Health Technology Review

Supporting Information for RapidAI Review

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Abbreviations

AI	artificial intelligence
ICH	intracranial hemorrhage
LVO	large vessel occlusion
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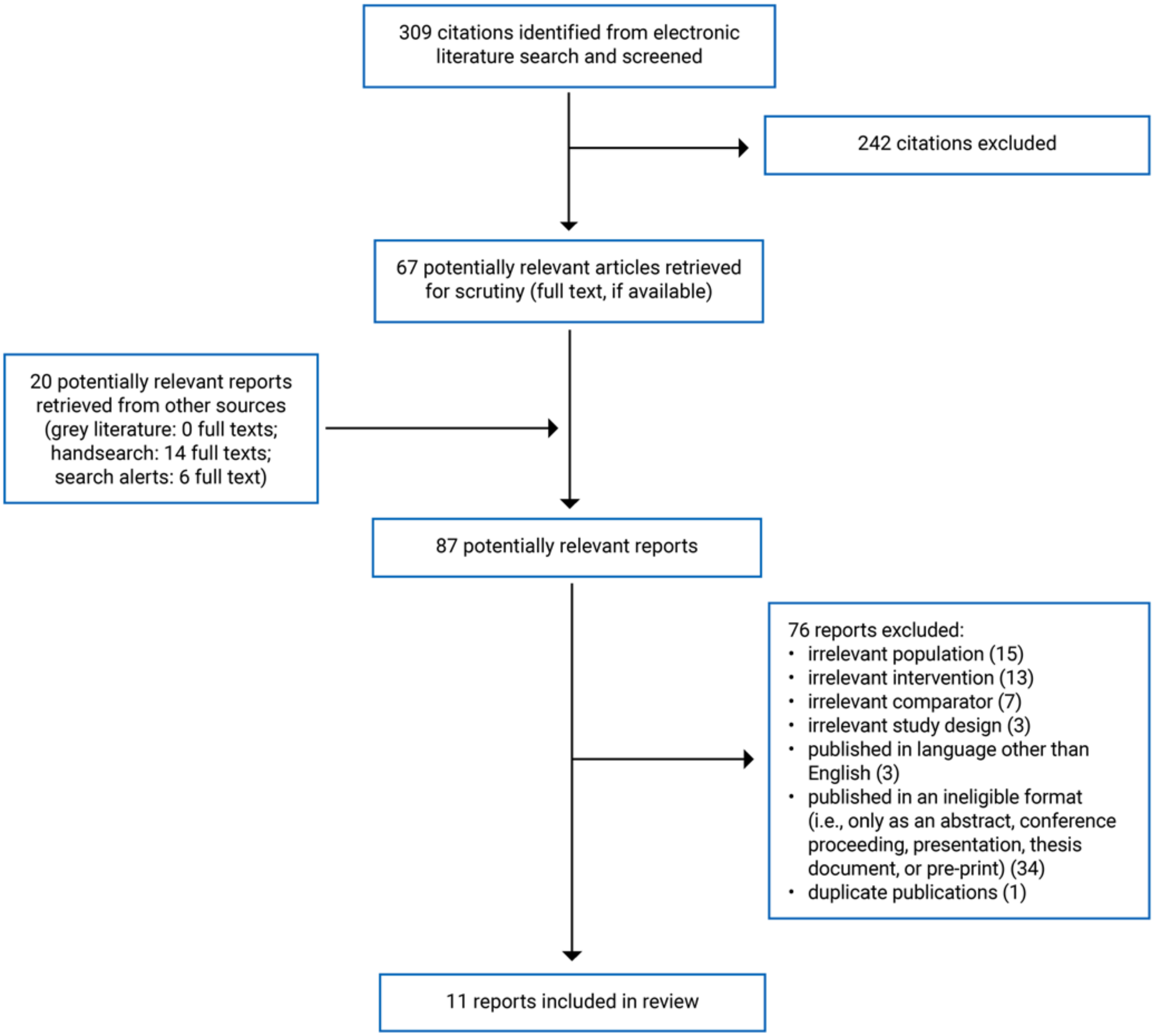
Selection of Included Studies

Figure 1: Selection of Included Studies



List of Included Publications

The citations provided in this list are the publications that were included in this rapid review (in reverse chronological and alphabetical order).

Delora A, Hadjialiakbari C, Percenti E, Torres J, Alderazi YJ, Ezzeldin R, Hassan AE, Ezzeldin M. Viz LVO versus Rapid LVO in detection of large vessel occlusion on CT angiography for acute stroke. J Neurointerv Surg. 2024 May 21;16(6):599 to 602. doi: 10.1136/jnis-2023-020445. PMID: 37355255.

Slater LA, Ravintharan N, Goergen S, et al. RapidAI compared with Human Readers of Acute Stroke Imaging for Detection of Intracranial Vessel Occlusion. Stroke: Vascular and Interventional Neurology. 2024;4:e001145

Chan N, Sibtain N, Booth T, de Souza P, Bibby S, Mah YH, Teo J, U-King-Im JM. Machine-learning algorithm in acute stroke: real-world experience. Clin Radiol. 2023 Feb;78(2):e45-e51. doi: 10.1016/j.crad.2022.10.007. Epub 2022 Nov 18. PMID: 36411087.

Soun JE, Zolyan A, McLouth J, et al. Impact of an automated large vessel occlusion detection tool on clinical workflow and patient outcomes. Frontiers in neurology [electronic resource]. 2023; 14():1179250. PubMed: 37305764

Yedavalli V, Heit JJ, Dehkharghani S, et al. Performance of RAPID noncontrast CT stroke platform in large vessel occlusion and intracranial hemorrhage detection. Front Neurol. 2023; 14():. PubMed:

Mallon DH, Taylor EJR, Vittay OI, Sheeka A, Doig D, Lobotesis K. Comparison of automated ASPECTS, large vessel occlusion detection and CTP analysis provided by Brainomix and RapidAI in patients with suspected ischemic stroke. J Stroke Cerebrovasc Dis. Oct 2022; 31(10):106702. PubMed: 35994882

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Adhya J, Li C, Eisenmenger L, Cerejo R, Tayal A, Goldberg M, Chang W. Positive predictive value and stroke workflow outcomes using automated vessel density (RAPID-CTA) in stroke patients: One year experience. Neuroradiol J. 2021 Oct;34(5):476 to 481. doi: 10.1177/19714009211012353. Epub 2021 Apr 28. PMID: 33906499; PMCID: PMC8559016.

Dehkharghani S, Lansberg M, Venkatsubramanian C, Cereda C, Lima F, Coelho H, Rocha F, Qureshi A, Haerian H, Mont'Alverne F, Copeland K, Heit J. High-Performance Automated Anterior Circulation CT Angiographic Clot Detection in Acute Stroke: A Multireader Comparison. Radiology. 2021 Mar;298(3):665 to 670. doi: 10.1148/radiol.2021202734. Epub 2021 Jan 12. PMID: 33434110.

Amukotuwa SA, Straka M, Smith H, Chandra RV, Dehkharghani S, Fischbein NJ, Bammer R. Automated Detection of Intracranial Large Vessel Occlusions on CT Angiography: A Single Center Experience. Stroke. 2019 Oct;50(10):2790 to 2798. doi: 10.1161/STROKEAHA.119.026259. Epub 2019 Sep 9. PMID: 31495328.

List of Excluded Publications and Reasons for Exclusion

The citations provided in this list are studies that were excluded after full-text review as part of the rapid review (in reverse chronological and alphabetical order).

Ineligible Population (n = 15)

Alwood BT, Meyer DM, Ionita C, et al. Multicenter comparison using 2 AI stroke CT perfusion software packages for determining thrombectomy eligibility. J Stroke Cerebrovasc Dis. 2024 Jul;33(7):107750. Epub 2024 May 2. PubMed: 38703875.

Pisani L, Haussen DC, Mohammaden M, et al. Comparison of CT Perfusion Software Packages for Thrombectomy Eligibility. Ann Neurol. 11 2023; 94(5):848 to 855. PubMed: 37584452

Yedavalli V, Hamam O, Mohseni A, et al. Pretreatment brain CT perfusion thresholds for predicting final infarct volume in distal medium vessel occlusions. J Neuroimaging. Nov-Dec 2023; 33(6):968 to 975. PubMed: 37357133

Xiong Y, Luo Y, Wang M, et al. Evaluation of Diffusion-Perfusion Mismatch in Acute Ischemic Stroke with a New Automated Perfusion-Weighted Imaging Software: A Retrospective Study. Neurol. Dec 2022; 11(4):1777 to 1788. PubMed: 36201112

Wouters A, Robben D, Christensen S, et al. Prediction of Stroke Infarct Growth Rates by Baseline Perfusion Imaging. Stroke. 02 2022; 53(2):569 to 577. PubMed: 34587794

Bouslama M, Ravindran K, Harston G, et al. Noncontrast CT e-Stroke Infarct Volume Is Similar to RAPID CT Perfusion in Estimating Postreperfusion Infarct Volumes. Stroke. 01 2021; 52(2):634 to 641. PubMed: 33430633

Maegerlein C, Fischer J, Monch S, et al. Automated Calculation of the Alberta Stroke Program Early CT Score: Feasibility and Reliability. Radiology. 04 2019; 291(1):141 to 148. PubMed: 30720400

Demeestere J, Scheldeman L, Cornelissen SA, et al. Alberta Stroke Program Early CT Score Versus Computed Tomographic Perfusion to Predict Functional Outcome After Successful Reperfusion in Acute Ischemic Stroke. Stroke. 10 2018; 49(10):2361 to 2367. PubMed: 30355098

Automated CT perfusion imaging to aid in the selection of patients with acute ischemic stroke for mechanical thrombectomy: A health technology assessment. Ont Health Technol Assess Ser. 2020; 20(13)():1 to 87. PubMed: 2005424949

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Kurmann CC, Kaesmacher J, Cooke DL, et al. Evaluation of time-resolved whole brain flat panel detector perfusion imaging using RAPID ANGIO in patients with acute stroke: Comparison with CT perfusion imaging. J Neurointerv Surg. 2023; 15(4):387 to 392. PubMed:

Pistocchi S, Strambo D, Bartolini B, et al. MRI software for diffusion-perfusion mismatch analysis may impact on patients' selection and clinical outcome. Eur Radiol. 2022; 32(2):1144 to 1153. PubMed:

Amukotuwa SA, Straka M, Dehkharghani S, Bammer R. Fast Automatic Detection of Large Vessel Occlusions on CT Angiography. Stroke. 2019 Dec;50(12):3431 to 3438. doi: 10.1161/STROKEAHA.119.027076. Epub 2019 Nov 4. PMID: 31679501; PMCID: PMC6878187.

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Siegler JE, Olsen A, Pulst-Korenberg J, Cristancho D, Rosenberg J, Raab L, Cucchiara B, Messé SR. Multicenter Volumetric Assessment of Artifactual Hypoperfusion Patterns using Automated CT Perfusion Imaging. J Neuroimaging. 2019 Sep;29(5):573 to 579. doi: 10.1111/jon.12641. Epub 2019 Jun 14. PMID: 31199025; PMCID: PMC6731139.

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Deshpande A, Elliott J, Jiang B, et al. End to end stroke triage using cerebrovascular morphology and machine learning. Front Neurol. 2023; 14(no pagination)():. PubMed: 2026464700

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Xiong Y, Huang CC, Fisher M, Hackney DB, Bhadelia RA, Selim MH. Comparison of Automated CT Perfusion Softwares in Evaluation of Acute Ischemic Stroke. J Stroke Cerebrovasc Dis. 2019 Dec;28(12):104392. doi: 10.1016/j.jstrokecerebrovasdis.2019.104392. Epub 2019 Sep 25. PMID: 31562038.

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John S, Hussain SI, Piechowski B, Dogar MA. Discrepancy in core infarct between non-contrast CT and CT perfusion when selecting for mechanical thrombectomy. J Cerebrovasc Endovasc Neurosurg. 2020; 22(1):8 to 14. PubMed:

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Miao KH, Miao JH. Enhancing Pain Management and Rehabilitation Outcomes in Stroke Patients with Artificial Intelligence and Medical Imaging. *J Investig Med*. 2021 April;69(4):935. PubMed: PM641217957

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Seo K, Kim GS, Yun PH, Suh SH. An introduction of the rapid software increased the number of mechanical thrombectomy with favourable outcome in stroke patients. Neuroradiology. 2019; 61(1)():S106. PubMed: 631878630

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Bouslama M, Rodrigues G, Ravindran K, Haussen D, Frankel M, Nogueira R. Ct perfusion and e-aspects automated noncontract CT ischemic core volumes: Correlations and clinical outcome prediction. Eur Stroke J. May 2019; 4(Supplement 1)():405. PubMed: 628560803

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Paz D, Yagoda D, Wein T. Single Site performance of AI software for stroke detection and Triage. medRxiv. 2021; ():2021.04.02.21253083. PubMed:

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Kamal H, Abdelhamid N, Zhu L, Sarraj A. Does RAPID reduce groin puncture times in acute, ischemic stroke? Presented at International Stroke Conference; 21 to 24 February 2017; Houston (TX). Stroke 2017;48(Suppl. 1):TP296.

Duplicate Publications (n = 1)

Hoving JW, Marquering HA, Majoie C, et al. Volumetric and Spatial Accuracy of CT Perfusion Estimated Ischemic Core Volume in Patients With Acute Ischemic Stroke. Stroke. 2018 10;49(10):2368 to 2375. PubMed: PM30355095

Characteristics of Included Publications

Table 1: Characteristics of Included Cohort Studies

Study citation, country, funding source	Study design and period	Population characteristics[a] and setting	Intervention and comparator(s)	Relevant clinical outcomes, length of follow-up
Soun et al. (2023)[1] United States **Funding source:** The Radiological Society of North America Research Scholar Grant	Retrospective non-concurrent cohort December 2019 to June 2020 (pre-Rapid LVO group) and December 2020 to June 2021 (post-Rapid LVO group)	**Population**: 760 patients presenting with suspected acute ischemic stroke who were imaged using CTA (with or without Rapid LVO)[b] **Age, median (IQR):** 75 (65 to 83) years vs. 71.5 (65 to 79) years **Sex or gender:** 55.2% vs. 45.2% female, other sexes or genders NR **Race:** African American (2.3% vs. 3.2%), Asian or Pacific Islander (32.6% vs. 38.7%), Hispanic (30.2% vs. 17.7%), white (30.2% vs. 40.3%), other or did not specify (4.7% vs. 0.0%) **Ethnicity, culture, or language:** NR **SES:** NR **Disability status:** NR **Setting:** A single comprehensive stroke centre in the US.	**Intervention:** Clinician interpretation of CTA imaging with Rapid LVO (Rapid 4.9) for the detection of M1 MCA and intracranial ICA LVO (i.e., post-Rapid LVO group) **Comparator**: Clinician interpretation of CTA imaging without Rapid LVO for the detection of M1 MCA and intracranial ICA LVO (i.e., pre-Rapid LVO group)	Radiology report turnaround time; time from door to image; time from door to intubation; time from door to needle (i.e., tPA therapy); time from door to puncture (i.e., thrombectomy); time from door to revascularization; stroke-related neurologic deficit (NIHSS scores); disability (mRS scores); response to therapy (TICI grades) **Follow-up**: Until discharge (mean time NR)
Adhya et al. (2021)[2] United States **Funding source:** No financial support was received for this work.	Retrospective non-concurrent cohort November 2018 to November 2019 (pre-Rapid CTA group) and November 2019 to November 2020 (post-Rapid CTA group)	**Population**: 146 patients who arrived at the emergency department for stroke or neurologic deficit and were imaged using CTA (with or without Rapid CTA post-processing) and subsequently underwent mechanical thrombectomy. **Age:** NR **Sex or gender:** NR **Race, ethnicity, culture, or language:** NR **SES:** NR **Disability status:** NR **Setting:** A large multi-hospital network in the US with comprehensive	**Intervention:** Clinician interpretation of CTA imaging with Rapid CTA (version NR) post-processing for the detection of LVO[c] (i.e., post-Rapid CTA group) **Comparator**: Clinician interpretation of CTA imaging without Rapid CTA for the detection of LVO[c] (i.e., pre-Rapid CTA group)	Disability (mRS scores); time from CTA to groin puncture (i.e., thrombectomy) **Follow-up:** 90 days

Study citation, country, funding source	Study design and period	Population characteristics[a] and setting	Intervention and comparator(s)	Relevant clinical outcomes, length of follow-up
		stroke centres and 24-hour neurointerventional coverage		

CTA = CT angiography; ICA = internal carotid artery; ICH = intracranial hemorrhage; IQR = interquartile range; LVO = large vessel occlusion; MCA = middle cerebral artery; mRS = modified Rankin Scale; NIHSS = US National Institutes of Health Stroke Scale; NR = not reported; SES = socioeconomic status; TICI = Thrombolysis in Cerebral Infarction; tPA = tissue plasminogen activator.

[a]Intervention group vs. comparator group, respectively.

[b]Baseline demographics were reported for patients who received acute therapies (i.e., tPA, thrombectomy, or both) and not the entire study population (n = 43 for post-Rapid LVO group; n = 62 for pre-Rapid LVO).

[c]Unclear which types of LVO were considered eligible. The study population included patients with occlusions of the ICA, carotid terminus, M1 MCA segment, or M2 MCA segment.

Table 2: Characteristics of Included Diagnostic Accuracy Studies

Study citation, country, funding source	Study design and period	Target condition	Population characteristics and setting	Index test and reference standard	Relevant outcomes
LVO					
Delora et al. (2024)[3] United States **Funding source**: The authors did not declare a specific grant for this research from any funding agency. HCA Health care supported this research and had financial interest in Viz.ai	Cross-sectional study with unclear selection January 2022 to January 2023	LVO[a]	**Population:** 360 patients who underwent CTA for suspected acute stroke **Age, mean (SD):** 65 (16.5) years **Sex or gender:** 44.4% males, other sexes or genders NR **Race, ethnicity, culture, or language:** NR **SES**: NR **Disability status**: NR **Setting:** Two community-based comprehensive stroke centers in the US	**Index test:** Evaluation of CTA by Rapid LVO (version 5.2.2) alone **Reference standard:** Interpretation of CTA by a single diagnostic or interventional neuroradiologist (with access to Rapid LVO results).	Sensitivity; specificity; TP; FP; TN; FN; PPV; NPV
Slater et al. (2024)[4] Australia **Funding source:** No financial support was received for this work.	Cohort selected cross-sectional study April 2021 to August 2021	LVO (defined as occlusions of the intracranial ICA, M1 or M2 MCA segments, basilar artery, or intracranial vertebral artery)	**Population:** 500 adult patients (aged ≥ 18 years) with clinical suspicion of ischemic stroke who underwent multimodality imaging (i.e., NCCT of the brain, CTA of the head, and CT perfusion) with RapidAI interpretation **Age, median (IQR):** 70 (56 to 80) years **Sex or gender:** 49.6% men, other sexes or genders NR **Race, ethnicity, culture,**	**Index test:** Rapid CTA (RapidAI 5.1) alone **Reference standard**: Independent assessment by 3 interventional neuroradiologists (with 10, 10, and 3 years of experience). Whenever the panel was not unanimous, a 4th neurointerventional radiologist (with 13	Sensitivity; specificity

Study citation, country, funding source	Study design and period	Target condition	Population characteristics and setting	Index test and reference standard	Relevant outcomes
			or language: NR **SES**: NR **Disability status**: NR **Setting:** A single comprehensive stroke centre in Australia	years of experience) made an additional independent assessment and disagreements were reviewed until consensus was reached.	
Chan et al. (2023)[5] UK **Funding source:** The funding source for this study was unclear. The authors declared financial interests and relationships with industry and medical research granting agencies	Cohort selected cross-sectional study January 2021 to March 2021	Terminal ICA and M1 MCA LVO	**Population**: 104 consecutive patients with suspected acute stroke who underwent imaging CT or CTA imaging **Age, median (range):** 62 (19 to 93) years **Sex or gender:** 41.3% women, other sexes or genders NR **Race, ethnicity, culture, or language:** NR **SES**: NR **Disability status**: NR **Setting:** A single tertiary neuroscience institution in the UK	**Index test:** Evaluation of CTA by Rapid CTA (version NR) alone **Reference standard**: Consensus assessment of LVO on CTA by 2 experienced neuroradiologists blinded to the initial report and the Rapid CTA interpretation	Sensitivity; specificity; TP; FP; TN; FN; PPV; NPV
Soun et al. (2023)[1] United States **Funding source:** The Radiological Society of North America Research Scholar Grant	Cohort selected cross-sectional study December 2020 to June 2021	M1 MCA and intracranial ICA LVO	**Population**: 321 patients presenting with suspected acute ischemic stroke who were imaged using CTA with Rapid LVO[b] **Age, median (IQR):** 75 (65 to 83) years **Sex or gender:** 55.2% female, other sexes or genders NR **Race:** 2.3% African American, 32.6% Asian or Pacific Islander, 30.2% Hispanic, 30.2% white, 4.7% other or did not specify **Ethnicity, culture, or language:** NR **SES:** NR **Disability status:** NR **Setting:** A single	**Index test:** Evaluation of CTA by Rapid LVO (Rapid 4.9) alone **Reference standard**: Assessment of LVO on CTA from the radiologist's reports (with Rapid LVO), which were verified by a board-certified neuroradiologist (with 9 years of experience). For complex cases where the reference standard was not clearly delineated, 2 additional 2 additional neuroradiologists (with 9 and 11 years of experience)	Sensitivity; specificity; PPV; NPV

Study citation, country, funding source	Study design and period	Target condition	Population characteristics and setting	Index test and reference standard	Relevant outcomes
			comprehensive stroke centre in the US	determined the reference standard	
Yedavalli et al. (2023)[6] United States **Funding source:** No financial support was received for this work	Cohort selected cross-sectional study Study period was NR	Distal intracranial ICA and M1 segment of the MCA	**Population:** 244 patients with suspected stroke who underwent NCCT and CTA imaging **Age, mean (SD):** NR **Sex or gender:** NR **Race, ethnicity, culture, or language:** NR **SES**: NR **Disability status**: NR **Setting**: Patient data from 7 hospitals (including academic and community hospitals) and 2 research studies that enrolled acute LVO patients were included	**Index test:** Evaluation of NCCT by Rapid NCCT Stroke platform (using the Rapid HVS to detect LVO) alone **Reference standard:** Consensus assessment of LVO on CTA by 2 of 3 neuroradiologists	Sensitivity; specificity; TP; FP; TN; FN.
Mallon et al. (2022)[7] UK **Funding source:** Imperial Health Charity and National Institute for Health Research Biomedical Research Centre based at Imperial College Health care NHS Trust and Imperial College London	Cohort selected cross-sectional study January 2016 and December 2020	LVO of the ICA and the M1 and M2 MCA segments	**Population:** 90 patients undergoing evaluation with CT perfusion for suspected anterior circulation LVO[c] **Age, median (IQR):** 70.5 (58 to 80) years **Sex or gender:** 48% female, 52% male, other sexes or genders NR **Race, ethnicity, culture, or language:** NR **SES**: NR **Disability status**: NR **Setting:** A single academic health science centre in the UK	**Index test:** Evaluation of CTA by RapidAI (version NR) alone **Reference standard:** Evaluation of CTA by a single neuroradiologist (with 4 years experience)	Sensitivity; specificity; TP; FP; TN; FN; PPV; NPV
Schlossman et al. (2022)[8] United States **Funding source**: Canon Medical	Cohort selected cross-sectional study December 2020 to June 2021	M1 and M2 MCA and intracranial ICA LVO	**Population:** 263 patients who underwent CTA for suspected acute ischemic stroke **Age, median (IQR):** 68 (56 to 79) years **Sex or gender:** 46.4% female, other sexes or genders NR **Race, ethnicity, culture, or language:** NR	**Index test:** Evaluation of CTA by Rapid LVO (RapidAI 4.9) alone **Reference standard**: Consensus assessment of LVO on CTA by 2 board-certified neuroradiologists (with 9 and 10 years of experience), with	Sensitivity; specificity; TP; FP; TN; FN; PPV; NPV

Study citation, country, funding source	Study design and period	Target condition	Population characteristics and setting	Index test and reference standard	Relevant outcomes
			SES: NR **Disability status**: NR **Setting:** A single comprehensive stroke centre in US	a 3rd board-certified neuroradiologist (with 11 years experience) to adjudicate disagreements	
Adhya et al. (2021)[2] United States **Funding source:** No financial support was received for this work	Cohort selected cross-sectional study November 2019 to November 2020	LVO[a]	**Population:** 310 patients who underwent CTA imaging for the evaluation of suspected acute ischemic stroke or neurologic deficit with relative vessel density of 60% or less **Age, mean (SD):** 70.0 (NR) years **Sex or gender:** 53% female, 47% male, other sexes or genders NR **Race, ethnicity, culture, or language:** NR **SES:** NR **Disability status:** NR **Setting:** A large multi-hospital network in the US with comprehensive stroke centres and 24-hour neurointerventional coverage	**Index test:** Evaluation of CTA by Rapid CTA (version NR) alone **Reference standard**: Consensus assessment of LVO on CTA by 2 board-certified neuroradiologists, with a 3rd board-certified neuroradiologist to adjudicate disagreements (although not required as there were no disagreements)	Sensitivity; specificity; TP; FP; TN; FN; PPV; NPV (at < 45% and < 60% thresholds for relative vessel density)
Dehkharghani et al. (2021)[9] United States **Funding source**: The authors received support from iSchemaView and the National Institute of Neurologic Disorders and Stroke	Case-control selected cross-sectional study Study period was NR	M1 MCA and intracranial ICA LVO	**Population**: 217 patients who underwent CTA imaging for suspected acute ischemic stroke **Age, mean (SD):** 64 (16) years **Sex or gender:** 46% female, 54% male, 1% unknown, other sexes or genders NR **Race, ethnicity, culture, or language:** NR **SES:** NR **Disability status**: NR **Setting**: Patient data from recent cerebrovascular trials and institutional registries from 11	**Index test:** Evaluation of CTA by Rapid LVO (version 1.0) alone **Reference standard**: Consensus assessment of LVO on CTA from up to 3 board-certified neuroradiologists with subspecialty certification (with 11, 7 and 7 years of experience)	Sensitivity; specificity; TP; FP; TN; FN

Study citation, country, funding source	Study design and period	Target condition	Population characteristics and setting	Index test and reference standard	Relevant outcomes
			worldwide sites were included		
Amukotuwa et al. (2019)[10] Australia **Funding source:** No financial support was received for this work.	Cohort selected cross-sectional study January 2017 to December 2018	LVO (defined as occlusions of the M1 MCA and intracranial ICA) and M2 MCA occlusions	**Population:** 477 patients who underwent multimodal brain CT (including NCCT, CT perfusion, and CTA) for suspected acute ischemic stroke. **Age, median (IQR):** 71 (60 to 80) years **Sex or gender:** 43.2% female, 56.8% male, other sexes or genders NR **Race, ethnicity, culture, or language:** NR **SES**: NR **Disability status**: NR **Setting:** A single regional hospital in Australia	**Index test:** Evaluation of CTA by Rapid CTA (RapidAI 4.9) alone. **Reference standard**: Consensus assessment of LVO on unenhanced CT, CTP, and CTA by 2 diagnostic neuroradiologists (with 8 and 9 years of post-fellowship experience), with a 3rd interventional neuroradiologist (with 7 years of experience) to verify decisions.	Sensitivity; specificity; TP; FP; TN; FN; PPV; NPV; AUC
ICH					
Eldaya et al. (2022)[11] United States **Funding source:** NR	Cohort selected cross-sectional study May 2020 to October 2020	ICH	**Population:** 308 patients presenting with acute neurologic deficit suspicious for acute stroke and underwent NCCT imaging with Rapid ICH **Age, mean (SD):** 61.0 (16.7) years **Sex or gender:** NR **Race, ethnicity, culture, or language:** NR **SES**: NR **Disability status**: NR **Setting:** A single large, tertiary comprehensive stroke centre in the US	**Index test:** Evaluation of NCCT by a board certified or board-eligible neuroradiologist, typically in conjunction with a radiology trainee, using Rapid ICH (version NR) **Reference standard**: When standalone Rapid ICH and neuroradiologist interpretation were concordant, it was considered the reference standard. In cases where there was disagreement between Rapid ICH and neuroradiologist interpretation, the reference standard was a consensus panel	Sensitivity; specificity; TP; FP; TN; FN; PPV; NPV

Study citation, country, funding source	Study design and period	Target condition	Population characteristics and setting	Index test and reference standard	Relevant outcomes
				of 3 board-certified neuroradiologists (with 3, 6, and 24 years of experience)	

AUC = area under the receiver operating characteristic curve; CT = CT; CTA = CT angiography; CTP = CT perfusion; FN = false negatives; FP = false positives; ICA = internal carotid artery; MCA = middle cerebral artery; NCCT = non-contrast CT; NPV = negative predictive value; NR = not reported; PPV = positive predictive value; SES = socioeconomic status; TN = true negatives; TP = true positives; tPA = tissue plasminogen activator.

[a]Unclear which types of LVO were considered eligible. In Delora et al. (2024),[3] the study population included patients with occlusions of the ICA, M1 MCA segment, and M2 MCA segment. The study population from Adhya et al. (2021) included patients with occlusions of the ICA, carotid terminus, M1 MCA segment, and M2 MCA segment.

[b]Baseline demographics were reported for patients who received acute therapies (i.e., tPA, thrombectomy, or both; n = 48) and not the entire study population.

[c]Baseline demographics were reported for patients with LVO according to the reference standard (n = 62) and not the entire study population.

Critical Appraisal of Included Studies

ROBINS-I Detailed Assessments

Table 3: Risk of Bias Assessment of Time to Intervention Outcomes Reported by Soun et al. (2023)[1] – ROBINS-I

Domain/question	Judgement	Comments
Decide whether to proceed with a risk-of-bias assessment		
1. Did the authors make any attempt to control for confounding?	No	There were no adjustments for confounding variables (e.g., age, sex or gender, race, ethnicity, disease severity, comorbidities, neurologist experience).
2. Is there sufficient potential for confounding that an unadjusted result should not be considered further?	Yes	Two cohorts of patients were enrolled during separate time periods. There were differences in patient disease characteristics at baseline and in the level of neurologist training between time periods which could affect the outcomes. This is particularly concerning as the study period partially overlapped with the COVID-19 pandemic, where many changes to the hospital system could have impacted time to treatment outcomes.
3. Was the method of measuring the outcome inappropriate?	NI	It was unclear who assessed time to intervention outcomes or how they were measured.
Risk of bias judgment	Critical (no further assessment is required)	For time to intervention outcomes, the study is at critical risk of bias due to confounding, as there were no attempts to control for differences across the 2 time periods which could have affected the outcomes.

NI = no information; ROBINS-I = Risk Of Bias In Nonrandomized Studies – of Interventions.

Table 4: Risk of Bias Assessment of Functional Status Outcomes Reported by Soun et al. (2023)[1] – ROBINS-I

Domain/question	Judgement	Comments
Decide whether to proceed with a risk-of-bias assessment		
1. Did the authors make any attempt to control for confounding?	Yes	For change in NIHSS score and NIHSS at discharge, there were adjustments for the effects of high cholesterol, heart disease, atrial fibrillation, therapies received, and NIHSS on admission. However, the authors provided no rationale for how these factors were selected, and it is unlikely that this would include all potential sources of baseline confounding. Additionally, there was no information as to how these confounding variables were measured. For the remaining measure of functional status, there were no adjustments for confounding variables.
2. Is there sufficient potential for confounding that an unadjusted result should not be considered further?	Yes	Two cohorts of patients were enrolled during separate time periods. There were differences in patient disease characteristics at baseline and in the level of neurologist training between time periods which could affect the outcomes. This is particularly concerning as the study period partially overlapped with the COVID-19 pandemic, where many changes to the hospital system could have impacted patient outcomes.
3. Was the method of measuring the outcome inappropriate?	Probably no	The tools used to assess outcomes related to functional status were reported, but it was unclear who conducted the assessments.
Risk of bias judgment	Critical (no further assessment is required)	For functional status outcomes, the study is at critical risk of bias due to confounding, as there were no or limited attempts to control for differences across the 2 time periods which could have affected the outcomes.

NIHSS = US National Institutes of Health Stroke Scale; ROBINS-I = Risk Of Bias In Nonrandomized Studies – of Interventions.

Table 5: Risk of Bias Assessment of Response to Therapy Outcomes Reported by Soun et al. (2023)[1] – ROBINS-I

Domain/question	Judgement	Comments
Decide whether to proceed with a risk-of-bias assessment		
1. Did the authors make any attempt to control for confounding?	No	There were no adjustments for confounding variables (e.g., age, sex or gender, race, ethnicity, disease severity, comorbidities, neurologist experience)
2. Is there sufficient potential for confounding that an unadjusted result should not be considered further?	Yes	Two cohorts of patients were enrolled during separate time periods. There were differences in patient disease characteristics at baseline and in the level of neurologist training between time periods which could affect the outcomes. This is particularly concerning as the study period partially overlapped with the COVID-19 pandemic, where many changes to the hospital system could have impacted patient outcomes.
3. Was the method of measuring the outcome inappropriate?	Probably no	The tools used to assess response to treatment outcomes were reported, but it was unclear who conducted the assessments.
Risk of bias judgment	Critical (no further assessment is required)	For response to treatment outcomes, the study is at critical risk of bias due to confounding, as there were no attempts to control for differences across the 2 time periods which could have affected the outcomes.

ROBINS-I = Risk Of Bias In Nonrandomized Studies – of Interventions.

Table 6: Risk of Bias Assessment of Time to Intervention Outcomes Reported by Adhya et al. (2021)[2] – ROBINS-I

Domain/question	Judgement	Comments
Decide whether to proceed with a risk-of-bias assessment		
1. Did the authors make any attempt to control for confounding?	No	There were no adjustments for confounding variables (e.g., age, sex or gender, race, ethnicity, disease severity, comorbidities, neurologist experience)
2. Is there sufficient potential for confounding that an unadjusted result should not be considered further?	Yes	Two cohorts of patients were enrolled during separate time periods. There could have been differences in patient disease characteristics at baseline and in the level of neurologist training between time periods which could affect the outcomes but insufficient information was reported to inform about these differences. This is particularly concerning as the study period partially overlapped with the COVID-19 pandemic, where many changes to the hospital system could have impacted time to treatment outcomes.
3. Was the method of measuring the outcome inappropriate?	NI	It was unclear who assessed time to intervention outcomes or how they were measured.
Risk of bias judgment	Critical (no further assessment is required)	For time to intervention outcomes, the study is at critical risk of bias due to confounding, as there were no attempts to control for differences across the 2 time periods which could have affected the outcomes.

NI = no information; ROBINS-I = Risk Of Bias In Nonrandomized Studies – of Interventions.

Table 7: Risk of Bias Assessment of Functional Status Outcomes Reported by Adhya et al. (2021)[2] – ROBINS-I

Domain/question	Judgement	Comments
Decide whether to proceed with a risk-of-bias assessment		
1. Did the authors make any attempt to control for confounding?	No	There were no adjustments for confounding variables (e.g., age, sex or gender, race, ethnicity, disease severity, comorbidities, neurologist experience)
2. Is there sufficient potential for confounding that an unadjusted result should not be considered further?	Yes	Two cohorts of patients were enrolled during separate time periods. There could have been differences in patient disease characteristics at baseline and in the level of neurologist training between time periods which could affect the outcomes but insufficient information was reported to inform about these differences. This is particularly concerning as the study period partially overlapped with the COVID-19 pandemic, where many changes to the hospital system could have impacted patient outcomes.
3. Was the method of measuring the outcome inappropriate?	Probably no	The tools used to assess outcomes related to functional status were reported, but it was unclear who conducted the assessments.
Risk of bias judgment	Critical (no further assessment is required)	For functional status outcomes, the study is at critical risk of bias due to confounding, as there were no attempts to control for differences across the 2 time periods which could have affected the outcomes.

ROBINS-I = Risk Of Bias In Nonrandomized Studies – of Interventions.

QUADAS-2 Detailed Assessments

Table 8: Risk of Bias Assessment of Delora et al. (2024)[3] – QUADAS-2

Domain/question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	Unclear	There is insufficient reporting of how the patient population was selected to determine if it was a consecutive or random sample.
Was a case-control design avoided?	Unclear	The methods for patient selection were unclear.
Did the study avoid inappropriate exclusions?	Unclear	The eligibility criteria were not reported. Some patients were excluded for missing data, but it was unclear which types of data were missing and for what reasons.
Risk of bias: Could the selection of patients have introduced bias?	Unclear	'Unclear' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the included patients do not match the review question?	Low	Patients were those who underwent multimodal CT for suspected acute ischemic stroke, which is directly relevant to the review question.

Domain/question	Judgement	Comments
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of Rapid LVO alone (which did not have access to the results of the reference standard).
If a threshold was used, was it pre-specified?	Unclear	The threshold of relative vessel density for detecting LVO was not described.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Unclear	There is insufficient information to determine whether the threshold of relative vessel density for detecting LVO was pre-specified.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was evaluation of CTA by Rapid LVO alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid LVO alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard diagnosis was interpretation of CTA by a single diagnostic or interventional neuroradiologist (with access to Rapid LVO results).
Were the reference standard results interpreted without knowledge of the results of the index test?	No	The reference standard results were interpreted with knowledge of the analysis by Rapid LVO and Viz LVO (2 automated LVO detection software that were running simultaneously).
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	High	Knowledge of the index test results could have influenced the interpretation of the reference standard, which may bias estimates of agreement between the index test and the reference standard results.
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	There were no indications that all patients did not receive a reference standard.
Did patients receive the same reference standard?	Yes	All patients received the same reference standard.

Domain/question	Judgement	Comments
Were all patients included in the analysis?	Yes	All 360 patients were included in the Rapid LVO confusion matrix and the calculation of diagnostic parameters.
Risk of bias: Could the patient flow have introduced bias?	Low	'Yes' or 'NA' for all signalling questions.

CT = CT; CTA = CT angiography; LVO = large vessel occlusion; NA = not applicable; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Table 9: Risk of Bias Assessment of Slater et al. (2024)[4] – QUADAS-2

Domain/question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	Yes	Patients who presented to a single comprehensive stroke centre over a 5-month interval with clinical suspicion of ischemic stroke and who underwent multimodality imaging with RapidAI interpretation were included. From this cohort, patients were excluded if they had incomplete imaging or if CT angiography was of inadequate quality (e.g., those with poor contrast bolus injection or patient motion artifact). Although not explicitly reported, it appears likely that all eligible patients were included.
Was a case-control design avoided?	Yes	Patient selection was independent of the results of the reference standard.
Did the study avoid inappropriate exclusions?	Yes	Although the study excluded patients with inadequate image quality, this is likely aligned with how the test would be used in practice.
Risk of bias: Could the selection of patients have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the included patients do not match the review question?	Low	Patients with clinical suspicion of ischemic stroke, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of RapidAI alone (which did not have access to the results of the reference standard).
If a threshold was used, was it pre-specified?	Yes	"We did not calculate the area under the receiver operating curve for RapidAI detection of arterial occlusion. The test has only 1 threshold, and receiver operating curves are better suited to perform in diagnostic tests with multiple thresholds" (p. 7).[4] The authors indicated that RapidAI only has 1 threshold, so they likely used the threshold specified by the manufacturer of the test.

Domain/question	Judgement	Comments
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was evaluation of CTA by RapidAI CTA module alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid CTA alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard diagnosis was made by a panel of 4 interventional neuroradiologists (with access to Rapid LVO results).
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear	"Three interventional neuroradiologists […] independently assessed all studies to determine the presence and site of arterial occlusions. Whenever this panel was not unanimous, a fourth neurointerventional radiologist […] made an additional independent assessment, and disagreements were reviewed. A consensus diagnosis was obtained for all cases" (p. 4).[4] It was not explicitly stated whether the reference standard assessments were conducted without knowledge of the index test results.
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear	Unclear if the neuroradiologists had knowledge of the results of the index test.
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	All 500 included patients were assessed by the reference standard (and a consensus diagnosis was obtained for each).
Did patients receive the same reference standard?	Yes	The reference standard was consistent for all patients.
Were all patients included in the analysis?	Yes	There were no indications to suggest that all patients were not included in the analysis.

Domain/question	Judgement	Comments
Risk of bias: Could the patient flow have introduced bias?	Low	'Yes' or 'NA' for all signalling questions.

CT = CT; CTA = CT angiography; LVO = large vessel occlusion; NA = not applicable; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Table 10: Risk of Bias Assessment of Chan et al. (2023)[5] – QUADAS-2

Domain/question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	Yes	"The CT and CTA images performed to exclude stroke for 104 consecutive adult patients presenting from January to March 2021 at a single tertiary neuroscience institution were analysed" (p. e46).[5]
Was a case-control design avoided?	Yes	Consecutive patients presenting with suspected acute stroke were included. Patient selection was independent of the results of the reference standard.
Did the study avoid inappropriate exclusions?	Yes	Only 2/104 patients were excluded at the time of enrollment. The rationale for exclusions were provided and reasonable.
Risk of bias: Could the selection of patients have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the included patients do not match the review question?	Low	Patients were those who were being assessed for possible acute stroke, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of Rapid CTA alone (which did not have access to the results of the reference standard).
If a threshold was used, was it pre-specified?	Unclear	The threshold of relative vessel density for detecting LVO was not described.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Unclear	There is insufficient information to determine whether the threshold of relative vessel density for detecting LVO was pre-specified.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was evaluation of CTA by Rapid CTA alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid CTA alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		

Domain/question	Judgement	Comments
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard diagnosis was determined by consensus among 2 experienced neuroradiologists.
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes	“Both readers were blinded to the report and the RAPID software interpretation” (p. e46).
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	Low	‘Yes’ for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	There were no indications that all patients did not receive a reference standard.
Did patients receive the same reference standard?	Yes	All patients received the same reference standard.
Were all patients included in the analysis?	No	13.7% (14 of 102) of patients were excluded from the analysis “due to technical difficulties” (p. e51).[5] It is not clear why these patients were excluded, and they may represent difficult to diagnose populations.
Risk of bias: Could the patient flow have introduced bias?	High	A large portion (13.7%) of the participants were excluded from the analysis for unknown reasons.

CT = CT; CTA = CT angiography; LVO = large vessel occlusion; NA = not applicable; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Table 11: Risk of Bias Assessment of Soun et al. (2023)[1] – QUADAS-2

Domain/question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	Yes	“This retrospective study included consecutive patients presenting with suspected acute ischemic stroke who had a CTA at a comprehensive stroke center” (p. 02).[1]
Was a case-control design avoided?	Yes	Consecutive patients presenting with suspected acute ischemic stroke were included. Patient selection was independent of the results of the reference standard.

Domain/question	Judgement	Comments
Did the study avoid inappropriate exclusions?	Yes	The study excluded patients with technically inadequate CTA (e.g., poor contrast bolus, significant motion, or other artifacts that would preclude evaluation by both human and automated assessment). However, this is likely aligned with how the test would be used in practice.
Risk of bias: Could the selection of patients have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the included patients do not match the review question?	Low	Patients with clinical suspicion of acute ischemic stroke, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of Rapid LVO alone (which did not have access to the results of the reference standard)
If a threshold was used, was it pre-specified?	Unclear	"The RAPID LVO algorithm which primarily relies on vessel density threshold assessment has been described previously" (p. 02).[1] The threshold of relative vessel density for detecting LVO was not described.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Unclear	There is insufficient information to determine whether the threshold of relative vessel density for detecting LVO was pre-specified.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was Rapid LVO alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid LVO alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard was assessment of LVO on CTA from the radiologist's reports (with access to Rapid LVO results), which were verified by a board-certified neuroradiologist. For complex cases where the reference standard was not clearly delineated, 2 additional neuroradiologists determined the reference standard.
Were the reference standard results interpreted without knowledge of the results of the index test?	No	The reference standard results were interpreted with knowledge of the analysis by Rapid LVO.
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	High	Knowledge of the index test results could have influenced the interpretation of the reference standard, which may bias estimates of agreement between the index test and the reference standard results.

Domain/question	Judgement	Comments
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	There were no indications that all patients did not receive a reference standard.
Did patients receive the same reference standard?	Yes	The reference standard was consistent for all patients.
Were all patients included in the analysis?	Unclear	The reporting related to the calculation of diagnostic performance metrics was limited. It was unclear if all 321 patients were included in the analysis.
Risk of bias: Could the patient flow have introduced bias?	Unclear	It is unclear if all patients were included in the analysis.

CT = CT; CTA = CT angiography; LVO = large vessel occlusion; NA = not applicable; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Table 12: Risk of Bias Assessment of Yedavalli et al. (2023)[6] – QUADAS-2

Domain/question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	Unclear	“Cases were obtained from consecutive emergency room (ER) scans obtained from Augusta University Medical Center and Riverside Regional Medical Center. Other hospitals that contributed cases included three community hospitals (Box Hill, Hospital de Clinicas, Olathe Medical Center) and two university centers (Kansas University Medical Center and, New York University). Two research studies that enrolled acute LVO patients, CRISP (9) and DEFUSE 3 (10) also contributed cases” (p. 02).[6] There is insufficient reporting of how the patient population was selected to determine if it was a consecutive or random sample.
Was a case-control design avoided?	Unclear	The methods for patient selection were unclear.
Did the study avoid inappropriate exclusions?	Unclear	The eligibility criteria were not reported.
Risk of bias: Could the selection of patients have introduced bias?	Unclear	‘Unclear’ for all signalling questions.
B. Concerns regarding applicability		

Domain/question	Judgement	Comments
Applicability: Is there concern that the included patients do not match the review question?	Low	Acutely presenting patients with suspected stroke, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of the Rapid NCCT Stroke platform alone (which did not have access to the results of the reference standard).
If a threshold was used, was it pre-specified?	Yes	"This AI software uses neural networks and automated segmentation techniques based on predefined thresholds for identification of ICH, HVS, and Alberta Stroke Program Early CT Score (ASPECTS)" (p. 03).[6] The authors indicated that the Rapid NCCT Stroke platform uses a predefined threshold for detecting the presence of a hyperdense vessel sign, so they likely used the threshold specified by the manufacturer of the test.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was evaluation of NCCT by the Rapid NCCT Stroke platform (using the Rapid HVS to detect LVO) alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid NCCT Stroke platform alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard diagnosis was based on a consensus of 2 of 3 neuroradiologists.
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes	"All readers performed interpretations blinded to the AI software results and clinical information. Readers then assessed for ICH, and if ICH was not present, they then assessed for suspected LVO. The reference truth for ICH was based on a consensus of two of three neuroradiologists evaluating the NCCT scan using the same parameters" (p. 03).[6]
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.

Domain/question	Judgement	Comments
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	Yes	"Stand-alone performance was based on the reference LVO assessment which was determined by a consensus of two of three neuroradiologists based on a CTA performed concurrently with the NCCT" (p. 03).[6] Images used for the index test and the reference standard were conducted concurrently.
Did all patients receive a reference standard?	Yes	There were no indications that all patients did not receive a reference standard.
Did patients receive the same reference standard?	Yes	All patients received the same reference standard.
Were all patients included in the analysis?	Unclear	"LVO: The software identified 73 true suspected LVOs (73/115, 63.5%) with 42 false negatives (42/115, 36.5%). It also correctly categorized 90 cases (90/115, 78.2%) where LVO was not present with five false positives (5/115, 4.3%). This resulted in a sensitivity of 63.5% (95% CI: 54.4–71.7%) and specificity of 95.1% (95% CI: 89.1–97.9%)" (p. 03).[6] There were inconsistencies in the reporting of the number of patients included in the analysis. The number of TP (n = 73), FP (n = 5), FN (n = 42), and TN (n = 90) sum to 210, but the total number of patients who had LVO or did not have LVO or ICH (the ICH-positive patients were considered in a separate analysis) was 218. The difference between these values was not explained.
Risk of bias: Could the patient flow have introduced bias?	Unclear	Unclear if all enrolled patients were included in the analysis; it appears as though data were missing for 8 (4%) patients, but no explanation is provided.

CT = CT; CTA = CT angiography; FN = false negative; FP = false positive; ICH = intracranial hemorrhage; LVO = large vessel occlusion; NA = not applicable; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2; TN = true negative; TP = true positive.

Table 13: Risk of Bias Assessment of Eldaya et al. (2022)[11] – QUADAS-2

Domain/question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	Yes	"Three hundred eight consecutive adult patients presenting with acute neurological deficit suspicious for acute stroke and undergoing NCCT with RAPID ICH processing at a single large tertiary comprehensive stroke center with a large catchment area between May, 19, 2020, and October 16, 2020, were included (Fig. 1)" (p. 70).[11]
Was a case-control design avoided?	Yes	Consecutive patients presenting with suspected acute stroke were included. Patient selection was independent of the results of the reference standard.

Domain/question	Judgement	Comments
Did the study avoid inappropriate exclusions?	Yes	“One patient was excluded from the study because of intravenous contrast administration a few hours before the NCCT confounding interpretation of a hyperdensity within the infarct as hemorrhage or contrast. The remaining 307 patients were included in the final analysis” (p. 771).[11] Only 1/308 patients were excluded from the analysis, and rationale for exclusion was provided and reasonable.
Risk of bias: Could the selection of patients have introduced bias?	Low	‘Yes’ for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the included patients do not match the review question?	Low	Patients were those presenting with acute neurologic deficit suspicious of acute stroke, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	“Two neuroradiology fellows (M.Z. and E.M.) reviewed the patients’ electronic medical records to determine […] presence and type of ICH reported in the neuroradiologist interpretation, and RAPID ICH result. For patients in whom RAPID ICH and neuroradiologist interpretation were concordant for the presence of ICH, the neuroradiologist interpretation was considered the reference standard. For patients in who RAPID ICH and neuroradiologist interpretation were discordant [...], a consensus panel of 3 board-certified neuroradiologists […] was then used as the reference standard” (p. 771).[11] The index test was conducted and interpreted before the reference standard.
If a threshold was used, was it pre-specified?	Unclear	No threshold was reported.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Unclear	‘Yes’ or ‘Unclear’ for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	Low	The index test was RAPID ICH + neuroradiologist, which is directly applicable to the review question (and use of the tool in practice).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	When standalone Rapid ICH and neuroradiologist interpretation were concordant, it was considered the reference standard. In cases where there was disagreement between Rapid ICH and neuroradiologist interpretation, the reference standard was a consensus panel of 3 neuroradiologists (with 3, 6, and 24 years of experience).

Domain/question	Judgement	Comments
Were the reference standard results interpreted without knowledge of the results of the index test?	No	"The consensus panel was not blinded to the neuroradiologist interpretation nor the RAPID ICH result" (p. 771).[11]
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	High	In cases of concordance, the index test served as the reference standard, which could inflate the diagnostic accuracy of the index test. Additionally, in cases of discordance, the consensus panel of neuroradiologists was aware of the neuroradiologist interpretation and Rapid ICH result, which may bias the test accuracy estimates.
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was intracranial hemorrhage (i.e., hemorrhagic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	"For patients in whom RAPID ICH and neuroradiologist interpretation were concordant for the presence of ICH, the neuroradiologist interpretation was considered the reference standard. For patients in who RAPID ICH and neuroradiologist interpretation were discordant [..], a consensus panel of 3 board-certified neuroradiologists […] was then used as the reference standard" (p. 771).[11]
Did patients receive the same reference standard?	No	In some patients, the index test was considered the reference standard, while in others the reference standard was a consensus panel of 3 neuroradiologists (i.e., there was differential verification).
Were all patients included in the analysis?	Yes	The reporting was limited, but there were no indications that all 307 enrolled patients were not included in the analyses.
Risk of bias: Could the patient flow have introduced bias?	High	Different reference standards were used depending on the results of the index test, which could bias the accuracy estimates.

CT = CT; CTA = CT angiography; ICH = intracranial hemorrhage; LVO = large vessel occlusion; NA = not applicable; NCCT = non-contrast CT; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Table 14: Risk of Bias Assessment of Mallon et al. (2022)[7] – QUADAS-2

Domain/question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		

Domain/question	Judgement	Comments
Was a consecutive or random sample of patients enrolled?	Yes	"In this single-centre retrospective study, the cohort included all patients with either a suspected or confirmed anterior circulation LVO who underwent a CTP study at Imperial College NHS Healthcare Trust between 1 January 2016 and 31 December 2020" (p. 2).[7]
Was a case-control design avoided?	Yes	Patient selection was independent of the results of the reference standard.
Did the study avoid inappropriate exclusions?	Yes	Only patients who did not have CTA imaging data available were excluded (4.4%; 4/90).
Risk of bias: Could the selection of patients have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the included patients do not match the review question?	Low	Patients were those who were being assessed for suspected or confirmed anterior circulation LVO, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of Rapid AI alone (which did not have access to the results of the reference standard).
If a threshold was used, was it pre-specified?	Unclear	The threshold of relative vessel density for detecting LVO was not described.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Unclear	The threshold of relative vessel density for detecting LVO was not described.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was evaluation of CTA by Rapid AI alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid AI alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard diagnosis was based assessment of CTA by a single neuroradiologist.
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear	"ASPECTS was determined on NCCT and the presence of LVO on CTA by a neuroradiologist with 4 years' experience. ASPECTS was determined as described previously. Images were reviewed with all available clinical and imaging data" (p.2).[7] It was not explicitly stated whether the reference standard assessments were conducted without knowledge of the index test results.

Domain/question	Judgement	Comments
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear	It is not clear whether the reference standard assessments were conducted without knowledge of the index test results.
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	There were no indications that all patients did not receive a reference standard.
Did patients receive the same reference standard?	Yes	All patients received the same reference standard.
Were all patients included in the analysis?	No	1 of 90 participants was not included in the analysis because the algorithm failed to give an output.
Risk of bias: Could the patient flow have introduced bias?	Low	While not all patients were included in the analysis, the number of excluded patients is small (1.1% of the study population) and is unlikely to meaningfully bias the result.

ASPECTS = Alberta Stroke Program Early CT score; CT = CT; CTA = CT angiography; CTP = CT perfusion; LVO = large vessel occlusion; NA = not applicable; NCCT = non-contrast CT; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Table 15: Risk of Bias Assessment of Schlossman et al. (2022)[8] – QUADAS-2

Domain/question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	Yes	"This was a retrospective, single center study performed at University of California, Irvine, a comprehensive stroke center, using anonymized data from December 2020 to June 2021. Inclusion criteria was as follows: (1) suspected acute stroke patients who had CT angiography (CTA) performed, (2) imaging done within 24 h of symptom onset, and (3) RAPID LVO output included with CTA acquisition. Patients who had either (1) imaging acquired at outside facilities or (2) technically inadequate CTA (e.g., poor contrast bolus, significant motion, or other artifact that would preclude evaluation by both human and automated assessment) were excluded" (p. 02).[8] Based on the description of the study population, it appears to be a consecutively enrolled cohort of patients who met the eligibility criteria.

Domain/question	Judgement	Comments
Was a case-control design avoided?	Yes	Patient selection was independent of the results of the reference standard.
Did the study avoid inappropriate exclusions?	Yes	The study excluded patients with technically inadequate CTA (e.g., poor contrast bolus, significant motion, or other artifacts that would preclude evaluation by both human and automated assessment). However, this is likely aligned with how the test would be used in practice.
Risk of bias: Could the selection of patients have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the included patients do not match the review question?	Low	The study included patients with suspected acute stroke, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of Rapid LVO alone (which did not have access to the results of the reference standard).
If a threshold was used, was it pre-specified?	Unclear	There is insufficient information to determine whether the threshold of relative vessel density for detecting LVO was pre-specified.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Unclear	It is unclear whether the threshold of relative vessel density for detecting LVO was pre-specified.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was evaluation of CTA by Rapid LVO alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid LVO alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard diagnosis was based on assessment of CTA by 2 neuroradiologists. Disagreements were adjudicated by a 3rd neuroradiologist.
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes	"Ground truth was based off interpretation of the raw data from the CTA by radiology reports and confirmed by two neuroradiologists" (p. 02).[8] Based on the above quote, it is likely that the reference standard was conducted using only the raw CTA data (i.e., without processing from Rapid LVO).
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	Low	'Yes' for all signalling questions.

Domain/question	Judgement	Comments
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	There were no indications that all patients did not receive a reference standard.
Did patients receive the same reference standard?	Yes	All patients received the same reference standard.
Were all patients included in the analysis?	Yes	All 253 patients were included in the Rapid LVO confusion matrix and the calculation of diagnostic parameters.
Risk of bias: Could the patient flow have introduced bias?	Low	'Yes' for all signalling questions.

CT = CT; CTA = CT angiography; LVO = large vessel occlusion; NA = not applicable; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Table 16: Risk of Bias Assessment of Adhya et al. (2021)[2] – QUADAS-2

Domain/ signalling question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	Yes	"All patients who received CTA for the evaluation of AIS or neurological deficit from November 2019–November 2020 that included RAPID-CTA with relative vessel density of 60% or less were included in the study" (p. 4).[2] Based on the description of the study population, it appears to be a consecutively enrolled cohort of patients who met the eligibility criteria.
Was a case-control design avoided?	Yes	Patient selection was independent of the results of the reference standard.
Did the study avoid inappropriate exclusions?	No	Patients with a relative vessel density of 60% or more were excluded, which makes for a selected population that is not reflective of clinical practice. These could represent patients who are negative for LVO or who have LVO but are difficult to diagnose populations.
Risk of bias: Could the selection of patients have introduced bias?	High	The study applied inappropriate exclusion criteria and selected for a population that is not reflective of clinical practice.
B. Concerns regarding applicability		

Domain/ signalling question	Judgement	Comments
Applicability: Is there concern that the included patients do not match the review question?	Low	Patients were those who underwent CTA for the evaluation of acute ischemic stroke or neurologic deficit, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of Rapid CTA alone (which did not have access to the results of the reference standard).
If a threshold was used, was it pre-specified?	Yes	Two thresholds were tested (i.e., < 45% relative vessel density and < 60% relative vessel density) and were likely pre-specified.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was evaluation of CTA by Rapid CTA alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid CTA alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard diagnosis was based on assessment of CTA by 2 neuroradiologists.
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear	It was not explicitly stated whether the reference standard assessments were conducted without knowledge of the index test results.
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	Unclear	It is not clear whether the reference standard assessments were conducted without knowledge of the index test results.
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	There were no indications that all patients did not receive a reference standard.
Did patients receive the same reference standard?	Yes	All patients received the same reference standard.

Domain/ signalling question	Judgement	Comments
Were all patients included in the analysis?	Yes	There were no indications to suggest that all patients were not included in the analysis.
Risk of bias: Could the patient flow have introduced bias?	Low	'Yes' or 'NA' for all signalling questions.

CT = CT; CTA = CT angiography; LVO = large vessel occlusion; NA = not applicable; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Table 17: Risk of Bias Assessment of Dehkharghani et al. (2021)[9] – QUADAS-2

Domain and questions	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	No	Patients were enrolled from recent cerebrovascular trials and institutional registries from 11 worldwide sites were included and selected for inclusion using LVO status, location, CT vendor, and baseline demographics (i.e., a nonrandom and non-consecutive sample).
Was a case-control design avoided?	No	The study population was enriched with patients who had known LVO status to achieve balance between LVO-positive and LVO-negative patients (i.e., it is a case-control selected cross-sectional study).
Did the study avoid inappropriate exclusions?	Yes	The study excluded patients who did not have "… technically adequate thin section (≤ 2 mm section thickness) contiguous cerebrovascular CTA source axial images free of artifacts that would degrade interpretation by human readers (e.g., those related to severe metallic streak or beam hardening)" (p. 666).[9] However, this is likely aligned with how the test would be used in practice.
Risk of bias: Could the selection of patients have introduced bias?	High	The study included a non-consecutive and nonrandom patient population and provided limited reporting on the methods used to select patients for inclusion.
B. Concerns regarding applicability		
Applicability: Is there concern that the included patients do not match the review question?	Low	The study included patients with suspected acute ischemic stroke who underwent CTA imaging, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of Rapid LVO alone (which did not have access to the results of the reference standard).
If a threshold was used, was it pre-specified?	Unclear	"A custom vessel tracking algorithm (RapidLVO, version 1.0; iSchemaView) was used to inform the course, caliber, opacity, and continuity of the filtered vasculature, and vascular opacification was quantified with density thresholding. The thresholding operation represents a tunable parameter described by a vessel density ratio. By

Domain and questions	Judgement	Comments
		default, a vascular segment failing to reach the terminus of a predefined region of interest is classified as a vessel density ratio of 0.0. With a potential vessel density ratio ranging from 0.00 to 1.00, a score less than 0.6 was classified as positive for the presence of LVO" (p. 666).[9] It was not stated whether the vessel density ratio threshold for the primary analyses was pre-defined or selected post-hoc.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Unclear	It is not clear whether the vessel density ratio threshold for the primary analyses was pre-defined or selected post-hoc.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was evaluation of CTA by Rapid LVO alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid LVO alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard diagnosis was based on assessment of CTA by consensus from up to 3 neuroradiologists.
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes	"Readers 1 and 2 independently scored all examinations for LVO and, when present, the side of the LVO, before receiving the automated output. Once submitted, reader scores could not be modified" (p. 666).[9]
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	There were no indications that all patients did not receive a reference standard.
Did patients receive the same reference standard?	Yes	All patients received the same reference standard.
Were all patients included in the analysis?	Yes	All 217 patients were included in the Rapid LVO confusion matrix and the calculation of diagnostic parameters.

Domain and questions	Judgement	Comments
Risk of bias: Could the patient flow have introduced bias?	Low	'Yes' or 'NA' for all signalling questions.

CT = CT; CTA = CT angiography; LVO = large vessel occlusion; NA = not applicable; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Table 18: Risk of Bias Assessment of Amukotuwa et al. (2019)[10] – QUADAS-2

Domain/ signalling question	Judgement	Comments
Domain 1: Patient Selection		
A. Risk of Bias		
Was a consecutive or random sample of patients enrolled?	Yes	"Consecutive patients who presented to our institution between January 1, 2017 and December 31, 2018 underwent multimodal brain CT for a suspected acute ischemic stroke and met the following inclusion criteria were retrospectively identified using our Picture Archiving and Communication System and electronic medical records" (p. 2791).[10]
Was a case-control design avoided?	Yes	Consecutive patients with suspected acute ischemic stroke were included. Patient selection was independent of the results of the reference standard.
Did the study avoid inappropriate exclusions?	Yes	"Exclusion criteria were (1) technically inadequate CTA (poor contrast bolus or substantial motion of metal artifact that precluded accurate assessment of the intracranial arteries to the level of the distal M2 segments of the middle cerebral arteries by an experienced neurologist) and (2) thin slide CTA images unavailable" (p. 2791).[10] However, this is likely aligned with how the test would be used in practice.
Risk of bias: Could the selection of patients have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the included patients do not match the review question?	Low	The study included patients with suspected acute ischemic stroke who underwent multimodal brain CT, which is directly relevant to the review question.
Domain 2: Index Test		
A. Risk of Bias		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	The study examined the diagnostic performance of Rapid CTA alone (which did not have access to the results of the reference standard).
If a threshold was used, was it pre-specified?	Yes	"A vessel density threshold of < 75% (inclusive of the 60%–75%, 45%–59%, and < 45% thresholds) was used in this study for LVO detection, as this was recommended by the software developers based on their prerelease testing" (p. 2792).[10] A rationale was provided for selecting the vessel density

Domain/ signalling question	Judgement	Comments
		threshold. It is likely that this was determined before conducting the analysis.
Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the index test, its conduct, or interpretation differ from the review question?	High	The index test was evaluation of CTA by Rapid CTA alone, which is different from our primary review question and how the tool is used in practice (i.e., Rapid CTA alongside clinician interpretation).
Domain 3: Reference Standard		
A. Risk of Bias		
Is the reference standard likely to correctly classify the target condition?	Yes	The reference standard diagnosis was based on consensus assessment of LVO on unenhanced CT, CTP, and CTA by 2 diagnostic neuroradiologists. A 3rd interventional neuroradiologist verified decisions.
Were the reference standard results interpreted without knowledge of the results of the index test?	Yes	"The multimodal computed tomographies were assessed by 2 neuroradiologists in consensus for the presence of an intracranial anterior circulation LVO or M2-segment middle cerebral artery occlusion (the reference standard). The patients' computed tomography angiographies were then processed using an automated LVO-detection algorithm (RAPID CTA)" (p. 2790).[10] Based on the above quote, it is likely that the reference standard was conducted before the index test (and therefore the results of the index test could not have influenced the reference standard).
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	Low	'Yes' for all signalling questions.
B. Concerns regarding applicability		
Applicability: Is there concern that the target condition as defined by the reference standard does not match the review question?	Low	The target condition was LVO (i.e., ischemic stroke), and was likely to be correctly classified by the reference standard, which is directly relevant to the review question.
Domain 4: Flow and Timing		
A. Risk of Bias		
Was there an appropriate interval between index test(s) and reference standard?	NA	Not applicable. The index test and the reference standard used the same CT images, and the timing of interpretation is not relevant.
Did all patients receive a reference standard?	Yes	There were no indications that all patients did not receive a reference standard.
Did patients receive the same reference standard?	Yes	All patients received the same reference standard.

Main Study Findings

Table 19: Study Results, by Outcome — Time to Intervention

Study citation	Study design	Intervention and comparator	Outcome	Outcome result		
				Pre-RapidAI	Post-RapidAI	P value
Soun et al. (2023)[1]	Retrospective non-concurrent cohort	**I:** Clinician interpretation of CTA imaging with Rapid LVO (i.e., post-RapidAI group) **C:** Clinician interpretation of CTA imaging without Rapid LVO (i.e., pre-RapidAI group)	Radiology report turnaround time (minutes),[a] mean (SD)	30.58 (29.85) (n ≤ 439)[b]	22 (35.07) (n ≤ 321)[b]	0.0005[c,d]
			Time from door to image (minutes), median (IQR)	11 (8 to 20) (n ≤ 62)[b]	13 (7 to 20) (n ≤ 43)[b]	0.75[e]
			Time from door to intubation (minutes), median (IQR)	64.5 (46 to 73) (n ≤ 62)[b]	69.5 (58 to 86) (n ≤ 43)[b]	0.15[e]
			Time from door to needle (i.e., tPA therapy) (minutes), median (IQR)	37 (25.5 to 44) (n ≤ 62)[b]	42 (30 to 53) (n ≤ 43)[b]	0.38[e]
			Time from door to groin puncture (i.e., thrombectomy) (minutes), median (IQR)	97 (80 to 107) (n ≤ 62)	101 (90 to 113) (n ≤ 43)[b]	0.32[e]
			Time from door to revascularization (minutes), median (IQR)	155 (123 to 197) (n ≤ 62)[b]	158 (131 to 191.5) (n ≤ 43)[b]	0.72[e]
Adhya et al. (2021)[2]	Retrospective non-concurrent cohort	**I:** Clinician interpretation of CTA imaging with Rapid CTA (i.e., post-RapidAI group) **C**: Clinician interpretation of CTA imaging without Rapid CTA (i.e., pre-RapidAI group)	Time from CTA to groin puncture (i.e., thrombectomy) (minutes), mean (SD)	92 (NR) (n = 74)	68 (NR) (n = 72)	< 0.05[c,d]

C = comparator; CTA = CT angiography; I = intervention; IQR = interquartile range; LVO = large vessel occlusion; NR = not reported; SD = standard deviation; tPA = tissue plasminogen activator.

[a]Defined as the time from when the CTA images are available for the radiologist to the earlier time of either the report being available or read-back verification was provided for the clinicians.

[b]The sample size for the analysis was not explicitly reported; as such, the amount of missing data are unknown.

[c]Statistically significant.

[d]Statistical test not reported (Student's t test or Mann–Whitney U test).

[e]Wilcoxon rank sum test.

Table 20: Study Results, by Outcome — Functional Status

Study citation	Study design	Intervention and comparator	Outcome	Outcome result		
				Pre-RapidAI	Post-RapidAI	P value
Soun et al. (2023)[1]	Retrospective non-concurrent cohort	**I:** Clinician interpretation of CTA imaging with Rapid LVO (i.e., post-RapidAI group) **C:** Clinician interpretation of CTA imaging without Rapid LVO (i.e., pre-RapidAI group)	36-hour post-treatment NIHSS score, median (IQR)[a]	9.5 (5 to 18) (n = NR)[b]	11 (2 to 20) (n = NR)[b]	0.71[c]
			NIHSS score at discharge, median (IQR)[a]	4.5 (1 to 11) (n = NR)[b]	8 (1.5 to 20) (n = NR)[b]	0.099[c]
			Change in NIHSS score from admission to discharge, median (IQR)[a]	−7 (−2 to −13) (n = NR)[b]	−3 (0 to −7) (n = NR)[b]	0.03[c,d]
			Proportion of patients with mRS score ≥ 5 at discharge, n/N[e,f]	11/62 (17.7%)	10/43 (23.3%)	0.62[c]
Adhya et al. (2021)[2]	Retrospective non-concurrent cohort	**I:** Clinician interpretation of CTA imaging with Rapid CTA (i.e., post-RapidAI group) **C**: Clinician interpretation of CTA imaging without Rapid CTA (i.e., pre-RapidAI)	90-day mRS score, mean (SD)[e]	4.47 (NR) (n = 74)	3.90 (NR) (n = 67)	0.07[g]
			Proportion of patients with 90-day mRS score ≤ 2, n/N[e,h]	17/74 (23.0%)	23/67 (34.3%)	0.15[g]

C = comparator; CTA = CT angiography; I = intervention; IQR = interquartile range; LVO = large vessel occlusion; mRS = modified Rankin Scale; NIHSS = US National Institutes of Health Stroke Scale; NR = not reported; SD = standard deviation.

[a]The National Institutes of Health Stroke Scale is a 15-item neurologic examination stroke scale used for evaluating stroke-related neurologic deficit. Total scores range from 0 to 42, with higher scores indicating more severe neurologic deficit.[12]

[b]The sample size for the analysis was not explicitly reported; as such, the amount of missing data are unknown. The analyses for Thrombolysis in Cerebral Infarction scores and mRS scores included 62 and 46 participants in the pre-RapidAI group and 46 and 34 participants in the post-RapidAI group, respectively, but it is unclear if these samples sizes are applicable to other clinical outcomes.

[c]Wilcoxon rank sum test. After adjusting for the effects of high cholesterol, heart disease, atrial fibrillation, therapies received, and NIHSS on admission via multivariate regression, the P value for the between-group difference in NIHSS score at discharge was < 0.01. The between-group difference for 36-hour post-treatment NIHSS score was not statistically significant when adjusted for the same variables (P value not reported).

[d]Statistically significant.

[e]The modified Rankin Scale is a clinician-reported tool for measuring the degree of disability and dependence in daily activities in people who have experienced stroke. Scores range from 0 (no symptoms at all) to 6 (death). A higher score indicates greater disability.[13]

[f]Considered 'significant morbidity/mortality'.

[g]Statistical test not reported (Student's t test or Mann–Whitney U test).

[h]Considered 'functionally independent'.

Table 21: Study Results, by Outcome — Response to Therapy

Study citation	Study design	Intervention and comparator	Outcome	Outcome result		
				Pre-RapidAI	Post-RapidAI	P value
Soun et al. (2023)[1]	Retrospective non-concurrent cohort	**I:** Clinician interpretation of CTA imaging with Rapid LVO (i.e., post-RapidAI group) **C:** Clinician interpretation of CTA imaging without Rapid LVO (i.e., pre-RapidAI group)	Proportion of patients with TICI score of 0, n/N[a]	2/46 (4.3%)	3/34 (8.8%)	0.51[b]
			Proportion of patients with TICI score of 1, n/N[a]	1/46 (2.2%)	0/34 (0%)	
			Proportion of patients with TICI score of 2A, n/N[a]	4/46 (8.7%)	4/34 (11.8%)	
			Proportion of patients with TICI score of 2B/C, n/N[a]	18/46 (39.1%)	17/34 (50.0%)	
			Proportion of patients with TICI score of 3, n/N[a]	21/46 (45.7%)	10/34 (29.4%)	

C = comparator; CTA = CT angiography; I = intervention; IQR = interquartile range; LVO = large vessel occlusion; NR = not reported; TICI = Thrombolysis in Cerebral Infarction.

[a]The Thrombolysis in Cerebral Infarction (TICI) scale is a grading system used to evaluate the degree of perfusion obtained following recanalization of an arterial occlusion. The TICI scale ranges from 0 (no reperfusion) to 3 (complete reperfusion).[14]

[b]Chi-square test.

Table 22: Study Results, by Outcome — Diagnostic Accuracy for the Detection of M1 MCA and ICA LVO

Study Citation	Index Test and Reference Standard	Type of LVO and Subgroup (if applicable)	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC (95% CI)
Chan et al. (2023)[5] (N = 88)	**IT:** Rapid CTA alone **RS:** Consensus	M1 MCA and terminal ICA LVO	12	11	1	64	92% (64 to 100)[b]	85% (75 to 92)[b]	52% (31 to 73)[b]	98% (92 to 100)[b]	86% (77 to 93)[b]	NR

Study Citation	Index Test and Reference Standard	Type of LVO and Subgroup (if applicable)	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC (95% CI)
	of 2 neuro-radiologists											
Soun et al. (2023)[1] (N = 321)	**IT**: Rapid LVO alone **RS**: Single radiologist report, verified by up to 3 additional neuro-radiologists	M1 MCA and intracranial ICA LVO	NR	NR	NR	NR	96% (NR)	85% (NR)	53% (NR)	99% (NR)	NR	NR
Yedavalli et al. (2023)[6] (N = 244)	**IT:** Rapid NCCT Stroke platform alone[c] **RS:** Consensus of 2 of 3 neuro-radiologists	M1 MCA and distal intracranial ICA LVO	73	5	42	90	63% (54 to 72)	95% (88 to 98)[c]	94% (86 to 98)[b,e]	68% (60 to 76)[b,e]	78% (71 to 83)[b]	NR
Schlossman et al. (2022)[8] (N = 253)	**IT**: Rapid LVO alone **RS**: Consensus of 2 neuro-radiologists	M1 MCA and intracranial ICA LVO	26	32	3	192	90% (73 to 98)[b]	86% (80 to 90)[b]	45% (32 to 58)[b]	98% (96 to 100)[b]	86% (81 to 90)[b]	NR
Dehkharghani et al. (2021)[9] (N = 217)	**Index test:** Rapid LVO alone **Reference standard**: Consensus of up to 3 neuro-radiologists	M1 MCA and intracranial ICA LVO	105	2	4	106	96% (91 to 99)	98% (94 to 100)	NA[f]	NA[f]	97% (94 to 99)[b]	NR

Study Citation	Index Test and Reference Standard	Type of LVO and Subgroup (if applicable)	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC (95% CI)
		M1 MCA and intracranial ICA LVO **Subgroup**: female (n = 100)	52	0	2	46	96% (87 to 100)	100% (92 to 100)	NA[f]	NA[f]	98% (93 to 100)[b]	NR
		M1 MCA and intracranial ICA LVO **Subgroup**: male (n = 116)	52	2	2	60	96% (87 to 100)	97% (89 to 100)	NA[f]	NA[f]	97% (91 to 99)[b]	NR
		M1 MCA and intracranial ICA LVO **Subgroup**: 20 to 39 years of age (n = 17)	7	0	0	10	100% (59 to 100)	100% (69 to 100)	NA[f]	NA[f]	100% (80 to 100)	NR
		M1 MCA and intracranial ICA LVO **Subgroup**: 40 to 59 years of age (n = 68)	29	1	0	38	100% (88 to 100)	97% (87 to 100)	NA[f]	NA[f]	99% (92 to 100)[b]	NR
		M1 MCA and intracranial ICA LVO **Subgroup**: ≥ 60 years of age (n = 131)	69	1	4	57	95% (87 to 98)	98% (91 to 100)	NA[f]	NA[f]	96% (91 to 99)[b]	NR
Amukotuwa et al. (2019)[10] (N = 477)	**IT:** Rapid CTA alone **RS:** Consensus	M1 MCA and intracranial ICA LVO	73	NR	5	NR	94% (86 to 98)	76% (72 to 80)	43% (39 to 48)	98% (96 to 99)	NR	0.85 (0.81 to 0.88)

Study Citation	Index Test and Reference Standard	Type of LVO and Subgroup (if applicable)	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC (95% CI)
	of 2 neuro-radiologists, verified by a 3rd neuroradiologist											

AUC = area under the receiver operating characteristic curve; CTA = CT angiography; FN = false negatives; FP = false positives; ICA = internal carotid artery; IT = index test; LVO = large vessel occlusion; MCA = middle cerebral artery; NCCT = non-contrast CT; NPV = negative predictive value; NR = not reported; PPV = positive predictive value; TN = true negatives; TP = true positives; RS = reference standard.

[a]Concordance refers to the overall rate of agreement between the index test and the reference standard. It measures how often the index test and the reference standard produced the same result (e.g., both positive or both negative) for the same set of cases, but does not assess the accuracy or correctness of either test relative to the absolute truth.

[b]Not reported in the publication. We calculated the value with Clopper-Pearson exact 95% confidence intervals from the available data via the EpiR package in R.[15]

[c]Unlike other index tests included in this table, the Rapid NCCT Stroke platform detects LVO using NCCT images (rather than CTA images).

[d]Reported as 95% (89 to 98) in the publication, but was calculated as 95% (88 to 98) via the EpiR package in R.[15]

[e]Patient selection methods were unclear.

[f]PPV and NPV values were not calculated for Dehkharghani et al. (2019) as it used a case-control selected cross-sectional design that artificially created a sample of equally divided LVO-positive and LVO-negative patients.

Table 23: Study Results, by Outcome — Diagnostic Accuracy for the Detection of M1 and M2 MCA and ICA LVO

Study Citation	Index Test and Reference Standard	Type of LVO and Subgroup (if applicable)	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC (95% CI)
Mallon et al. (2022)[7] (N = 84)	**IT:** RapidAI alone **RS:** A single neuroradiologist	M1 and M2 MCA and terminal ICA LVO	45	8	16	15	74% (61 to 84)[b]	65% (43 to 84)[b]	85% (72 to 93)[b]	48% (30 to 67)[b]	71% (61 to 81)[b]	NR
Amukotuwa et al. (2019)[10] (N = 477)	**IT:** Rapid CTA alone **RS:** Consensus of 2 neuroradiologists, verified by a 3rd neuroradiologist	M1 and M2 MCA and intracranial ICA LVO	97	71	9	300	92% (85 to 96)	81% (77 to 85)	58% (52 to 63)	97% (95 to 98)	83% (80 to 86)[b]	0.86 (0.83 to 0.90)

AUC = area under the receiver operating characteristic curve; FN = false negatives; FP = false positives; ICA = internal carotid artery; IT = index test; LVO = large vessel occlusion; MCA = middle cerebral artery; NPV = negative predictive value; NR = not reported; PPV = positive predictive value; TN = true negatives; TP = true positives; RS = reference standard.

[a]Concordance refers to the overall rate of agreement between the index test and the reference standard. It measures how often the index test and the reference standard produced the same result (e.g., both positive or both negative) for the same set of cases, but does not assess the accuracy or correctness of either test relative to the absolute truth.

[b]Not reported in the publication. We calculated the value with Clopper-Pearson exact 95% confidence intervals from the available data via the EpiR package in R.[15]

Table 24: Study Results, by Outcome — Diagnostic Accuracy for the Detection of M1 MCA LVO

Study Citation	Index Test and Reference Standard	Type of LVO and Subgroup (if applicable)	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC (95% CI)
Mallon et al. (2022)[7] (N = 84)	**IT:** RapidAI alone **RS:** A single neuroradiologist	M1 MCA LVO (n = 73)	33	8	4	27	89% (75 to 97)[b]	77% (60 to 90)[b]	80% (65 to 91)[b]	87% (70 to 96)[b]	83% (73 to 91)[b]	NR
Schlossman et al. (2022)[8] (N = 253)	**IT**: Rapid LVO alone **RS**: Consensus of 2 neuroradiologists	M1 MCA LVO (n = 247)	21	32	2	192	91% (72 to 99)[b]	86% (80 to 90)[b]	40% (26 to 54)[b]	99% (96 to 100)[b]	86% (81 to 90)[b]	NR

AUC = area under the receiver operating characteristic curve; FN = false negatives; FP = false positives; IT = index test; LVO = large vessel occlusion; MCA = middle cerebral artery; NPV = negative predictive value; NR = not reported; PPV = positive predictive value; TN = true negatives; TP = true positives; RS = reference standard.

[a]Concordance refers to the overall rate of agreement between the index test and the reference standard. It measures how often the index test and the reference standard produced the same result (e.g., both positive or both negative) for the same set of cases, but does not assess the accuracy or correctness of either test relative to the absolute truth.

[b]Not reported in the publication. We calculated the value with Clopper-Pearson exact 95% confidence intervals from the available data via the EpiR package in R.[15]

Table 25: Study Results, by Outcome — Diagnostic Accuracy for the Detection of M2 MCA LVO

Study Citation	Index Test and Reference Standard	Type of LVO and Subgroup (if applicable)	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC (95% CI)
Schlossman et al. (2022)[8] (N = NR)	**IT**: Rapid LVO alone **RS**: Consensus of 2 neuroradiologists	M2 MCA LVO	8	NR	2	NR	80% (NR)	NR	NR	NR	NR	NR
Amukotuwa et al. (2019)[10] (N = 477)	**IT:** Rapid CTA alone **RS:** Consensus of 2 neuroradiologists, verified by a 3rd neuroradiologist	M2 MCA LVO	24	NR	4	NR	86% (67 to 96)	68% (63 to 72)	14% (12 to 17)	99% (97 to 100)	NR	0.77 (0.70 to 0.84)

AUC = area under the receiver operating characteristic curve; FN = false negatives; FP = false positives; IT = index test; LVO = large vessel occlusion; MCA = middle cerebral artery; NPV = negative predictive value; NR = not reported; PPV = positive predictive value; TN = true negatives; TP = true positives; RS = reference standard.

[a]Concordance refers to the overall rate of agreement between the index test and the reference standard. It measures how often the index test and the reference standard produced the same result (e.g., both positive or both negative) for the same set of cases, but does not assess the accuracy or correctness of either test relative to the absolute truth.

Table 26: Study Results, by Outcome — Diagnostic Accuracy for the Detection of Other LVO

Study Citation	Index Test and Reference Standard	Type of LVO and Subgroup (if applicable)	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC (95% CI)
Delora et al. (2024)[3] (N = 360)	**IT:** Rapid LVO alone **RS:** Interpretation by a single neuroradiologist	LVO[b]	41	48	6	265	87% (74 to 95)[c]	85% (80 to 88)[c]	46% (35 to 57)[c]	98% (95 to 99)[c,d]	85% (81 to 89)[c]	NR
Slater et al. (2024)[4] (N = 500)	**IT**: Rapid LVO alone **RS**: Consensus of 3 or 4 neuroradiologists	LVO of the intracranial ICA, M1 or M2 MCA segments, basilar artery, or intracranial vertebral artery	NR	NR	NR	NR	62% (48 to 75)	93% (90 to 95)	NR	NR	NR	NR
Schlossman et al. (2022)[8] (N = 253)	**IT**: Rapid LVO alone **RS**: Consensus of 2 neuroradiologists	Intracranial ICA LVO (n = 235)	9	32	2	192	82% (48 to 98)[c]	86% (80 to 90)[c]	22% (11 to 38)[c]	99% (96 to 100)[c]	86% (80 to 90)[c]	NR
Adhya et al. (2021)[2] (N = 310)	**IT**: Rapid CTA alone at < 45% relative vessel density threshold **RS**: Consensus of 2 neuroradiologists	LVO[b]	129	43	32	106	80% (73 to 86)[c]	71% (63 to 78)[c]	75% (68 to 81)[c]	77% (69 to 84)[c]	76% (71 to 80)[c]	NR

Study Citation	Index Test and Reference Standard	Type of LVO and Subgroup (if applicable)	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC (95% CI)
	IT: Rapid CTA alone at ≤ 60% relative vessel density threshold **RS**: Consensus of 2 neuroradiologists	LVO[b]	161	149	0	0	NE[e]	NE[e]	NE	NE	52% (46 to 58)[c]	NR

AUC = area under the receiver operating characteristic curve; FN = false negatives; FP = false positives; ICA = internal carotid artery; IT = index test; LVO = large vessel occlusion; MCA = middle cerebral artery; NE = not estimable; NPV = negative predictive value; NR = not reported; PPV = positive predictive value; TN = true negatives; TP = true positives; RS = reference standard.

[a]Concordance refers to the overall rate of agreement between the index test and the reference standard. It measures how often the index test and the reference standard produced the same result (e.g., both positive or both negative) for the same set of cases, but does not assess the accuracy or correctness of either test relative to the absolute truth.

[b]Unclear which types of LVO were considered eligible. In Delora et al. (2024),[3] the study population included patients with occlusions of the ICA, M1 MCA segment, and M2 MCA segment. The study population from Adhya et al. (2021) included patients with occlusions of the ICA, carotid terminus, M1 MCA segment, and M2 MCA segment.

[c]Not reported in the publication. We calculated the value with Clopper-Pearson exact 95% confidence intervals from the available data via the EpiR package in R.[15]

[d]NPV was reported as 97% in the publication, but was calculated as 98% via the EpiR package in R.[15]

[e]Patient eligibility was determined using the results of the index test (i.e., only patients who tested positive using the index test at a relative vessel density of 60% or less were included); as such, the values for sensitivity and specificity were not calculated as the sample was selected to exclude any true negatives and false negatives.

Table 27: Study Results, by Outcome — Diagnostic Accuracy for the Detection of ICH

Study Citation	Index Test and Reference Standard	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Concordance (95% CI)[a]	AUC
Eldaya et al. (2022)[11] (N = 307)	**IT**: Rapid ICH + neuroradiologist **RS**: Either a neuroradiologist (in the case of concordance) or a consensus panel of 3 neuroradiologists (in the case of discordance)	34	1	3	269	92% (78 to 98)	100% (98 to 100)	97% (85 to 100)	99% (97 to 100)	99% (97 to 100)[a]	NR

AUC = area under the receiver operating characteristic curve; FN = false negatives; FP = false positives; ICH = intracranial hemorrhage; IT = index test; NPV = negative predictive value; NR = not reported; PPV = positive predictive value; TN = true negatives; TP = true positives; RS = reference standard.

[a]Concordance refers to the overall rate of agreement between the index test and the reference standard. It measures how often the index test and the reference standard produced the same result (e.g., both positive or both negative) for the same set of cases, but does not assess the accuracy or correctness of either test relative to the absolute truth.

Reasons for Certainty of Evidence Ratings

Table 28: Certainty of Evidence Ratings for CTA With RapidAI Versus CTA Without RapidAI for People With Suspected Acute Stroke

Outcome	Certainty	Reason for Rating
Time to intervention		
Radiology report turnaround	Low *(due to risk of bias)*	Due to the NRS design and critical risk of bias due to baseline confounding as assessed via ROBINS-I, the certainty of evidence was started at low. We based our judgment of imprecision on the optimal information size, which was exceeded.
Door to intervention	Very low *(due to risk of bias and imprecision)*	Due to the NRS design and serious risk of bias due to baseline confounding as assessed via ROBINS-I, the certainty of evidence was started at low. Rated down 1 level for serious imprecision due to the small sample size.
CTA to groin puncture	Very low *(due to risk of bias and imprecision)*	Due to the NRS design and serious risk of bias due to baseline confounding as assessed via ROBINS-I, the certainty of evidence was started at low. Rated down 1 level for serious imprecision due to the small sample size.
Functional status		
Neurologic deficit (per NIHSS score)	Very low *(due to risk of bias and imprecision)*	Due to the NRS design and serious risk of bias due to baseline confounding as assessed via ROBINS-I, the certainty of evidence was started at low. Rated down 1 level for serious imprecision due to the small sample size
Proportion of patients with significant morbidity or mortality (defined as mRS score ≥ 5) at discharge	Very low *(due to risk of bias and imprecision)*	Due to the NRS design and serious risk of bias due to baseline confounding as assessed via ROBINS-I, the certainty of evidence was started at low. Rated down 2 levels for very serious imprecision. Using the null as the threshold, the 95% CI included the possibility of no difference and benefit.
Disability and dependence in daily activities (per 90-day mRS score)	Very low *(due to risk of bias and imprecision)*	Due to the NRS design and serious risk of bias due to baseline confounding as assessed via ROBINS-I, the certainty of evidence was started at low. Rated down 1 level for serious imprecision due to the small sample size
Proportion of patients considered to be functionally independent (defined as mRS score ≤ 2) at 90 days	Very low *(due to risk of bias and imprecision)*	Due to the NRS design and serious risk of bias due to baseline confounding as assessed via ROBINS-I, the certainty of evidence was started at low. Rated down 2 levels for very serious imprecision. Using the null as the threshold, the 95% CI included the possibility of no difference and harm.
Response to therapy		
Proportion of patients with TICI scores of 0, 1, 2A, 2B/C, or 3	Very low *(due to risk of bias and imprecision)*	Due to the NRS design and serious risk of bias due to baseline confounding as assessed via ROBINS-I, the certainty of evidence was started at low. Rated down 1 level for serious imprecision due to the small sample size.
Patient Harms		
NR	NA	NA

CI = confidence interval; CTA = CT angiography; mRS = modified Rankin Scale; NA = not applicable; NIHSS = US National Institutes of Health Stroke Scale; NR = not reported; NRS = nonrandomized study; TICI = Thrombolysis in Cerebral Infarction.

Source: Soun et al. (2023)[2] and Adhya et al. (2021).[2]

Table 29: Certainty of Evidence Ratings for the Diagnostic Accuracy of RapidAI with Clinician Interpretation Relative to Clinician Interpretation (or Clinician Consensus) for Suspected Acute Stroke

Index Test	Certainty	Reason for Rating
ICH		
Rapid ICH (version NR) with interpretation by a neuroradiologist	Low *(due to risk of bias and imprecision)*	Serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project

CI = confidence interval; ICH = intracranial hemorrhage; NR = not reported; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

Source: Eldaya et al. (2022).[11]

Table 30: Certainty of Evidence Ratings for the Diagnostic Accuracy of RapidAI Alone Relative to Clinician Interpretation (or Clinician Consensus) for Suspected Acute Stroke

Index Test	Certainty	Reason for Rating
M1 MCA and ICA LVO		
Rapid LVO (RapidAI v4.9) alone	Low *(due to risk of bias and imprecision)*[b]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project). The 95% CI for 1 study was neither reported nor calculable, precluding a comprehensive judgment about the precision of the estimates.
Rapid LVO (v1.0) alone	Moderate *(due to risk of bias)*[d]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2.
Rapid CTA (RapidAI v4.9) alone	Moderate *(due to imprecision)*[e]	Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project)
Rapid CTA (version NR) alone	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).
Rapid NCCT Stroke platform (version NR) alone[g]	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).

Index Test	Certainty	Reason for Rating
M1 and M2 MCA and ICA LVO		
RapidAI alone (version NR)	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).
Rapid CTA alone (RapidAI v4.9)	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).
M1 MCA LVO		
RapidAI alone (version NR)	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).
Rapid LVO alone (as part of RapidAI v4.9)	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).
M2 MCA LVO		
Rapid LVO (RapidAI v4.9) alone	Insufficient information to judge[h]	The certainty of evidence could not comprehensively be judged owing to incomplete reporting in the study. The number of false negatives and true negatives, the specificity, and the 95% CIs for sensitivity were neither reported nor calculable. The study was at high risk of bias as assessed via QUADAS-2
Rapid CTA (RapidAI v4.9) alone	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).
ICA LVO		
Rapid LVO (RapidAI v4.9) alone	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).

Index Test	Certainty	Reason for Rating
LVO of the ICA, M1 or M2 MCA, basilar artery, or intracranial vertebral artery		
Rapid LVO alone (RapidAI v5.1)	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).
Undefined LVO[a]		
Rapid LVO (v5.2.2) alone	Low *(due to risk of bias and imprecision)*[f]	Rated down 1 level for serious risk of bias, as all contributing studies were at high risk as assessed via QUADAS-2. Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).
Rapid CTA (version NR) alone at < 45% relative vessel density threshold	Very low *(due to risk of bias and imprecision)*[j]	Rated down 2 levels for very serious risk of bias, as all contributing studies were at high risk with concerns related to patient selection as assessed via QUADAS-2. Patient eligibility was determined using the results of the index test (i.e., only patients who tested positive using the index test at a relative vessel density of 60% or less were included); as such, the values calculated for sensitivity and specificity are drawn from a sample of patients that is not representative of clinical practice (as the sample excludes anyone with a relative vessel density of greater than 60%). Rated down 1 level for serious imprecision, as the ranges of the 95% CIs included values that may lead to different conclusions about value of the index test (i.e., values both above and below a sensitivity or specificity of 90%, a threshold suggested by a clinical expert that we consulted for this project).

CI = confidence interval; CTA = CT angiography; ICA = internal carotid artery; LVO = large vessel occlusion; MCA = middle cerebral artery; NCCT = non-contrast CT; NR = not reported; QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies 2.

[a]Unclear which types of LVO were considered eligible. In Delora et al. (2024), the study population included patients with occlusions of the ICA, M1 MCA segment, and M2 MCA segment. The study population from Adhya et al. (2021) included patients with occlusions of the ICA, carotid terminus, M1 MCA segment, and M2 MCA segment.

Source: Delora et al. (2024),[3] Slater et al. (2024),[4] Chan et al. (2023),[5] Soun et al. (2023),[1] Yedavalli et al. (2023),[6] Mallon et al. (2022),[7] Schlossman et al. (2022),[8] Adhya et al. (2021),[2] Dehkharghani et al. (2021),[9] and Amukotuwa et al. (2019).[10]

Patient Engagement

Table 31: Summary of Patient Engagement Using the Guidance for Reporting Involvement of Patients and the Public (version 2) Short Form Reporting Checklist[16]

Section and topic	Item	Report section
Aim	One patient contributor participated in a 1-hour interview during the drafting phase of the report to highlight her experiences, perspectives, and priorities for the use of AI in stroke detection.	Methods
Methods	After giving informed consent, 1 patient contributor discussed her experience of a stroke and her perspectives on the use of AI in stroke detection.	Methods

Section and topic	Item	Report section
Results of engagement	**Perspectives Shared:** The patient contributor shared her personal experience of having a hemorrhagic stroke, the emergency treatment she received, and her recovery. She did not know whether AI had been used in her diagnosis. **RapidAI:** RapidAI was described to the patient contributor, and she shared her thoughts on its use in stroke detection, relating to perceived potential outcomes and ethical considerations as described below. **Outcomes to Measure** **Speed:** Two of the potential benefits that the patient contributor hoped for was speed and accuracy. She was hopeful that if the use of AI meant a speedier and more accurate diagnosis, perhaps clinicians could initiate the most appropriate treatment sooner. She hoped that this would reduce the damage being caused by the stroke and improve outcomes. **Accuracy:** When asked to expand on her comment about accuracy being crucial to the success of using AI, the patient contributor posited that, while ensuring the accuracy of the AI technology was a concern, she was curious about whether AI could accurately identify issues earlier than a clinician, or perhaps prevent human error. **Other Outcomes:** When asked specifically about outcomes of interest, speed and accuracy were the patient contributor's priorities. However, she also identified minimizing the damage caused by strokes and mortality rates as other factors to consider. **Ethical Considerations** **Equitable Access:** The patient contributor expressed concern about the accessibility of RapidAI technologies outside of major stroke centres and wondered whether all major hospitals could benefit from this technology to assist in triaging (and potentially transferring) patients more quickly. She also had concerns about services in rural and remote community hospitals. **Privacy:** The patient contributor suggested that, in a crisis, she felt that most people wouldn't be thinking of ethical considerations like privacy and data sharing – they would be focused on diagnosis, treatment, and survival. The patient contributor reflected that some people may be more reluctant to have their personal information shared with the manufacturer, while others may be used to sharing their personal information with cell phone or computer software manufacturers. She suggested that there may be a divide, with some individuals being more protective of their personal information and others more familiar with novel technologies and sharing their data. Regardless of the level of patient comfort with sharing data, the patient contributor shared concerns about privacy, safety of information, accuracy, and reliability of storage. **Informing the Patient:** The patient contributor expressed curiosity about whether patients will be informed that their clinicians used AI in their diagnosis. She herself did not know whether the technology was in use at the time of her stroke.	Summary of Evidence

Section and topic	Item	Report section
Discussion and conclusions	Success of engagement in this review is related to several factors. First, there was outreach through several organizations. Second, the patient contributor was briefed on the objectives of the project in an introductory call and supported by a Patient Engagement Officer. Third, 3 of the project team members attended the interview to hear from the individual directly and to engage her in conversation. Fourthly, a gift card was offered as a gesture of appreciation for her contribution. Finally, the patient contributor was offered the opportunity to be thanked by name in the acknowledgements section of the report or to remain anonymous. She preferred to remain anonymous. However, there were limitations. Though we had intended to engage with 3 individuals, 2 patients and a clinician, we had limited response to our outreach, and the sole clinician who responded to our initial request ultimately declined to participate due to time constraints.	Summary of Evidence
Critical Reflections	The patient contributor was highly engaged in the discussion, sharing her experience, thoughts, and priorities. Questions were sent ahead of time so that she could prepare. A summary of the discussion was drafted and sent to the patient contributor. She was able to share feedback and approve the summary as an accurate reflection of the conversation. One limitation of our approach is that people need access to reliable technology, phone, and internet access to contribute to our work, which may exclude some voices.	NA

AI = artificial intelligence; NA = not applicable.

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