/S = liver to spleen attenuation ratio, NA = not available, NCCT = noncontrast CT, VNC = virtual noncontrast.

* Unless otherwise specified, data are means ± SDs.

† Value is median age (y), with the IQR in parentheses.

Quality Assessment

Tables 4 and 5 present the detailed QUADAS-2 tool quality assessments of each article. The primary sources of potential bias concerns were the index test, reference standard, and flow and timing domains. The risk of bias for seven included studies was unclear for the index test domain because the investigators' blinding status to the reference standard was not specified or not enough data were provided about the CT device, which hindered reproducibility (42,44,48,51,52,64,65). Eight of the included studies used NCCT as the reference standard (65–68,75–78).

Meta-Analysis of the Diagnostic Accuracy of NCCT

A total of 23 studies involving 14 287 CT examinations were analyzed to determine the diagnostic accuracy of NCCT compared with either biopsy or PDFF as the reference standard. Fourteen studies focused on liver donor candidates, and seven studies were conducted in patients with known liver disease. In two studies, the reasons for imaging were not specified. The studies included a diverse range of patients. In all patients, the interpretation of NCCT images was conducted without prior knowledge of the biopsy or PDFF results. The maximum duration between NCCT and the reference standard was 5 months, although in the majority of studies, it was less than 1 month.

Any degree of steatosis.—In a total of 17 studies with 8304 participants, 3518 of whom had hepatic steatosis, the sensitivity of NCCT in detecting any degree of steatosis based on biopsy or PDFF was 72% (95% CI: 60.9, 80.4) ($P < .001$), with a

Table 4: QUADAS-2 Assessment of Noncontrast CT

	Risk of Bias				Applicability Concerns		
Study	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Limanond et al, 2004 (43)	✓	✓	✓	✓	✓	✓	✓
Park et al, 2006 (46)	✓	✓	✓	✓	✓	✓	✓
Cho et al, 2008 (57)	✓	✓	✓	✓	✓	✓	✓
Lee et al, 2010 (45)	✓	✓	✓	✓	✓	✓	✓
van Werven et al, 2010 (50)	✓	✓	✓	✓	✓	✓	✓
Marsman et al, 2011 (53)	X	✓	✓	✓	✓	✓	✓
Pickhardt et al, 2012 (49)	✓	✓	✓	✓	✓	✓	✓
Kan et al, 2014 (55)	✓	✓	✓	✓	✓	✓	✓
Kuzu et al, 2015 (52)	✓	✓	✓	✓	✓	?	✓
Rogier et al, 2015 (47)	✓	✓	✓	✓	✓	✓	✓
Saba et al, 2015 (48)	✓	✓	✓	✓	✓	?	✓
Byun et al, 2018 (62)	✓	✓	✓	✓	✓	✓	✓
Pickhardt et al, 2018 (59)	✓	✓	✓	?	✓	✓	✓
Adalı et al, 2019 (44)	✓	?	✓	✓	✓	?	✓
Haberal et al, 2019 (42)	✓	?	✓	✓	✓	?	✓
Şeker et al, 2019 (51)	✓	?	✓	✓	✓	?	✓
Ahn and Yun et al, 2020 (60)	✓	✓	✓	✓	✓	✓	✓
Jirapatnakul et al, 2020 (58)	✓	✓	✓	✓	✓	✓	✓
Chaudhary et al, 2021 (56)	✓	✓	✓	✓	✓	✓	✓
Bae et al, 2022 (54)	✓	✓	✓	✓	✓	✓	✓
Choi et al, 2022 (36)	✓	✓	✓	✓	✓	✓	✓
Atef et al, 2023 (61)	✓	✓	✓	✓	✓	✓	✓
Kim and Jeon et al, 2023 (37)	✓	✓	✓	?	✓	✓	✓

Note.—QUADAS = Quality Assessment of Diagnostic Accuracy Studies, ✓ = low risk, X = high risk, ? = unclear risk.

specificity of 88% (95% CI: 81.1, 92.6) ($P < .001$) (Fig 2). The I^2 statistic for sensitivity and specificity was 93%.

At least moderate steatosis.—Fifteen studies involving 5983 patients assessed at least moderate hepatic steatosis. NCCT had a sensitivity of 82% (95% CI: 66.9, 91.4) ($P < .001$) in the detection of at least moderate steatosis based on histologic criteria or PDFF, whereas the specificity was 94% (95% CI: 87.8, 96.6) ($P < .001$) (Fig 2). The I^2 statistics for the estimates of sensitivity and specificity were 58% and 93%, respectively.

The correlation coefficients for the sensitivity and specificity variables were −0.08471 for the detection of steatosis and −0.26743 for the detection of at least moderate steatosis. The summary receiver operating characteristic curve showed an asymmetric pattern for detecting any degree of steatosis and symmetrical pattern for detecting at least moderate steatosis (Figs 3, 4).

The sensitivity analysis results indicated that excluding individual studies resulted in minor variations in the pooled sensitivity and specificity and heterogeneity metrics for both grades, indicating that no single study disproportionately impacted the overall results. This consistency reinforced the robustness of the meta-analysis findings despite the high heterogeneity observed.

Thresholds.—The liver attenuation cutoffs used for the detection of steatosis at NCCT were further examined. Table 1 and Figures 5 and 6 summarize the thresholds used. The large variation in these thresholds was at least partly due to the different tasks they were designed for (ie, aiming for high specificity vs high sensitivity).

Meta-Analysis of the Diagnostic Accuracy of CECT

The diagnostic accuracy of CECT, compared with that of biopsy, PDFF, or NCCT as the reference standard, was evaluated by analyzing nine studies involving 3958 scans. Three studies focused on liver donor candidates, and four studies focused on individuals with preexisting liver disease. The purpose of imaging was not specified in two studies. The longest time period between CECT and the reference standard was 5 months, whereas in most studies, it was less than 1 month.

Any degree of steatosis (biopsy or PDFF as the reference standard).—In the detection of any degree of steatosis, the overall sensitivity of CECT (when biopsy or PDFF was used as the reference standard) was 66% (95% CI: 50.4, 79.3) ($P < .05$), and the overall specificity was 90% (95% CI: 84.3, 93.3) ($P = .94$) (Fig 7). The I^2 statistics for sensitivity and specificity were 69% and 0%, respectively.

At least moderate steatosis (biopsy or PDFF as the reference standard).—In the detection of at least moderate steatosis, the pooled sensitivity of CECT (when biopsy or PDFF was

Table 5: QUADAS-2 Assessment of CECT and DECT Studies

Modality and Study	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
CECT							
Panicek et al, 1997 (69)	✓	✓	X	✓	✓	?	X
Jacobs et al, 1998 (65)	✓	✓	X	✓	✓	?	X
Cho et al, 2008 (57)	✓	✓	✓	✓	✓	✓	✓
Kim et al, 2010 (63)	✓	✓	✓	?	✓	✓	✓
Lawrence et al, 2012 (66)	✓	✓	X	✓	✓	✓	X
da Fonseca Monjardim et al, 2013 (67)	✓	✓	X	?	✓	✓	X
Sagir Kahraman et al, 2017 (64)	✓	?	✓	✓	✓	?	✓
Şeker et al, 2019 (51)	✓	?	✓	✓	✓	?	✓
Pickhardt et al, 2023 (68)	✓	✓	X	?	✓	✓	X
DECT							
Hyodo et al, 2017 (18)	✓	✓	✓	✓	✓	✓	✓
Choi et al, 2021 (72)	✓	✓	✓	✓	✓	✓	✓
Corrias et al, 2021 (74)	✓	✓	✓	✓	✓	✓	✓
Kang et al, 2021 (71)	✓	✓	✓	✓	✓	✓	✓
Beck et al, 2022 (78)	✓	✓	X	?	✓	?	X
Hong et al, 2022 (73)	✓	✓	✓	?	✓	✓	✓
Niehoff et al, 2022 (76)	✓	✓	X	?	✓	✓	X
Zhang et al, 2022 (70)	✓	✓	✓	✓	✓	✓	✓
Demondion et al, 2023 (75)	✓	✓	✓	?	✓	✓	✓
Catania et al, 2024 (77)	✓	✓	X	?	✓	✓	X

Note.—QUADAS = Quality Assessment of Diagnostic Accuracy Studies, CECT = contrast-enhanced CT, DECT = dual-energy CT, ✓ = low risk, X = high risk, ? = unclear risk.

used as the reference standard) was 68% (95% CI: 25.8, 92.6) (P = .10), and the pooled specificity was 93% (95% CI: 87.6, 96.8) (P < .001) (Fig 7). The I^2 statistics for sensitivity and specificity were 88% and 56%, respectively.

The correlation coefficients for the sensitivity and specificity variables were 0.6568 for detecting steatosis and 0.5366 for detecting at least moderate steatosis. The summary receiver operating characteristic curve did not show a symmetrical pattern for detecting steatosis or at least moderate steatosis, indicating heterogeneity among the studies (Figs 8, 9).

Any degree of steatosis (NCCT as the reference standard).—In the detection of any degree of steatosis, the pooled sensitivity of CECT (when NCCT was used as the reference standard) was 80% (95% CI: 41, 95.6) (P < .001), whereas the pooled specificity was 99% (95% CI: 80.1, 100) (P < .001). The I^2 statistics for sensitivity and specificity were 73% and 98%, respectively.

The sensitivity analysis results suggested that the overall sensitivity estimates and heterogeneity measures vary depending on the study that was excluded, highlighting the influence of individual studies on the meta-analysis outcomes. However, the pooled specificity estimates were relatively stable regardless of which study was excluded, and no significant heterogeneity was observed among the studies.

Thresholds.—Various cutoff values for hepatic steatosis were used in the studies (Table 2) (51).

Meta-Analysis of the Diagnostic Accuracy of DECT

A meta-analysis of the diagnostic accuracy of DECT is included in Appendix S2.

Meta-Regression

Meta-regression findings indicated that grade, timeframe, and cutoff basis were not moderators of diagnostic accuracy (nonsignificant P values) with either of the CT modalities, suggesting that other unmeasured factors contributed to variability. The high residual heterogeneity warrants further study into other potential moderators (Table 6).

Discussion

This meta-analysis describes the performance of CT for the detection of hepatic steatosis. Noncontrast CT showed better performance for the detection of at least moderate steatosis (with a pooled sensitivity and specificity of 82% and 94%, respectively) than for the detection of any degree of steatosis (with a pooled sensitivity and specificity of 72% and 88%). There are fewer studies regarding performance of contrast-enhanced CT (CECT) and with higher variability in the reference standard, which makes the conclusions less accurate. The pooled sensitivity and specificity of the CECT studies were 66% and 90% for the detection of any degree of steatosis and 68% and 93% for the detection of at least moderate steatosis.

The worldwide prevalence of SLD is increasing. US-based and MRI-based techniques are preferred imaging methods for

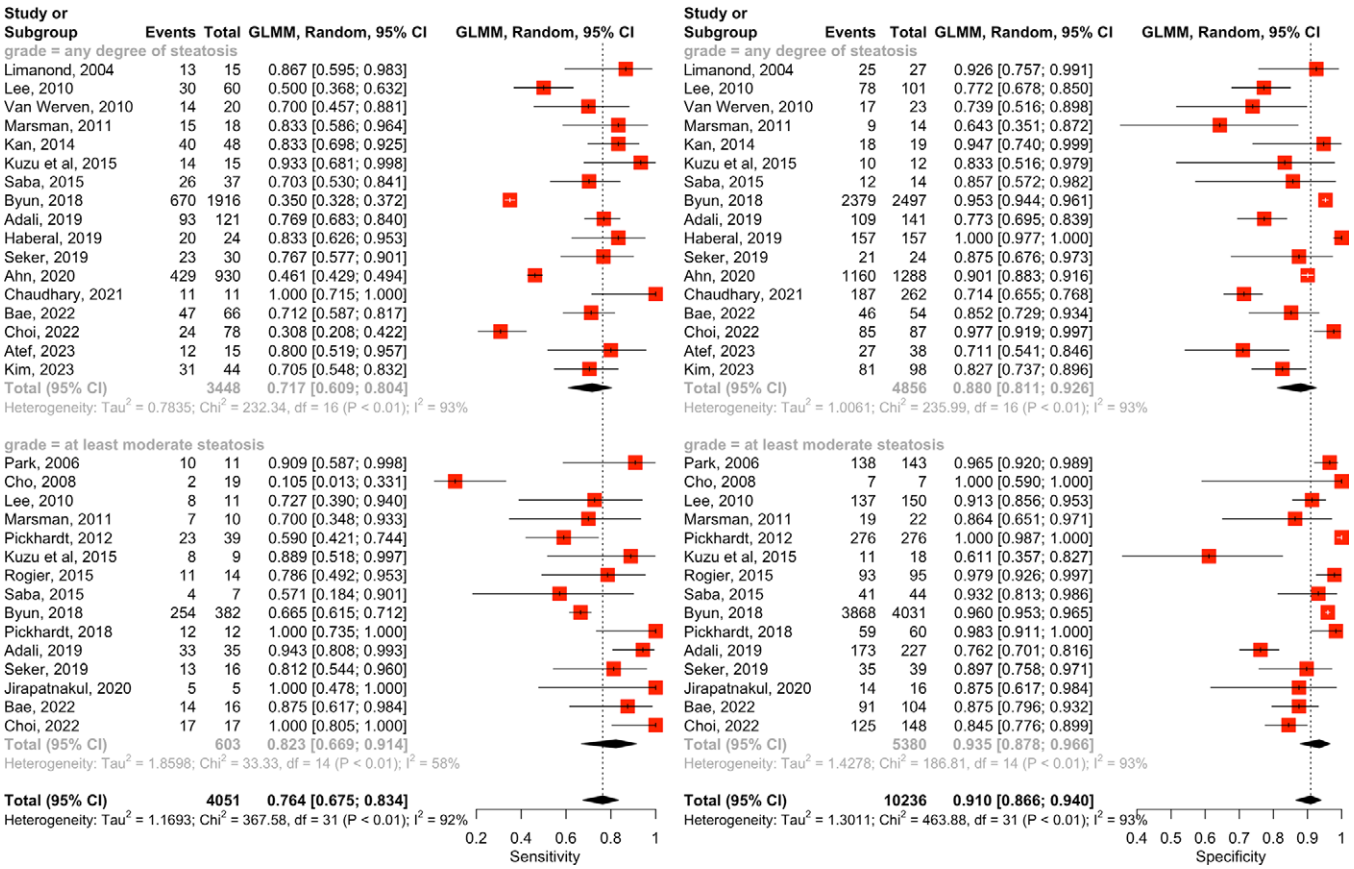


Figure 2: Forest plots show overall sensitivity (left) and specificity (right) of noncontrast CT for the detection of any degree of and at least moderate hepatic steatosis. The vertical dotted line represents the pooled sensitivity and specificity estimate. The horizontal bars indicate the 95% CI. The black diamond represents the pooled effect, with its width showing the CI. The red squares represent the observed study effect size. GLMM = generalized linear mixed model.

the assessment of steatosis. These methods are typically used as screening tools in patients at risk and for longitudinal surveillance. A substantial proportion of patients with SLD are unaware of their underlying liver condition. As such, opportunistic identification of steatosis plays a major role in this population (79). CT is a widely accessible imaging technique, with over 80 million scans acquired annually in the United States (80). Although not currently considered a screening tool for this task, CT can play an important role in opportunistic identification of steatosis when patients undergo scanning for other indications. These patients can be referred for clinical and laboratory assessment to screen for risk factors for advanced fibrosis that would require more advanced care.

At least moderate steatosis has emerged as the optimal focus for opportunistic CT screening (49). The currently accepted definition of at least moderate steatosis is more than 33% lipid content at biopsy or more than 17% PDFF at MRI. Less stringent definitions were used in many prior studies, with thresholds in the range of 20%–33% to distinguish mild from moderate steatosis. This level of steatosis is associated with an increased risk of fibrosis progression, considerably influencing overall prognosis and increasing the risk of major cardiovascular events (81). A mild degree of steatosis may not cause a considerable decrease in liver attenuation to be consistently detectable at NCCT. As such, aiming to detect mild steatosis with reasonable sensitivity will inadvertently result in a high rate of false positivity. Given the high prevalence of hepatic steatosis and the high risk of false positivity, opportunistic detection of all degrees of steatosis and the allocation of diagnostic work-ups for all patients may lack scientific justification within the current management guidelines. Notably, a heterogeneous and wide range of definitions for moderate steatosis, ranging from at least 20% to at least 33% fat at biopsy, was used in the studies included in this meta-analysis.

Results of this meta-analysis support the utility of NCCT in detecting hepatic steatosis. Although the literature on the value of CECT and DECT for the detection of steatosis is encouraging, more data are needed to support their use. Interestingly, the calculated pooled performance of NCCT based on our study is similar to that reported for US in a previous meta-analysis (82). Notably, the performance of CT is better than that of currently available serum markers (83). Other noninvasive biomarkers have been proposed for the diagnosis of steatohepatitis; however, data on their true clinical performance are limited (84).

Prior studies on CT-based detection of steatosis used different parameters (absolute liver attenuation, liver-spleen attenuation differences, and liver to spleen attenuation ratio), with substantial heterogeneity in the thresholds used (24). This stemmed mainly from their different goals of optimum sensitivity, optimum specificity, or a balance between the two. Continued debate revolves around whether to prioritize sensitivity or specificity.

Establishing reliable thresholds is essential for clinically meaningful screening of steatosis. With the emergence and

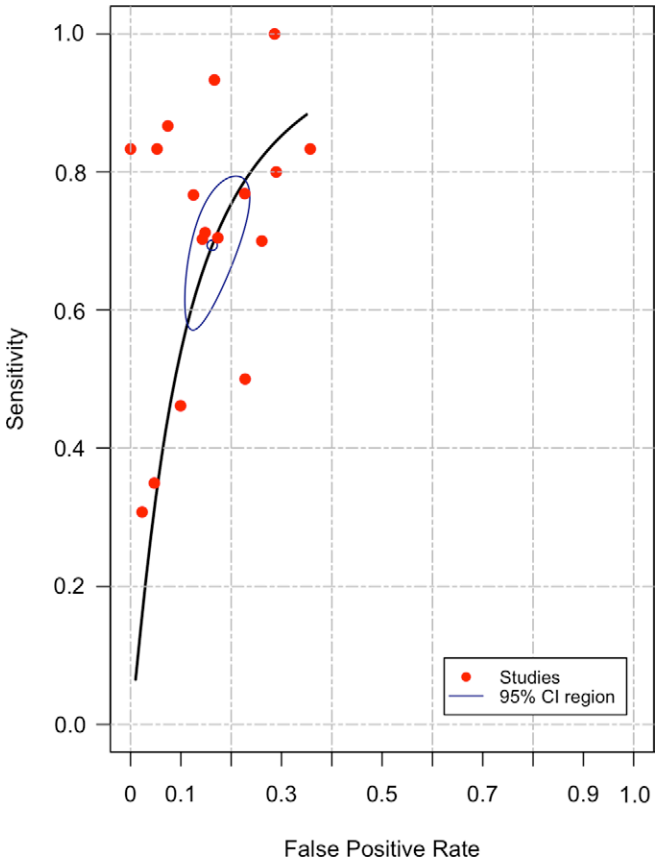


Figure 3: Summary receiver operating characteristic curve shows the test accuracy of noncontrast CT compared with that of biopsy or proton density fat fraction for the detection of any degree of hepatic steatosis.

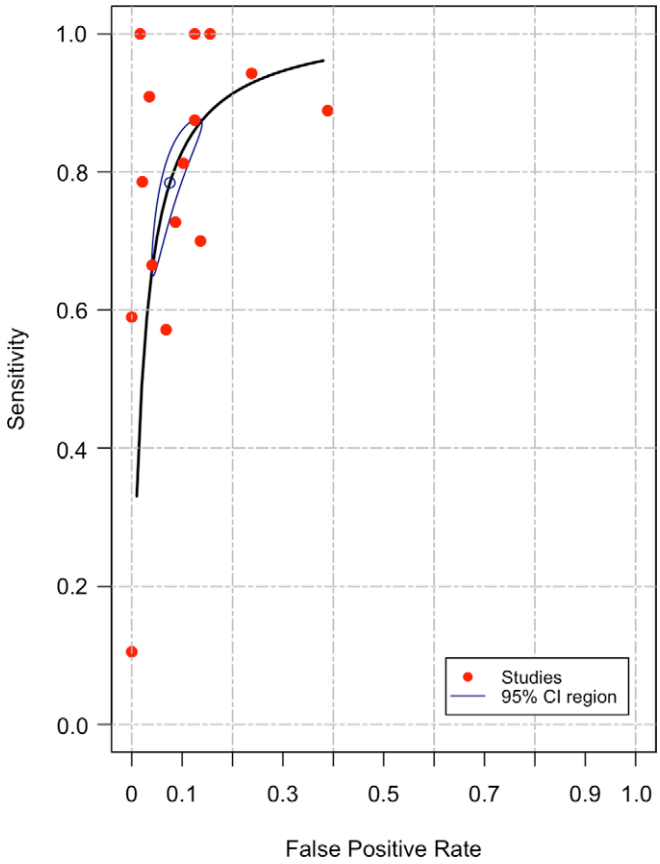


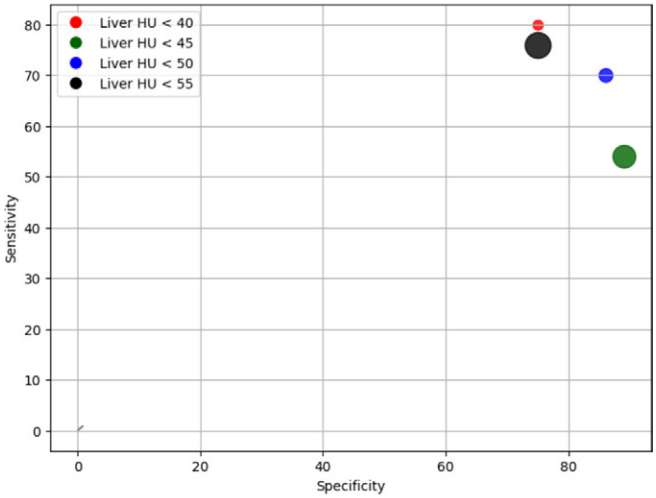
Figure 4: Summary receiver operating characteristic curve shows the test accuracy of noncontrast CT compared with that of biopsy or proton density fat fraction for the detection of at least moderate steatosis.

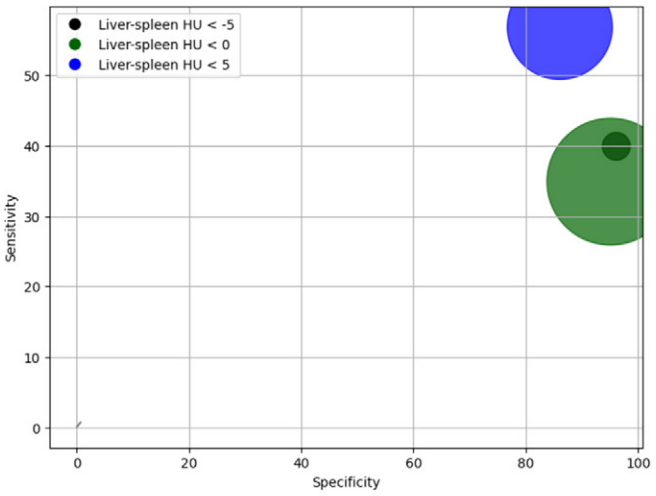
rapidly increasing use of artificial intelligence solutions for automated opportunistic identification, the importance of defining practical and evidence-based thresholds is multifold. A commonly used threshold of liver attenuation of less than 40 HU at NCCT correlates with a liver PDFF of 15% or greater, based on regression formula proposed by a study (49), and can be used to diagnose moderate hepatic steatosis. Few studies focused on subjective signs such as pericholecystic fat sparing and the visibility of intrahepatic vessels (42) or compared liver attenuation with muscle attenuation, which resulted in high specificity but very low sensitivity (66,69). In several large sample studies, absolute liver attenuation under 40–45 HU, liver-spleen attenuation differences less than −5 to 0 HU, or a liver to spleen attenuation ratio under 0.9–1 achieved high specificity (with variable sensitivities) for the detection of at least moderate steatosis.

On the basis of the existing data, it is difficult to conclude which parameter is the preferred one for the detection of steatosis at NCCT. The difference in liver and spleen attenuation appeared to be the most consistent. This parameter is also theoretically less prone to variations with CT tube voltage and scanner type (46).

Owing to the limited number of published studies, high heterogeneity, and inconsistencies in reference standards, insufficient evidence exists to establish thresholds for CECT and DECT. Particularly in the case of DECT, there are inherent technical differences between platforms and reconstructions, which makes it difficult to reach a concrete and generalizable conclusion. Despite these limitations, CECT and DECT methods show encouraging results, highlighting the need for future studies to address knowledge gaps and define reliable thresholds. Interestingly, we found that the heterogeneity between DECT studies that used PDFF or biopsy as a reference was low, and these studies showed good performance with high sensitivity and specificity. This further highlights the need to investigate this emerging modality.

Our study has several limitations. First, reference studies were published from 1998 to 2024. Some of the variability in study results may be attributed to rapid changes in CT acquisition and reconstruction techniques over this period. Second, variability in studies and other liver conditions, such as fibrosis and hepatic iron overload, were not addressed in this meta-analysis. Third, there was no consistent threshold for the definition of "at least moderate" steatosis among studies, and many studies used arbitrary thresholds lower than the currently accepted threshold of 33% at biopsy. Given the small number of articles included in this meta-analysis, we did not exclude those studies. Theoretically, the performance of CT for the detection of at least moderate steatosis would have been better if the 33% threshold had been used in all studies. Fourth, variations in biopsy results, such as microvascular versus macrovascular steatosis, were not assessed in our study. Finally, several studies lacked crucial information regarding the CT protocol and acquisition techniques, which can impact the attenuation values.





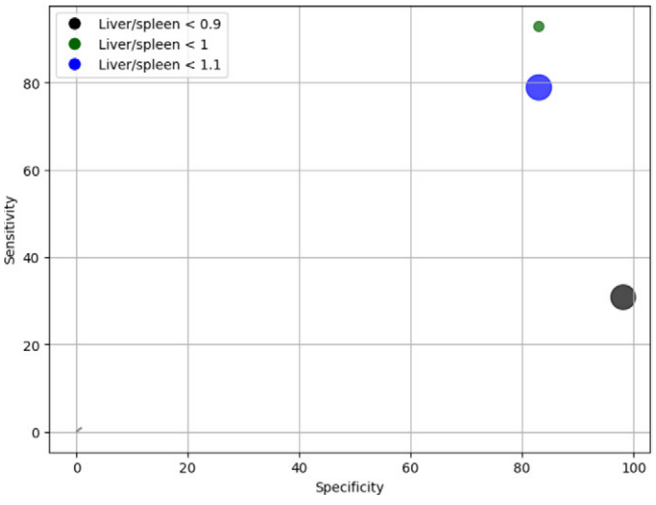
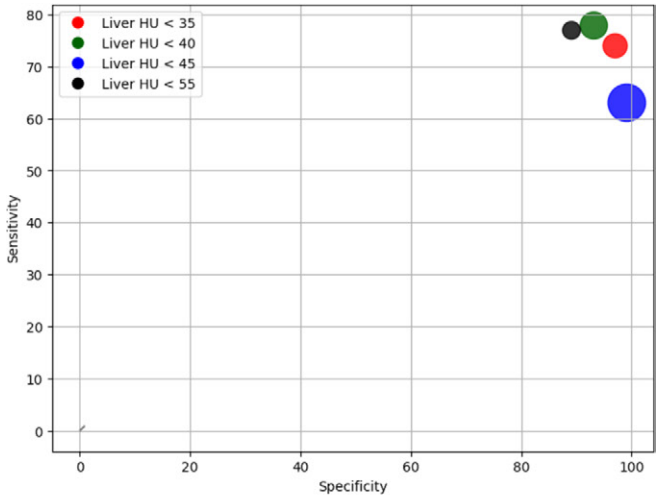
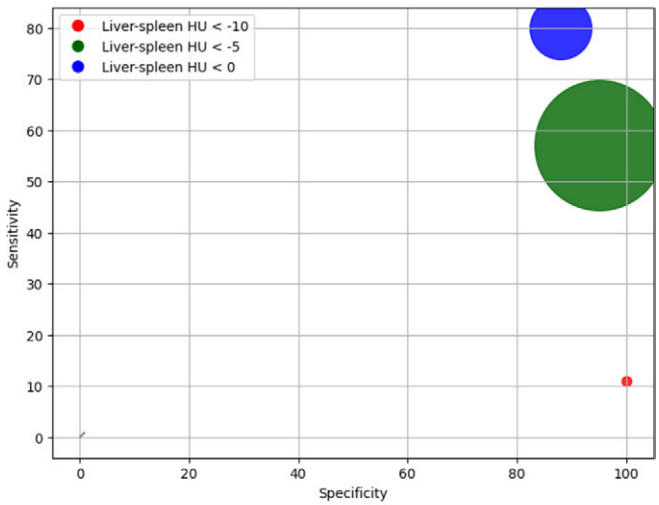


Figure 5: Plot shows sensitivity and specificity of different thresholds for the detection of any degree of hepatic steatosis at noncontrast CT; the size of the circles corresponds to the size of the cohort(s). Liver HU = liver attenuation, liver-spleen HU = liver-spleen attenuation difference, liver/spleen = liver to spleen attenuation ratio.





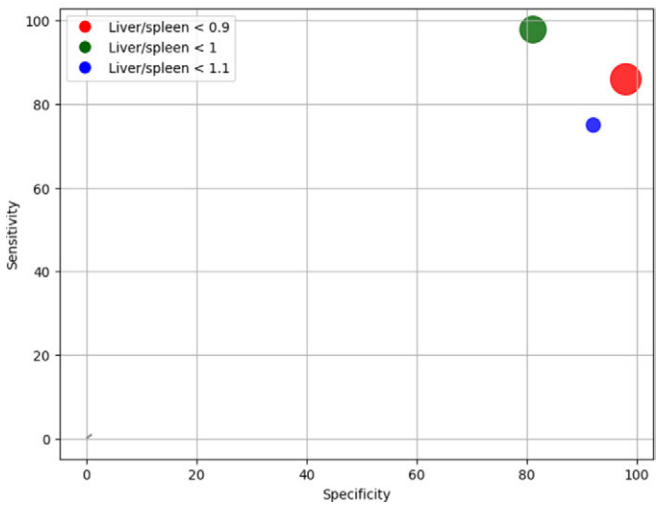


Figure 6: Plot shows sensitivity and specificity of different thresholds for the detection of at least moderate hepatic steatosis at noncontrast CT; the size of the circles corresponds to the size of the cohort(s). Liver HU = liver attenuation, liver-spleen HU = liver-spleen attenuation difference, liver/spleen = liver to spleen attenuation ratio.

In conclusion, our meta-analysis demonstrated that noncontrast CT is a reliable method for detecting at least moderate steatosis. We propose the use of an absolute liver attenuation of less than 40–45 HU, liver-spleen attenuation differences less than −5 to 0 HU, or a liver to spleen attenuation ratio under 0.9–1 for the detection of at least moderate steatosis. The supporting evidence for contrast-enhanced CT and dual-energy CT is insufficient for strong evidence-based conclusions at this time, although the initial results are promising, highlighting the need for further investigations.

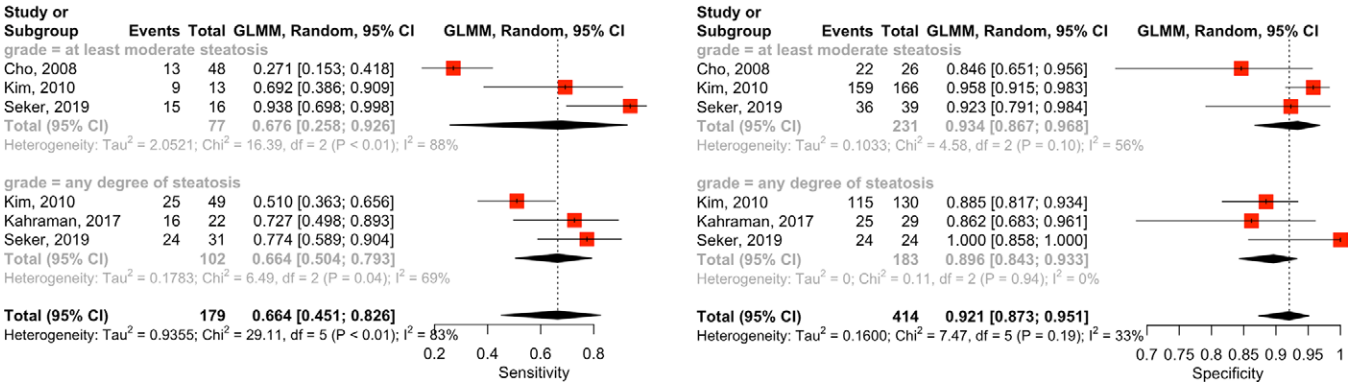


Figure 7: Forest plot shows overall sensitivity (left) and specificity (right) of contrast-enhanced CT for the detection of at least moderate hepatic steatosis or any degree of hepatic steatosis on the basis of proton density fat fraction or biopsy. The vertical dotted line represents the pooled sensitivity and specificity estimate. The horizontal bars indicate the 95% CI. The black diamond represents the pooled effect, with its width showing the CI. The red squares represent the observed study effect size. GLMM = generalized linear mixed model.

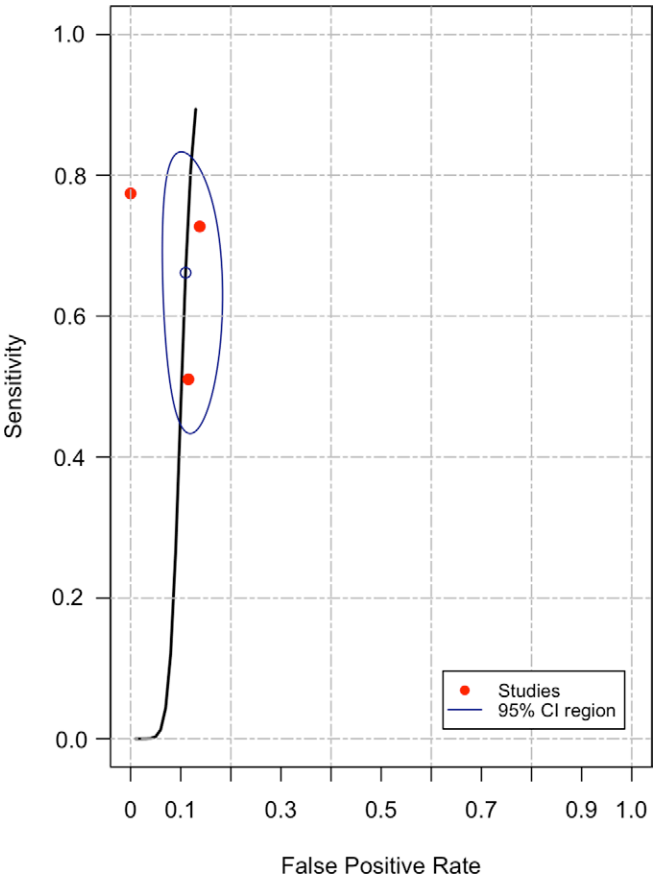


Figure 8: Summary receiver operating characteristic curve shows the test accuracy of contrast-enhanced CT compared with biopsy or the proton density fat fraction for the detection of hepatic steatosis.

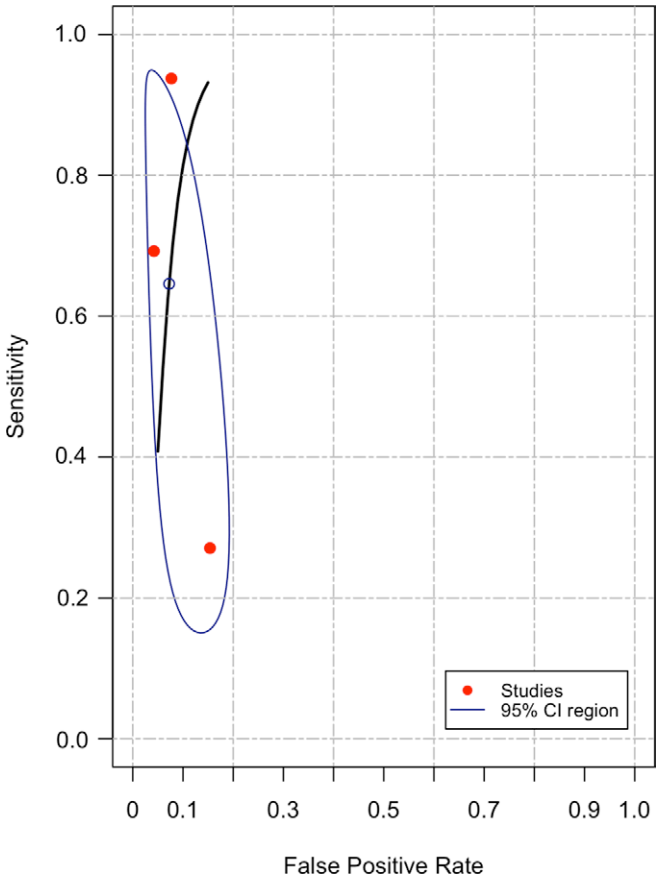


Figure 9: Summary receiver operating characteristic curve plot shows the test accuracy of contrast-enhanced CT compared with biopsy or the proton density fat fraction for the detection of at least moderate steatosis.

Table 6: Meta-Regression Analysis of NCCT, CECT, and DECT Studies

Modality	*P* Value for Grade Sensitivity	*P* Value for Grade Specificity	*P* Value for Cutoff Sensitivity	*P* Value for Cutoff Specificity	*P* Value for Time Frame Sensitivity	*P* Value for Time Frame Specificity
NCCT	.29	.22	.49	.22	.24	.13
CECT	.86	.22	NA	NA	.16	.10
DECT	NA	NA	.16	.10	.16	.10

Note.—CECT = contrast-enhanced CT, DECT = dual-energy CT, NA = not available, NCCT = noncontrast CT.

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Author contributions: Guarantors of integrity of entire study, **M.H., A.A.B.**; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, **M.H., D.A., F.H.M., A.A.B.**; clinical studies, **M.H., A.D.S., F.H.M.**; statistical analysis, **M.H., A.A.B.**; and manuscript editing, **M.H., A.D.S., S.T., F.H.M., A.A.B.**

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