

Table S1 Detailed search strategy

Database	Search strategy
PubMed	(((((CEUS) OR (contrast-enhanced ultrasound)) OR ((contrast enhanced ultrasound) AND ((HCC) OR (Carcinomas, Hepatocellular))) 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 (((perflubutane) OR (Sonazoid)) OR (fluorocarbons))
Embase	<ol style="list-style-type: none"> 1 exp liver cell carcinoma/ 2 exp contrast-enhanced ultrasound/ 3 (CEUS or contrast enhanced ultrasound).tw. 4 2 or 3 5 exp perflubutane/ 6 4 and 5 7 (LI-RADS or LIRADS).tw,kw,kf. 8 (liver imaging reporting and data system).mp. 9 (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. 10 7 or 8 or 9 11 6 and 10 12 1 and 11
MEDLINE	<ol style="list-style-type: none"> 1 exp Carcinoma, Hepatocellular/ 2 (CEUS or contrast enhanced ultrasound).tw,kw,kf. 3 (LI-RADS or LIRADS).tw,kw,kf. 4 (liver imaging reporting and data system).tw,kw,kf. 5 (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,kw,kf. 6 3 or 4 or 5 7 1 and 2 and 6 8 perflubutane.mp. 9 Sonazoid.mp. 10 8 or 9 11 7 and 10
Web of Science	<ol style="list-style-type: none"> 1.((ALL=(Carcinoma, Hepatocellular) OR ALL=(Cholangiocarcinoma) OR ALL=(HCC) 2.(((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) 3.(((ALL=(ultrasound)) OR ALL=(CEUS)) OR ALL=(contrast-enhanced ultrasound)) OR ALL=(contrast enhanced ultrasound) 4. #3 AND #2 AND #1 5. ((ALL=(Sonazoid)) OR ALL=(perflubutane)) OR ALL=(fluorocarbons) 6. #5 AND #4
Cochrane Central Register of Controlled Trials	((('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')): ti,ab,kw AND (('Carcinoma, Hepatocellular' or 'Cholangiocarcinoma' or 'hepatocellular carcinoma*' or 'hepatocellular neoplasm*' or 'hepatocellular cancer' or 'hepatic cell carcinoma*' or HCC or cholangiocarcinoma* or 'hepatic nodule*' or 'liver lesion*' or 'liver nodule*' or 'liver neoplasm*')): ti,ab,kw AND (('CEUS' or 'contrast enhanced ultrasound' or 'contrast-enhanced ultrasound')): ti,ab,kw AND (('perflubutane' or 'Sonazoid' or 'fluorocarbons')): ti,ab,kw with publication year from 2016 to 2023, in trials (word variations have been searched)

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

Covariate	Subgroup	Sensitivity (95% CI)	P values	Specificity (95% CI)	P values
Study Design	Retrospective (n=6)	0.71 (0.64–0.77)	0.20	0.86 (0.80–0.92)	<0.01
	Prospective (n=2)	0.66 (0.54–0.79)		0.96 (0.92–1.00)	
Reviewer	Multi-reviewer (n=7)	0.71 (0.66–0.76)	0.49	0.89 (0.83–0.95)	<0.01
	Single reviewer (n=1)	0.52 (0.34–0.70)		0.92 (0.81–0.97)	

ACR, American College of Radiology; LR-5, Liver Imaging Reporting and Data System category 5; HCC, hepatocellular carcinoma; 95% CI, 95% confidence interval.

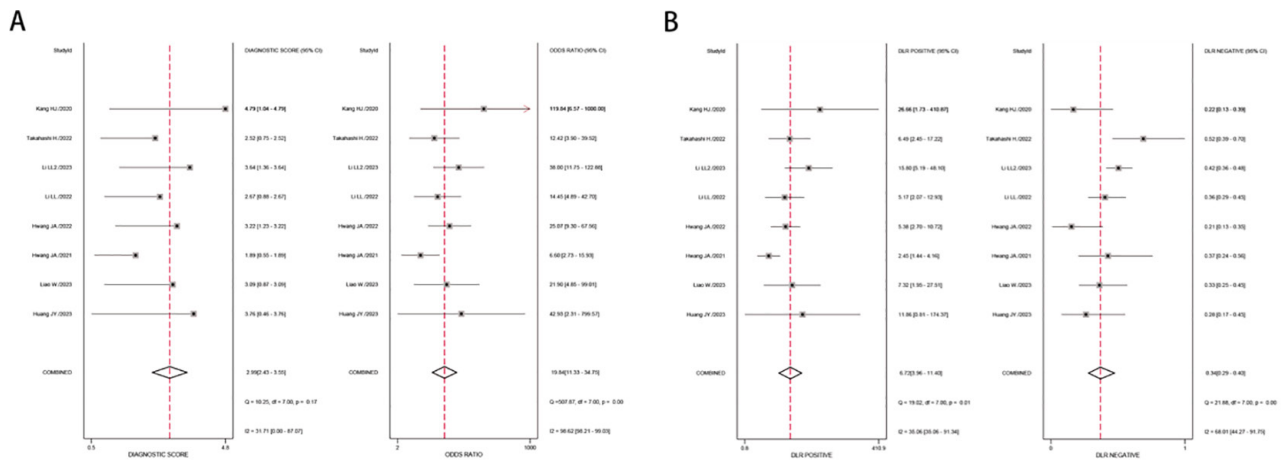


Figure S1 Forest plots of the LR-5 for HCC. (A) Pooled DOR of the ACR LR-5 algorithm. (B) Pooled +LR and -LR of the ACR LR-5 algorithm. 95% CI, 95% confidence interval; LR-5, Liver Imaging Reporting and Data System category 5; HCC, hepatocellular carcinoma; ACR, American College of Radiology; DOR, diagnostic odds ratio; +LR, positive likelihood ratio; -LR, negative likelihood ratio.

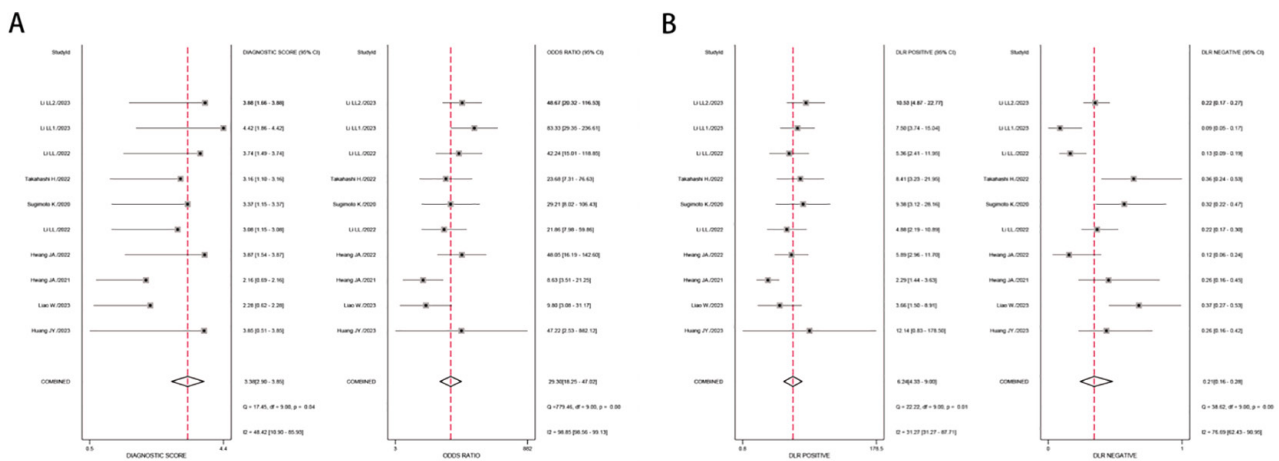


Figure S2 Forest plots of the LR-5 for HCC. (A) Pooled DOR of the modified LR-5 algorithm. (B) Pooled +LR and -LR of the modified LR-5 algorithm. 95% CI, 95% confidence interval; LR-5, Liver Imaging Reporting and Data System category 5; HCC, hepatocellular carcinoma; DOR, diagnostic odds ratio; +LR, positive likelihood ratio; -LR, negative likelihood ratio.

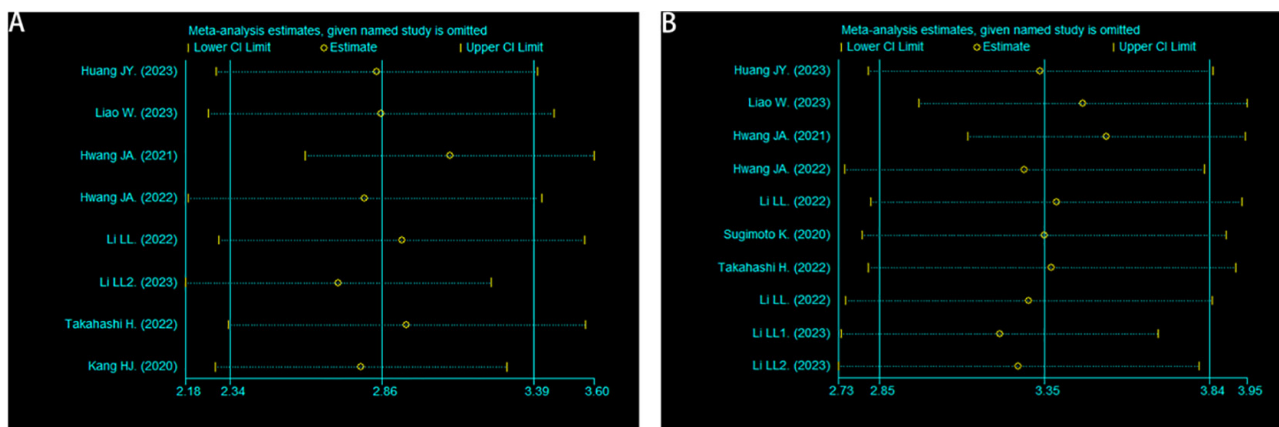


Figure S3 Results of sensitivity analysis of ACR and the modified LR-5 algorithms. (A) Sonazoid ACR LR-5 algorithm and (B) Sonazoid modified LR-5 algorithm. ACR, American College of Radiology; LR-5, Liver Imaging Reporting and Data System category 5.

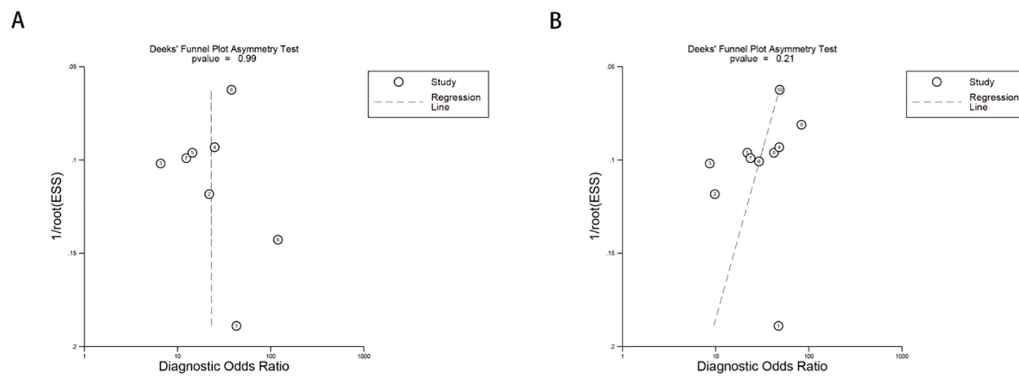


Figure S4 Results of publication bias and quality assessment. (A) Deeks funnel plot of Sonazoid ACR LI-RADS. (B) Deeks funnel plot of Sonazoid modified LI-RADS. ACR, American College of Radiology; LI-RADS, Liver Imaging Reporting and Data System.