

Table S1 Literature search strategy

Database	Search strategy
Pubmed	((CEUS) OR (contrast-enhanced ultrasound)) OR (contrast enhanced ultrasound) AND (((LI-RADS) OR (LIRADS)) OR (liver imaging reporting and data system)) OR (LR-1 or LR-2 or LR-3 or LR-4 or LR-5 or LR-TIV or LR-M or LR1 or LR2 or LR3 or LR4 or LR5 or LRTIV or LRM)) AND ((HCC) OR (Carcinomas, Hepatocellular))
Embase	<ol style="list-style-type: none"> (LI-RADS or LIRADS). tw, kw, k f. (liver imaging reporting and data system). mp. (LR-1 or LR-2 or LR-3 or LR-4 or LR-5 or LR-TIV or LR-M or LR1 or LR2 or LR3 or LR4 or LR5 or LRTIV or LRM). tw. 1 or 2 or 3 exp liver cell carcinoma/ exp contrast-enhanced ultrasound/ (CEUS or contrast enhanced ultrasound). tw. 6 or 7 4 and 5 and 8
Medline	<ol style="list-style-type: none"> (LI-RADS or LIRADS). tw, kw, kf. (liver imaging reporting and data system).tw,kw. (LR-1 or LR-2 or LR-3 or LR-4 or LR-5 or LR-TIV or LR-M or LR1 or LR2 or LR3 or LR4 or LR5 or LRTIV or LRM). tw. 1 or 2 or 3 Radiology Information Systems/ Carcinoma, Hepatocellular/ or Cholangiocarcinoma/ (hepatocellular carcinoma* or hepatocellular neoplasm* or hepatocellular cancer or hepatic cell carcinoma* or HCC or cholangiocarcinoma* or hepatic nodule* or liver lesion* or adrenocortical carcinoma*). tw, kw, kf. Liver Neoplasms/dg exp Liver Diseases/dg or liver disease*. tw, kw, kf. Liver/dg [Diagnostic Imaging] liver imaging. tw, kw. 6 or 7 or 8 or 9 or 10 or 11 5 and 12 4 or 13 Ultrasonography, Doppler, Color/ (CEUS or contrast enhanced ultrasound). tw, kw. 15 or 16 14 and 17
Web of Science	<ol style="list-style-type: none"> ((ALL=(Carcinoma, Hepatocellular)) OR ALL=(Cholangiocarcinoma)) OR ALL=(HCC) ((ALL=(LI-RADS)) OR ALL=(LIRADS)) OR ALL=(liver imaging reporting and data system)) AND ALL=(LR-1 or LR-2 or LR-3 or LR-4 or LR-5 or LR-5V or LR-OM or LR-TIV or LR-M or LR1 or LR2 or LR3 or LR4 or LR5 or LR5v or LRTIV or LRM or LROM) #2 AND #1 ((ALL=(ultrasound)) OR ALL=(CEUS)) OR ALL=(contrast-enhanced ultrasound)) OR ALL=(contrast enhanced ultrasound) #4 AND #3
Cochrane Central Register of Controlled Trials	<ol style="list-style-type: none"> ('LI-RADS' or 'LIRADS' or 'Liver Imaging Reporting and Data System' or 'LR-1' or 'LR-2' or 'LR-3' or 'LR-4' or 'LR-5' or 'LR-5V' or 'LR-TIV' or 'LR-M' or 'LR1' or 'LR2' or 'LR3' or 'LR4' or 'LR5' or 'LRTIV' or 'LRM'): ab, ti, kw ('Carcinoma, Hepatocellular' or 'Cholangiocarcinoma' or 'hepatocellular carcinoma*' or 'hepatocellular neoplasm*' or 'hepatocellular cancer' or 'hepatic cell carcinoma*' or 'hepatic nodule*' or 'liver lesion*' or 'liver nodule*' or 'liver neoplasm*'): ab, ti, kw ('CEUS' or 'contrast enhanced ultrasound' or 'contrast-enhanced ultrasound'): ab, ti, kw 1 and 2 and 3 publication year from 2016-2023

HCC, hepatocellular carcinoma; LI-RADS, liver imaging reporting and data system; CEUS, contrast-enhanced ultrasound.

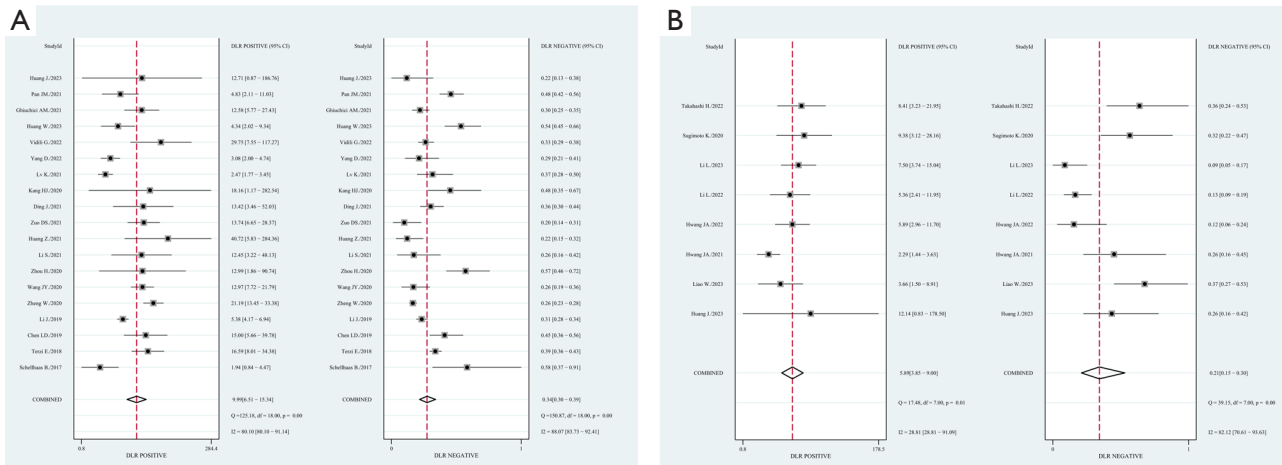


Figure S1 Forest plots of LR-5 for HCC. (A) Pooled +LR and -LR of the SonoVue LR-5 algorithm. (B) Pooled +LR and -LR of the Sonazoid modified LR-5 algorithm. LR-5, LI-RADS category 5; HCC, hepatocellular carcinoma; +LR, positive likelihood ratio; -LR, negative likelihood ratio; LI-RADS, liver imaging reporting and data system.

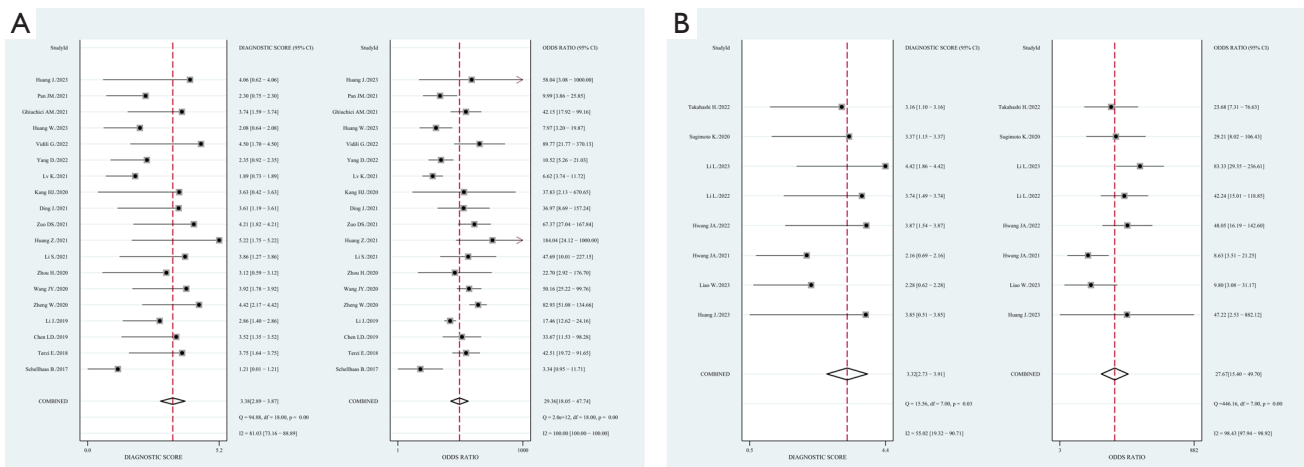


Figure S2 Forest plots of LR-5 for HCC. (A) Pooled DOR of the SonoVue LR-5 algorithm. (B) Pooled DOR of the Sonazoid modified LR-5 algorithm. LR-5, LI-RADS category 5; HCC, hepatocellular carcinoma; DOR, diagnostic odds ratio; LI-RADS, liver imaging reporting and data system.

Table S2 Results of the meta-regression analysis of SonoVue LR-5 for the detection of HCC

Covariates	Subgroup	Studies (n)	Meta-analysis summary estimates of SonoVue LR-5			
			Sensitivity (95% CI)	P	Specificity (95% CI)	P
Study design	Prospective	3	0.53 (0.41–0.65)	<0.01	0.93 (0.83–1.00)	0.34
	Retrospective	16	0.70 (0.66–0.74)		0.93 (0.90–0.96)	
Study type	Cohort	17	0.68 (0.64–0.73)	0.15	0.92 (0.89–0.96)	0.69
	Case-control	2	0.68 (0.55–0.82)		0.97 (0.93–1.00)	
Center	Multi-center	3	0.63 (0.52–0.75)	0.24	0.92 (0.84–1.00)	0.18
	Single center	16	0.69 (0.65–0.74)		0.93 (0.90–0.96)	
Subject enrollment*	Consecutive	16	0.69 (0.64–0.74)	0.16	0.93 (0.90–0.96)	0.04
	Selective	2	0.68 (0.54–0.83)		0.97 (0.93–1.00)	
Lesions	<100	4	0.64 (0.53–0.75)	0.19	0.97 (0.94–1.00)	0.05
	≥100	15	0.69 (0.64–0.74)		0.92 (0.89–0.96)	
LI-RADS version	v2016	2	0.62 (0.47–0.76)	0.51	0.91 (0.79–1.00)	0.73
	v2017	17	0.69 (0.65–0.74)		0.93 (0.90–0.96)	
Reference standard	Pathology	8	0.67 (0.60–0.73)	0.01	0.90 (0.85–0.95)	0.01
	Pathology and imaging follow-up	11	0.70 (0.64–0.75)		0.95 (0.92–0.97)	

*, the study conducted by Schellhaas et.al did not explicitly mention the subject enrollment method employed and was thus excluded from the meta-analysis. LR-5, LI-RADS category 5; HCC, hepatocellular carcinoma; CI, confidence interval; LI-RADS, liver imaging reporting and data system; v2016, version 2016; v2017, version 2017.

Table S3 Results of the meta-regression analysis of Sonazoid modified LR-5 for the detection of HCC

Covariates	Subgroup	Studies (n)	Meta-analysis summary estimates of Sonazoid modified LR-5			
			Sensitivity (95% CI)	P	Specificity (95% CI)	P
Center	Multi-center	1	0.90 (0.78–1.00)	0.08	0.85 (0.69–1.00)	0.51
	Single center	7	0.80 (0.73–0.87)		0.86 (0.80–0.93)	
Lesions	<100	1	0.77 (0.54–1.00)	0.31	1.00 (1.00–1.00)	<0.01
	≥100	7	0.82 (0.75–0.89)		0.85 (0.79–0.92)	
LI-RADS version	Version 1	2	0.90 (0.86–0.95)	0.18	0.87 (0.76–0.92)	0.15
	Version 2	6	0.77 (0.71–0.82)		0.86 (0.79–0.93)	
Reference standard	Pathology	2	0.83 (0.71–0.95)	0.12	0.86 (0.75–0.98)	0.17
	Pathology and imaging follow-up	6	0.81 (0.73–0.89)		0.86 (0.79–0.93)	

LR-5, LI-RADS category 5; HCC, hepatocellular carcinoma; CI, confidence interval; LI-RADS, liver imaging reporting and data system.

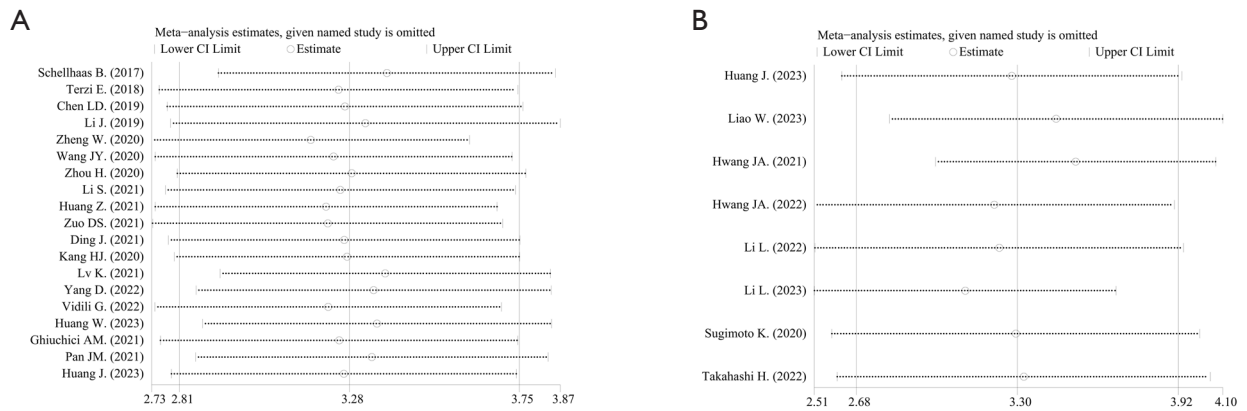


Figure S3 Results of the sensitivity analysis of the SonoVue LR-5 and Sonazoid modified LR-5 algorithms. (A) Sonazoid LR-5 algorithm and (B) Sonazoid modified LR-5 algorithm. LR-5, LI-RADS category 5; LI-RADS, Liver Imaging Reporting and Data System.

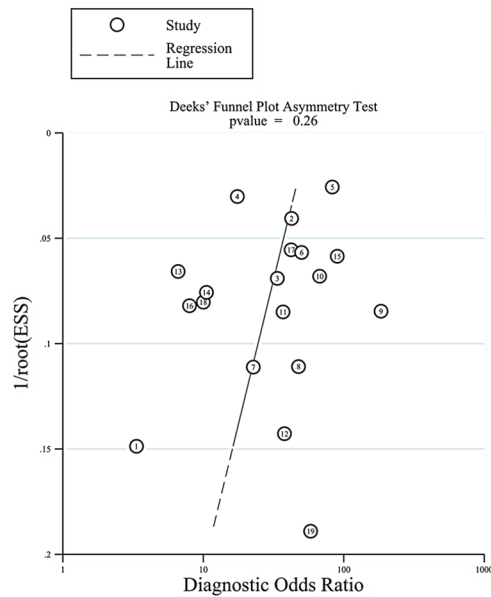


Figure S4 Results of the publication bias and quality assessment. (A) Deeks' funnel plot of SonoVue LR-5. (B) Deeks' funnel plot of Sonazoid modified LR-5. ESS, effective sample sizes; LR-5, LI-RADS category 5; LI-RADS, liver Imaging Reporting and Data System.