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AUTOMATED PREDICTION OF LARGE VESSEL OCCLUSION USING ARTIFICIAL INTELLIGENCE IN NON-CONTRAST COMPUTED TOMOGRAPHY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background: Acute ischemic stroke due to large vessel occlusion (LVO) requires rapid identification. Reducing the time to diagnosis and treatment of stroke patients is an important goal to improve clinical outcomes. Non-contrast computed tomography (NCCT) is widely used in clinical practice for suspected stroke patients. Automated analysis using artificial intelligence in NCCT may be a solution to accelerate the early detection of LVO.
Objective: To determine the accuracy of artificial intelligence in NCCT to predict LVO.
Methods: A systematic literature search was conducted based on the PRISMA flow chart in four databases (PubMed, ProQuest, ScienceDirect, Cochrane Library) until June 2024. Data extraction was performed to evaluate the accuracy of predicting LVO. Quality assessment was performed using QUADAS-2. All data were analyzed using Review Manager 5.4 and MetaDTA 2.0.
Results: Five studies involving 4.862 patients were enrolled. The quality of all the studies was high and had a low risk of bias. All studies used different software. Artificial intelligence in NCCT had fairly good accuracy with a sensitivity and specificity of 0.83 (95% CI; 0.78-0.87) and 0.73 (95% CI; 0.52-0.87). NCCT plus clinical status (NIHSS, stroke onset) in two studies slightly improved overall accuracy with a sensitivity and specificity of 0.85 (95% CI; 0.80-0.89) and 0.74 (95% CI; 0.54-0.88). Two studies reported that machine learning took less than two minutes.
Conclusion: Artificial intelligence in NCCT was reasonably accurate and took a short time to predict LVO. There are still opportunities for machine learning to improve performance. Further research is still needed.

Keywords: artificial intelligence, automated prediction, large vessel occlusion, non-contrast computed tomography

Introduction

Ischemic stroke was the most prevalent type of stroke, accounting for 62.4% of cases.[1] Large vessel occlusion (LVO) was identified in 24-46% of all acute ischemic strokes.[2] LVO requires a special approach due to its high morbidity and mortality rates.[3] The American Heart Association (AHA)/American Stroke Association (ASA) guidelines recommend mechanical thrombectomy within 24 hours of stroke onset due to LVO. Despite the high prevalence of LVO, only a small proportion of patients undergo recommended therapy.[4]

LVO requires early detection and prompt treatment. Reducing the time required for detection will facilitate intervention and improve clinical outcomes. Radiological imaging, such as magnetic resonance imaging (MRI) and computed tomography angiography (CTA), is the primary modality to determine LVO.[5,6] However, these examinations have limitations such as restricted accessibility, procedural delays, expense, risk of contrast agent, and the necessity for radiologist expertise.[7,8]

Non-contrast computed tomography (NCCT) is a widely used imaging technique in clinical practice for suspected acute stroke patients. NCCT has high accessibility, a fast procedure, and numerous benefits. Some research has found that specific characteristics visible on NCCT can be signs of LVO, including hyperdense artery signs.[9,10] Loss of gray-white matter differentiation and sulcal effacement.[11,12] In conjunction with the patient's clinical status, there is an increased likelihood of suspecting LVO.[10,13]

Neuroimaging is a crucial tool in the management of stroke patients. The application of artificial intelligence (AI) in neuroimaging has recently attracted considerable attention. AI-driven automated analysis has the potential to facilitate early detection in emergency settings where radiology is unavailable. This study aims to assess the accuracy of AI in NCCT in predicting LVO.

Methods

Search strategy

This study was conducted per the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[14] A comprehensive literature search was performed to determine artificial intelligence's accuracy in NCCT predicting LVO. The search was conducted on June 9, 2024, using four databases (PubMed, ProQuest, ScienceDirect, Cochrane-Library) using combination keywords that included “artificial intelligence” or “deep learning” or machine learning” and “large vessel occlusion” and “non-contrast computed tomography”.

Inclusion criteria were studies that (1) evaluated artificial intelligence for LVO prediction on NCCT, (2) were available in English, (3) were original research, and (4) contained outcome measures. All study designs were included. We excluded non-original studies and those with insufficient data for analysis.

Data extraction

The authors independently screened the studies, including titles and abstracts, based on the inclusion criteria. The full-text article was reviewed when uncertain or if it met the inclusion criteria. Data extraction included publication year, study location and design, number of patients, the slice thickness of NCCT, AI methods, performance results, and 2x2 table extraction.

Analysis data

The methodological quality of the studies was assessed by the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) criteria.[15] The extracted data were analyzed using Cochrane Review Manager 5.4. Bivariate model analysis performed by MetaDTA 2.0.[16] The analysis data used a 95% confidence interval (CI) using the random effect model. The results are forest plots and summary receiver operating characteristic (SROC) curves.

Results

Study selection

An initial literature search yielded 123 articles. After excluding duplicates, we reviewed 98 potential studies in detail. A total of 35 articles were read for the abstract, and eight were read for the full-text. Two studies have no outcome of interest, and one study does not have enough data for analysis. Five studies were identified for quantitative analysis. The selection process and reasons for the studies identified are shown in Figure 1.

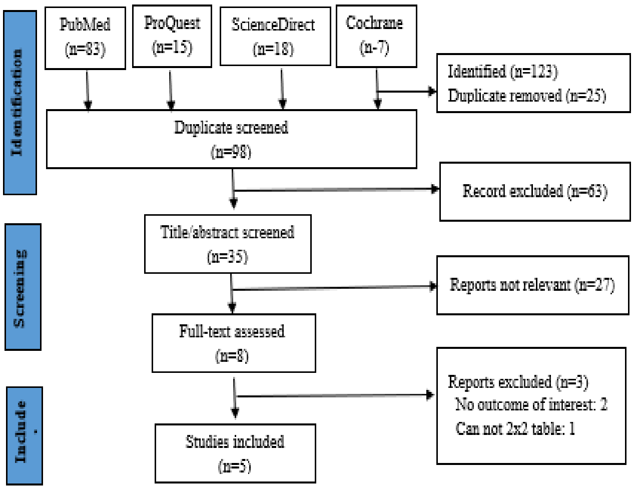


Figure 1. Study the flow diagram

Characteristics of the Included Studies

All included studies had a retrospective cohort design, involving 4,862 patients across five studies from various countries. Each study used different AI software on NCCT to predict LVO, with four utilizing Convolutional Neural Network (CNN) models and one using the ExtraTrees model (Table 1).

Three studies focused specifically on imaging-based AI. Chan et al. used the ASPECTS score to predict LVO, showing high sensitivity (87.5%) but low specificity (30.9%). In acute LVO, the hyperdense artery sign is visible on NCCT. Tolhuisen ML et al. and Weyland et al. used AI to detect this sign, reporting 86% and 77% sensitivities, respectively.

Table 1. Study characteristics

Study	Country	Study Design	Sample	LVO (%)	Slice	AI Method/ Software	Time	Detection	Performance Scores	
Chan N, 2022	Single center, United Kingdom	Cohort retrospective	104	26.1	0.625 mm	CNN; RAPID ASPECTS	NA	ASPECTS	AUC: NA Se: 87.5% Spe: 30.9%	
Kim PE, 2024	Five centers, South Korea	Cohort retrospective	2.919	26.3	3-5 mm	ExtraTrees; JLK-CTL, JLK-CTL+	NA	1. Modified 4 ASPECTS and HAS 2. Adding NIHSS	JLK-CTL AUC: 0.88 Se: 80.1% Spe: 88.6%	JLK-CTL+ AUC: 0.92 Se: 92.1% Spe: 81.5%
Olive-Gadea M, 2020	Two centers, Spain	Cohort retrospective	1.453	56.6	3-5 mm	CNN; MethinksLVO, MethinksLVO+	< 2m	1. Acute ischemic tissue and HAS 2. Adding NIHSS and stroke onset	MethinksLVO AUC: 0.87 Se: 83.2% Spe: 71.3%	MethinksLVO+ AUC: 0.91 Se: 83.1% Spe: 85.1%
Tolhuisen ML, 2020	Multicenter, Netherland	Cohort retrospective	232	57.4	≤ 2.5 mm	CNN	< 2m	Asymmetry and HAS	AUC: NA Se: 86% Spe: 65%	
Weyland CS, 2022	Three centers, Germany	Cohort retrospective	154	54.5	≤ 1 mm	CNN	NA	HAS	AUC: 0.85 Se: 77% Spe: 87%	

CNN: Convolutional Neural Network; NA: Not available; ASPECTS: Alberta Stroke Program Early CT Score; NIHSS: National Institutes of Health Stroke Scale Score; AUC: area under curve; Se: sensitivity; Spe: specificity

Two studies (Kim PE et al. and Olive-Gadea M et al.) employed NCCT with clinical status, enhancing detection performance. Kim PE et al. modified four ASPECTS and identified the clot sign for predicting LVO with a sensitivity of 80.1% and specificity of 88.6% (AUC 0.88). Adding imaging features to the National Institutes of Health Stroke Scale (NIHSS) score enhanced performance, with a sensitivity of 92.1% and specificity of 81.5% (AUC 0.92).[13] Similarly, Olive-Gadea M et al programmed AI to detect acute ischemic tissue and hyperdense clot signs, achieving a sensitivity of 83.2% and specificity of 71.3% (AUC 0.87). Incorporating patient clinical status, including the NIHSS score and stroke onset, increased the specificity of AI to 85.1% (AUC 0.91).[10]

Methodological quality

A QUADAS-2 assessment revealed that all studies exhibited a low risk of bias and applicability concerns, with clear patient selection reported. Moreover, all LVOs were consistently confirmed by CTA examinations conducted by experienced neuroradiologists, ensuring diagnostic reliability (Figure 2).

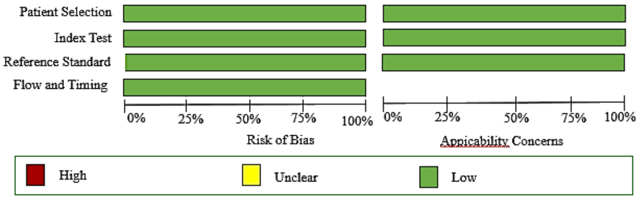
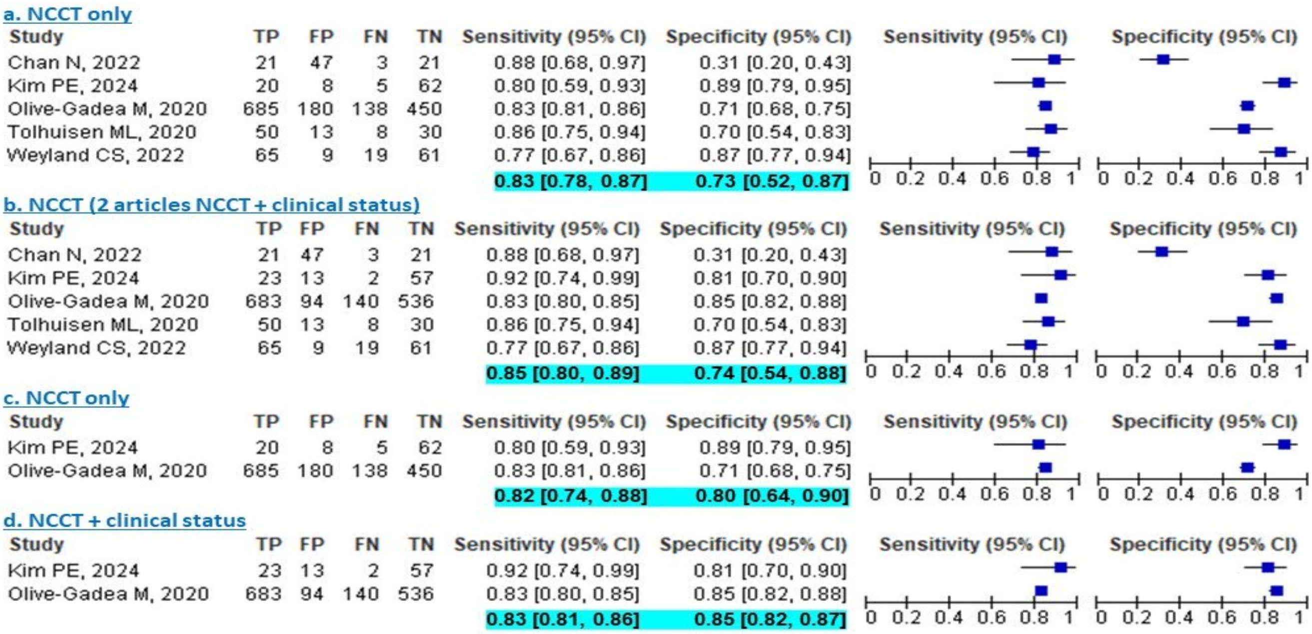


Figure 2. Methodological quality

Diagnostic accuracy

A meta-analysis was conducted on five studies to evaluate the accuracy of artificial intelligence (AI) in diagnosing stroke using non-contrast CT (NCCT) examination. The analysis was divided into four subgroups. The use of AI on NCCT examination alone demonstrated satisfactory performance, with a sensitivity of 0.83 (95% CI, 0.78-0.87) and specificity of 0.73 (95% CI, 0.52-0.87). The false positive rate remains high at 27.4%. Two studies performed additional analysis in which the NCCT examination was added to the input data set, incorporating patient clinical status (NIHSS and stroke onset), slightly improving the overall pooling results. The sensitivity was 0.85 (95% CI, 0.80-0.89), and the specificity was 0.74 (95% CI, 0.54-0.88). The false positive rate decreased to 25.8%.

In a separate analysis encompassing two studies, it was observed that the performance of AI improved when compared to NCCT only (sensitivity 0.82 and specificity 0.80) with NCCT plus clinical status (sensitivity 0.83 and specificity 0.87). The false positive rate decreased from 19.9% to 15.3%. The results of the forest plot analysis are illustrated in Figure 3. The summary receiver operating characteristic (SROC) curves are shown in Figure 4.



a. NCCT only

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chan N, 2022	21	47	3	21	0.88 [0.68, 0.97]	0.31 [0.20, 0.43]
Kim PE, 2024	20	8	5	62	0.80 [0.59, 0.93]	0.89 [0.79, 0.95]
Olive-Gadea M, 2020	685	180	138	450	0.83 [0.81, 0.86]	0.71 [0.68, 0.75]
Tolhuisen ML, 2020	50	13	8	30	0.86 [0.75, 0.94]	0.70 [0.54, 0.83]
Weyland CS, 2022	65	9	19	61	0.77 [0.67, 0.86]	0.87 [0.77, 0.94]
					0.83 [0.78, 0.87]	0.73 [0.52, 0.87]

b. NCCT (2 articles NCCT + clinical status)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chan N, 2022	21	47	3	21	0.88 [0.68, 0.97]	0.31 [0.20, 0.43]
Kim PE, 2024	23	13	2	57	0.92 [0.74, 0.99]	0.81 [0.70, 0.90]
Olive-Gadea M, 2020	683	94	140	536	0.83 [0.80, 0.85]	0.85 [0.82, 0.88]
Tolhuisen ML, 2020	50	13	8	30	0.86 [0.75, 0.94]	0.70 [0.54, 0.83]
Weyland CS, 2022	65	9	19	61	0.77 [0.67, 0.86]	0.87 [0.77, 0.94]
					0.85 [0.80, 0.89]	0.74 [0.54, 0.88]

c. NCCT only

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kim PE, 2024	20	8	5	62	0.80 [0.59, 0.93]	0.89 [0.79, 0.95]
Olive-Gadea M, 2020	685	180	138	450	0.83 [0.81, 0.86]	0.71 [0.68, 0.75]
					0.82 [0.74, 0.88]	0.80 [0.64, 0.90]

d. NCCT + clinical status

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kim PE, 2024	23	13	2	57	0.92 [0.74, 0.99]	0.81 [0.70, 0.90]
Olive-Gadea M, 2020	683	94	140	536	0.83 [0.80, 0.85]	0.85 [0.82, 0.88]
					0.83 [0.81, 0.86]	0.85 [0.82, 0.87]

Figure 3. Forest plot of AI to predict LVO: (a) NCCT only, (b) NCCT (2 articles NCCT + clinical status), (c) 2 articles with NCCT only, and (d) 2 articles with NCCT + clinical status

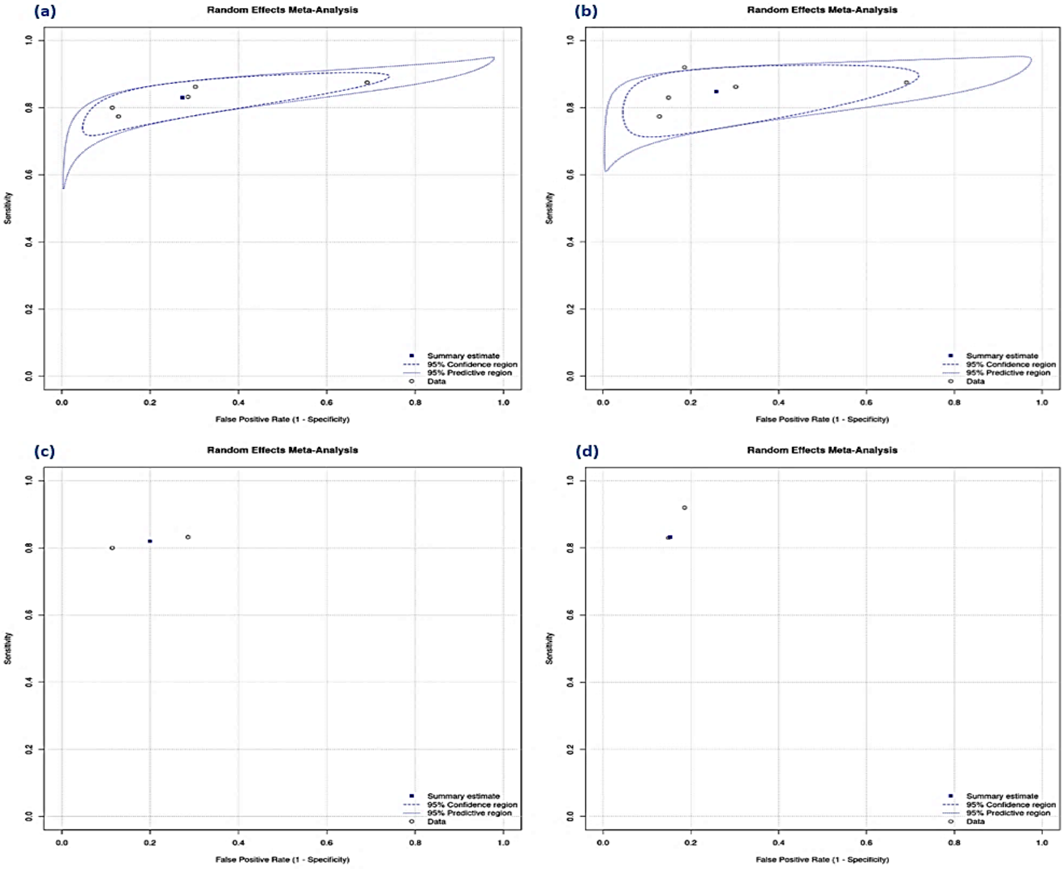


Figure 4. Summary receiver operating characteristic (SROC) curve of AI to predict LVO: (a) NCCT only, (b) NCCT (2 articles NCCT + clinical status), (c) 2 articles with NCCT only, and (d) 2 articles with NCCT + clinical status

Discussion

The ability of AI on NCCT to predict LVO had fairly good accuracy with a sensitivity and specificity of 0.83 (95% CI; 0.78-0.87) and 0.73 (95% CI; 0.52-0.87). One study employed the use of ASPECTS for machine learning. Chan et al. utilized the ASPECTS to predict LVO, exhibiting a high sensitivity of 87.5%, yet a low specificity of 30.9%. The false positive rate was 51.1%, with most cases exhibiting an ASPECTS score ≥ 8 and some instances reporting infarcts in the incorrect hemisphere. This indicates that the software frequently overcalled (1-2 scores) the presence of isolated ischemia without any imaging abnormalities. In cases where LVO was confirmed, the software correctly identified the affected hemisphere.[17]

Two studies used the hyperdense artery sign (HAS) in software to predict LVO. HAS is known to be present in acute ischemic stroke due to LVO, with a sensitivity of 52.4% and specificity of 94.9%. Using smaller CT scan slices can increase the sensitivity to 62%.[19] The ability to detect HAS by AI demonstrated superior sensitivity results as a marker of LVO. Studies conducted by Tolhuisen ML et al. and Weyland CS et al. obtained a sensitivity of 86% and 77%, respectively, with specificity that requires improvement, namely 65% and 87%. Automated detection of HAS by AI was demonstrated to be comparable to expert neuroradiologists. False positives can be found in focal atherosclerosis, while false negatives are observed in very distal or distal LVO cases.[9,18]

Two studies, Kim PE et al. and Olive-Gadea M et al., using a combination of acute ischemic picture and HAS as a marker of LVO, achieved a relatively high level of performance, with 80.1% and 83.2% sensitivity, respectively (AUC 0.88 and 0.87).[10,13] In addition to imaging, incorporating clinical data can assist in diagnosing LVO. The two studies added the patient's clinical status (NIHSS, stroke onset) into the AI input data, which enhanced the diagnostic performance, even in Kim PE et al. A high sensitivity of 92.1% and an AUC of 0.92 were achieved.[13] Adding NIHSS and stroke onset also resulted in a 14% reduction in false positives.[10] The results of the meta-analysis also demonstrated that the addition of NCCT to the patient's clinical status resulted in an improvement in the diagnostic performance.

The timely identification of LVO is crucial for improving clinical outcomes. However, in emergency settings, the interpretation of radiological images may not be readily available. AI-powered analysis offers a potential solution, as it can facilitate the detection of LVO in various clinical scenarios and minimize the impact of human reading errors, which may arise due to fatigue or a lack of accuracy. Two studies have demonstrated that machine learning algorithms can process images in less than two minutes.[10,18] Additionally, a study reported that automated platforms halve the processing time for imaging for stroke patients.[20] Furthermore, machine learning can be an early warning system and a failsafe mechanism to ensure no LVO is overlooked.

The performance of AI in detecting LVO may be further enhanced in the future. Integrating combination detection on NCCT imaging, such as acute infarction and HAS images, can augment the detection capability. Incorporating patient clinical status, including NIHSS and stroke onset, may also prove beneficial.[10,13] The study by You et al. using combined demographics, clinical status, and images on NCCT showed good diagnostic performance with a sensitivity of 93% (AUC 0.85, specificity 68.4%).[21] AI can be utilized independently or in conjunction with readout. In a study conducted by Delio et al., it was demonstrated that the diagnostic accuracy of radiologists reading imaging studies was significantly enhanced when machine learning was incorporated into the process, increasing from 72% to 78% ($p < 0.0001$).[22]

The present meta-analysis is subject to several limitations. Firstly, the number of studies included is relatively small, and the samples are limited. Secondly, the software used in the studies varied. Thirdly, all of the included studies were of a retrospective design. Finally, further research is needed to determine the benefits of AI in emergency settings in clinical practice.

Conclusion

The application of AI to NCCT imaging examinations demonstrated a relatively high degree of accuracy in predicting LVO. Incorporating patient clinical status data into the AI model yielded enhanced performance. There remain avenues for further improvement in AI performance. The deployment of AI may serve as a solution to accelerate the triage and detection of LVO, thereby enhancing the speed of management and clinical outcomes for patients. Further research is necessary to determine the clinical impact in emergency settings.

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