Supplementary

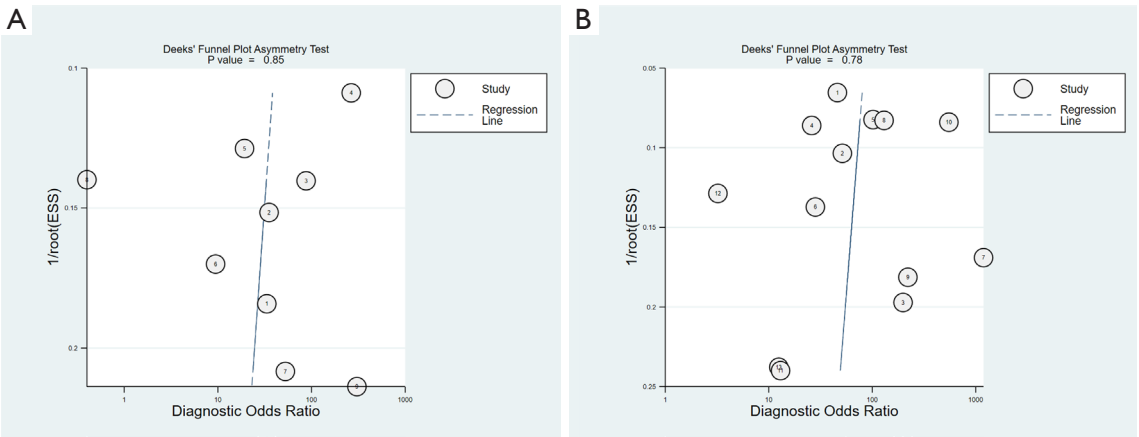

Figure S1 Deeks funnel plots of (A) CEUS and (B) HR-MRI. ESS, effective sample size; CEUS, contrast-enhanced ultrasound; HR-MRI, high-resolution magnetic resonance imaging.

Table S1 Search strategy

Database	CEUS	HR-MRI
PubMed	((("contrast-enhanced ultrasound" [Title/Abstract] OR "CEUS" [Title/Abstract]) AND (("carotid arteries" [MeSH]) AND ("atherosclerotic plaque" [MeSH] OR "atherosclerosis" [MeSH] OR "carotid stenosis" [MeSH]))))	((("magnetic resonance imaging" [Title/abstract] OR "MRI" [Title/abstract])) AND (("carotid arteries" [MeSH]) AND ("atherosclerotic plaque" [MeSH] OR "atherosclerosis" [MeSH] OR "carotid stenosis" [MeSH]))))
Cochrane library	1.MeSH descriptor: [carotid arteries] explode all tree 2.MeSH descriptor: [atherosclerotic plaque] explode all tree 3. MeSH descriptor: [atherosclerosis] explode all tree 4. MeSH descriptor: [atherosclerotic plaque] explode all tree 5."contrast-enhanced ultrasound": ti,ab,kw (word variations have been searched) 6."CEUS": ti,ab,kw (word variations have been searched) 7. 2 or 3 or 4 8. 5 or 6 9. 1 and 7 and 8	1.Mesh descriptor: [carotid arteries] explode all tree 2.MeSH descriptor: [atherosclerotic plaque] explode all tree 3. MeSH descriptor: [atherosclerosis] explode all tree 4. MeSH descriptor: [atherosclerotic plaque] explode all tree 5."magnetic resonance imaging": ti,ab,kw (word variations have been searched) 6. "MRI": ti,ab,kw (word variations have been searched) 7. 2 or 3 or 4 8. 5 or 6 9. 1 and 7 and 8
Embase	(("carotid arteries").ti. or ("carotid arteries").ab. or ("carotid arteries").kw.) and (("atherosclerotic plaque" or "atherosclerosis" or "atherosclerotic plaque"). ti. or ("atherosclerotic plaque" or "atherosclerosis" or "atherosclerotic plaque").ab. or ("atherosclerotic plaque" or "atherosclerosis" or "atherosclerotic plaque").kw.) and (("CEUS" or "contrast-enhanced ultrasound").ti. or ("CEUS" or "contrast-enhanced ultrasound").ab. or("CEUS" or "contrast-enhanced ultrasound").kw.)	(("carotid arteries").ti. or ("carotid arteries").ab. or ("carotid arteries").kw.) and (("atherosclerotic plaque" or "atherosclerosis" or "atherosclerotic plaque"). ti. or ("atherosclerotic plaque" or "atherosclerosis" or "atherosclerotic plaque").ab. or ("atherosclerotic plaque" or "atherosclerosis" or "atherosclerotic plaque").kw.) and (("MRI" or "magnetic resonance imaging").ti. or ("MRI" or "magnetic resonance imaging").ab. or ("MRI" or "magnetic resonance imaging").kw.)
Web of Science	1.TS= (plaque, atherosclerotic OR plaque, stenosis OR atherosclerosis) 2.TS= (carotid OR carotid artery OR carotid arteries OR artery carotid OR arteries carotid) 3.TS= (contrast-enhanced ultrasound OR CEUS) 4.1 AND 2 AND 3	1.TS= (plaque, atherosclerotic OR plaque, stenosis OR atherosclerosis) 2.TS= (carotid OR carotid artery OR carotid arteries OR artery carotid OR arteries carotid) 3.TS= (magnetic resonance imaging OR MRI) 4.1 AND 2 AND 3

CEUS, contrast-enhanced ultrasound; HR-MRI, high-resolution magnetic resonance imaging.

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Table S2 Details of QUADAS-2 assessment for the included studies

Studies (year)	ROB																
	Domain 1: patient selection					Domain 2: index test				Domain 3: reference standard				Domain 4: flowing and timing			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)
Fresilli D (2022)	L	Y	Y	Y	L	L	Y	Y	L	UN	Y	UN	L	L	Y	Y	Y
D'Oria (2018)	UN	UN	Y	UN	UN	L	Y	Y	L	L	Y	Y	L	UN	UN	Y	Y
Huang S (2021)	UN	UN	Y	Y	UN	UN	UN	Y	UN	UN	Y	UN	UN	L	Y	Y	Y
Iezz R (2015)	L	Y	Y	Y	L	L	Y	Y	L	UN	Y	UN	UN	UN	UN	Y	Y
Lyu Q (2021)	L	Y	Y	Y	L	L	Y	Y	L	L	Y	Y	L	UN	UN	Y	Y
Uchihara Y (2023)	UN	Y	Y	UN	UN	L	Y	Y	L	L	Y	Y	L	H	Y	Y	N
Di Leo (2018)	UN	Y	Y	UN	UN	UN	Y	UN	UN	UN	Y	UN	UN	UN	UN	Y	Y
Cai JM (2002)	L	Y	Y	Y	L	L	Y	Y	L	L	Y	Y	Y	UN	UN	Y	Y
Cappendijk VC (2004)	UN	UN	Y	UN	UN	L	Y	Y	L	L	Y	Y	L	L	Y	Y	Y
Chu B (2004)	UN	UN	Y	UN	UN	L	Y	Y	L	L	Y	Y	L	L	Y	Y	Y
Kampschulte A (2004)	UN	UN	Y	UN	UN	L	Y	Y	L	L	Y	Y	L	H	Y	Y	N
Moody AR (2003)	H	N	Y	UN	H	L	Y	Y	L	L	Y	Y	L	UN	UN	Y	Y
Hideki O (2010)	L	Y	Y	Y	L	UN	Y	UN	UN	L	Y	Y	L	UN	UN	Y	Y
Puppini G (2006)	UN	UN	Y	UN	UN	UN	UN	Y	UN	UN	Y	UN	UN	L	Y	Y	Y
Tapis P (2020)	UN	UN	Y	Y	UN	UN	UN	Y	UN	L	Y	Y	L	H	UN	Y	N
Qiao Y (2011)	UN	UN	Y	UN	UN	L	Y	Y	L	L	Y	Y	L	H	Y	Y	N
Narumi S (2015)	UN	Y	Y	UN	UN	UN	Y	UN	UN	UN	Y	UN	UN	UN	UN	Y	Y
Chai JT (2017)	UN	UN	Y	UN	UN	L	Y	Y	L	L	Y	Y	L	L	Y	Y	Y
Motoyama R (2019)	UN	Y	Y	UN	UN	L	Y	Y	L	L	Y	Y	L	L	Y	Y	Y
Zhao KQ (2018)	UN	UN	Y	Y	UN	UN	UN	UN	Y	UN	UN	Y	UN	UN	UN	Y	Y

(1) Could the selection of patients have introduced bias? (2) Was a consecutive or random sample of patients enrolled? (3) Was a case control design avoided? (4) Did the study avoid inappropriate exclusions? (5) Applicability: are there concerns that the included patients and setting do not match the review question? (6) Could the conduct or interpretation of the index test have introduced bias? (7) Were the index test results interpreted without knowledge of the results of the reference standard? (8) If a threshold was used, was it prespecified? (9) Applicability: are there concerns that the index test, its conduct, or its interpretation differ from the review question? (10) Could the reference standard, its conduct, or its interpretation have introduced bias? (11) Is the reference standard likely to correctly classify the target condition? (12) Were the reference standard results interpreted without knowledge of the results of the index test? (13) Applicability: are there concerns that the target condition as defined by the reference standard does not match the question? (14) Could the patient flowing have introduced bias? (15) Was there an appropriate interval between the index test and reference standard? (16) Did all patients receive the same reference standard? (17) Were all patients included in the analysis? QUDAS-2, Quality Assessment of Diagnostic Accuracy Studies 2; ROB, risk of bias; L, low risk or low concerns; Y, yes; UN, unclear or unclear risk or unclear concerns; H, high risk or high concerns; N, no.

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Table S3 Subgroup analyses for pooled values for identifying plaque vulnerability of CEUS studies

Subgroup	No. of studies	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR (95% CI)	AUC (SE)	Heterogeneity, I^2 (%) (P)
Region								
Asia	5	0.93 (0.89–0.96)	0.80 (0.69–0.88)	4.12 (2.30–7.40)	0.11 (0.06–0.19)	41.43 (17.62–97.41)	0.95 (0.03)	0.0 (0.44)
Europe	4	0.77 (0.70–0.83)	0.73 (0.61–0.82)	2.57 (0.70–9.45)	0.24 (0.05–1.22)	12.57 (0.73–215.56)	0.85 (0.16)	92.1 (<0.001)
Study design								
Prospective	5	0.77 (0.70–0.83)	0.71 (0.61–0.80)	2.66 (1.05–6.72)	0.19 (0.04–0.88)	15.16 (1.55–148.01)	0.82 (0.11)	89.9 (<0.001)
Retrospective	4	00.92 (0.87–0.96)	0.84 (0.73–0.93)	5.26 (1.49–18.59)	0.11 (0.06–0.22)	57.49 (10.28–321.62)	0.95 (0.04)	63.7 (0.04)
Sample size								
≥50	6	0.84 (0.79–0.88)	0.78 (0.69–0.85)	3.77 (1.29–11.00)	0.14 (0.04–0.55)	31.08 (3.18–303.68)	0.90 (0.08)	90.7 (<0.001)
<50	3	0.89 (0.80–0.95)	0.71 (0.52–0.86)	2.76 (1.61–4.72)	0.16 (0.08–0.32)	19.29 (6.42–57.97)	0.96 (0.08)	0.0 (0.43)
Plaque composition								
IPN	6	0.83 (0.77–0.87)	0.76 (0.65–0.84)	3.37 (1.06–10.74)	0.16 (0.04–0.60)	24.85 (2.37–260.85)	0.87 (0.10)	89.4 (<0.001)
Others	3	0.92 (0.84–0.96)	0.77 (0.65–0.86)	3.64 (1.76–7.50)	0.12 (0.06–0.23)	32.91 (12.98–83.49)	0.95 (0.03)	0.0 (0.43)
Mechanical index								
>0.2	4	0.94 (0.89–0.97)	0.72 (0.57–0.84)	3.09 (1.96–4.87)	0.10 (0.05–0.20)	34.10 (13.06–89.04)	0.86 (0.15)	0.0 (0.39)
≤0.2	5	0.78 (0.72–0.84)	0.78 (0.69–0.85)	3.46 (0.99–12.07)	0.22 (0.05–0.85)	18.33 (1.53–219.54)	0.88 (0.10)	91.3 (<0.001)
JCR region								
1	4	0.81 (0.74–0.86)	083 (0.73–0.90)	5.40 (0.45–65.32)	0.16 (0.02–1.02)	37.19 (0.83–1668.75)	0.92 (0.09)	93.9 (<0.001)
≤2	5	0.91 (0.85–0.95)	0.68 (0.56–0.79)	2.72 (1.93–3.83)	0.14 (0.08–0.23)	21.57 (10.01–46.46)	0.91 (0.09)	0.0 (0.72)

CEUS, contrast-enhanced ultrasound; CI, confidence interval; LR+, positive likelihood ratio; LR–, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the curve; SE, standard error; IPN, intraplaque neovascularization; JCR, Journal Citation Reports.

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Table S4 Subgroup analyses for pooled values for identifying plaque vulnerability of HR-MRI studies

Subgroup	No. of studies	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)	DOR (95% CI)	AUC (SE)	Heterogeneity, I^2 (%) (P)
Region								
Asia	6	0.87 (0.83–0.91)	0.88 (0.84–0.92)	7.71 (1.38–43.07)	0.18 (0.11–0.29)	54.44 (10.27–288.43)	0.92 (0.02)	79.8 (<0.001)
Europe	7	0.88 (0.84–0.90)	0.90 (0.86–0.93)	7.36 (4.09–13.24)	0.16 (0.10–0.27)	53.72 (28.90–99.87)	0.94 (0.01)	29.0 (0.20)
Study design								
Prospective	10	0.89 (0.87–0.92)	0.87 (0.84–0.90)	6.08 (2.54–14.57)	0.15 (0.10–0.21)	43.12 (19.12–97.25)	0.94 (0.02)	67.5 (0.001)
Retrospective	3	0.79 (0.71–0.85)	0.96 (0.92–0.99)	16.33 (3.82–69.73)	0.23 (0.09–0.58)	81.39 (12.30–538.53)	0.80 (0.33)	61.1 (0.08)
Sample size								
≥50	8	0.88 (0.85–0.90)	0.89 (0.86–0.91)	7.49 (2.70–20.79)	0.16 (0.12–0.22)	45.74 (20.08–104.21)	0.94 (0.02)	74.8 (<0.001)
<50	5	0.86 (0.79–0.92)	0.93 (0.81–0.99)	5.71 (2.49–13.11)	0.11 (0.02–0.55)	68.08 (12.54–369.51)	0.95 (0.03)	36.0 (0.18)
Plaque composition								
IPH	5	0.87 (0.83–0.90)	0.89 (0.85–0.92)	8.77 (1.59–48.45)	0.17 (0.13–0.23)	44.48 (10.86–182.24)	0.93 (0.01)	83.7 (<0.001)
Others	8	0.88 (0.85–0.91)	0.89 (0.85–0.93)	6.78 (4.88–9.44)	0.14 (0.07–0.27)	54.40 (28.21–104.90)	0.94 (0.01)	17.3 (0.29)
Strength field								
1.5T	7	0.89 (0.87–0.92)	0.88 (0.84–0.91)	6.43 (4.26–9.72)	0.13 (0.09–0.20)	49.24 (28.77–84.26)	0.94 (0.01)	22.5 (0.26)
Others	6	0.83 (0.77–0.88)	0.91 (0.86–0.94)	7.75 (0.81–74.44)	0.23 (0.12–0.44)	41.73 (6.76–257.45)	0.92 (0.02)	80.8 (0.0001)
JCR region								
1	8	0.89 (0.86–0.91)	0.90 (0.87–0.93)	7.54 (4.72–12.04)	0.15 (0.10–0.21)	54.16 (33.77–86.87)	0.94 (0.01)	16.3 (0.30)
≤2	5	0.84 (0.78–0.89)	0.85 (0.78–0.91)	7.96 (0.43–146.43)	0.22 (0.08–0.58)	41.07 (3.62–465.84)	0.92 (0.03)	82.2 (0.0002)

HR-MRI, high-resolution magnetic resonance imaging; CI, confidence interval; LR+, positive likelihood ratio; LR–, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the curve; SE, standard error; IPH, intraplaque hemorrhage; JCR, Journal Citation Reports.

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