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REVIEW ARTICLE

Cincinnati Prehospital Stroke Scale (CPSS) as a Screening Tool for Early Identification of Cerebral Large Vessel Occlusions; a Systematic Review and Meta-analysis

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Abstract: **Introduction:** Large vessel occlusion (LVO) strokes are associated with worse functional outcomes and higher mortality rates. In the present systematic review and meta-analysis, we evaluated the diagnostic yield of the Cincinnati Prehospital Stroke Scale (CPSS) in detecting LVO. **Methods:** We performed an extensive systematic search among online databases including Medline, Embase, Web of Science, and Scopus, until July 31st, 2023. We also conducted a manual search on Google and Google scholar, along with citation tracking to supplement the systematic search in retrieving all studies that evaluated the diagnostic accuracy of the CPSS in detecting LVO among patients suspected to stroke. **Results:** Fourteen studies were included in the present meta-analysis. CPSS showed the sensitivity of 97% (95% CI: 87%–99%) and the specificity of 17% (95% CI: 4%–54%) at the cut-off point of ≥1. The optimal threshold was determined to be ≥2, with a sensitivity of 82% (95% CI: 74%–88%) and specificity of 62% (95% CI: 48%–74%) in detecting LVO. At the highest cut-off point of ≥3, the CPSS had the lowest sensitivity of 60% (95% CI: 51%–69%) and the highest specificity of 81% (95% CI: 71%–88%). Sensitivity analyses showed the robustness of the results regardless of study population, inclusion of hemorrhagic stroke patients, pre-hospital or in-hospital settings, and the definition of LVO. **Conclusion:** A very low level of evidence demonstrated that CPSS, with a threshold set at ≥2, is a useful tool for identifying LVO stroke and directing patients to CSCs, both in prehospital and in-hospital settings.

Keywords: Brain infarction; Arterial occlusive diseases; Clinical decision rules; Diagnosis; Intracranial arteriosclerosis; Ischemic stroke

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1. Introduction

Globally, ischemic stroke, especially with large vessel occlusion (LVO), is a major cause of mortality and disability. LVO strokes, constituting 24% to 46% of acute ischemic stroke cases, often lead to higher dependence and deficits (1, 2). The evolution of LVO definition focuses on specific vessel occlusions. These vessels are intracranial internal carotid artery, M1/M2 segments of the middle cerebral artery, posterior cerebral artery, intracranial segment of vertebral artery, or basilar artery, as observed on the baseline computed tomography angiography (CTA) or magnetic resonance angiography (MRA) (1, 3, 4).

Intravenous thrombolysis (IVT) is the conventional treatment for acute ischemic stroke if it is not contraindicated and is performed in a time window of up to 4.5 hours (5). Along with IVT, Endovascular thrombectomy (EVT) has been shown to contribute to a substantially more favorable functional outcome in a subset of LVO stroke patients (6-10). IVT is a widely available intervention at many stroke centers. However, EVT requires specialized capabilities and is only available at Comprehensive Stroke Centers (CSC).

Ischemic stroke patients are usually directed to the nearest Primary Stroke Center (PSC). If eligible for EVT, they are referred to a CSC for treatment, causing potential delays and

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risking a missed EVT window during inter-facility transfer (3, 11). Therefore, early LVO detection in suspected stroke cases is crucial for quick decision-making, directing patients to CSC rather than the nearest PSC.

Implementing prehospital scoring for early-stage EVT eligibility can enhance outcomes, providing en-route notifications to the Emergency Department for faster critical care staff and equipment assembly, expediting EVT delivery (12, 13). While new scores can detect LVO stroke, cost considerations prompt researchers to assess the performance of existing stroke diagnostic tools repurposed for LVO screening. The Cincinnati Prehospital Stroke Scale (CPSS), commonly used by EMS personnel, initially aimed at screening acute stroke cases, evaluates facial paralysis, arm weakness, and speech disorders based on NIHSS assessment items (14).

Despite primary studies on CPSS's diagnostic accuracy for cerebral vessel occlusion, a conclusive determination is lacking, emphasizing the need for a consensus. Our systematic review and meta-analysis aim to audit CPSS's predictive performance in detecting LVO among stroke patients.

2. Methods

2.1. Study design and search strategy

In the present study, we investigated the diagnostic accuracy of the pre-hospital Cincinnati scale in identifying patients with large cerebral artery occlusion. The researchers followed preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 statement during conducting and reporting the current systematic review (15). We formulated the study question using PICO (Problem, Index test, Comparison, Outcome) framework. P referred to suspected or confirmed acute stroke patients, I to the CPSS, C to CTA or MRA, and O to the diagnostic accuracy of CPSS in detecting LVO.

We performed a comprehensive search in each database, including Medline (using PubMed), Embase, Scopus, and Web of Science by the end of July 2023. That was done by utilizing relevant keywords extracted form MeSH and Emtree terms and their synonyms, guided by field experts and review of literature. No language or time restrictions were applied. We also conducted a manual search on Google and Google scholar, along with citation tracking of the retrieved articles. The search strings are provided in Supplementary Material 1.

2.2. Selection criteria

We included the peer-reviewed articles investigating the value of CPSS in detecting LVO among adults with suspected or confirmed stroke, whether applied in a pre-hospital or in-hospital setting, and regardless of LVO definition. Exclusion criteria were reviews, abstracts, duplicate publications, retracted articles, studies on pediatrics, app-based diagnosis studies, not reporting CPSS cut-off points, lack of a non-LVO control group, and not reporting the required data for meta-analysis of diagnostic accuracy studies. If one study reported the data in multiple articles with overlapping samples, we included the article with larger sample size and broader patient selection, as far as it met our selection criteria. In cases of failure to retrieve the full-text articles or not reporting the required data, we contacted the corresponding author and asked for full-text or further data, before excluding those studies.

2.3. Data collection

We exported the search results to EndNote X9 software. After removing duplicates, two authors independently conducted the screening and data collection steps, starting with reviewing the titles and abstracts of the records. Any discrepancies among the two reviewers were resolved through discussion with a third reviewer. Based on inclusion criteria, the full-text of the potentially eligible articles were retrieved. By carefully reading the retrieved articles, exclusion criteria were applied to gain the final included articles. Articles were summarized in an excel sheet. The extracted data were first author's surname, publication year, country, study design, sample size, age and sex distribution of patients, the number of LVO patients, study population (i.e., suspected vs. confirmed stroke), CPSS cutoff point, CPSS assessment setting, CPSS assessor, reference standard, and LVO definition used in the study. We also gathered the diagnostic performance data including true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN).

2.4. Risk of bias assessment and certainty of evidence

Two authors independently assessed the quality of included articles using QUADAS-2 tool (16). Again, any disagreements were resolved through discussion with a third reviewer. The certainty of evidence was determined using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach (17).

2.5. Statistical analysis

We conducted the analyses using STATA 17.0 statistical software. The analyses were stratified based on the reported CPSS cut-off points. For each cut-off point, the area under the receiver operating characteristic curve (AUC), sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and diagnostic score were calculated with 95% confidence interval (CI). If one article had multiple reports for different LVO definitions (both anterior and posterior circulation or isolated anterior circulation) or population (suspected or confirmed stroke), the report with wider definition was entered to the main analysis. Regarding the considerable methodological and clinical variability among the studies, we applied a random-effect model for meta-analysis. The heterogeneity among the studies was assessed using the visual inspection of the plots along with I2 index. To investigate the potential sources of heterogeneity, we initially aimed to con-

duct a subgroup analysis based on the clinical setting where CPSS was assessed, LVO definition, and initial medical condition (i.e., suspected vs. confirmed stroke), and final diagnosis of enrolled patients. However, the limited number of studies and participants in each subgroup rendered subgroup analysis infeasible or untrustworthy.

We assessed the possibility of publication bias using Deek's funnel plot asymmetry test for every reported CPSS cut-off. Moreover, we conducted sensitivity analyses based on study population (suspected or confirmed stroke), stroke type (ischemic or ischemic and hemorrhagic), the setting in which CPSS was assessed (pre-hospital or in-hospital), and ischemic area (isolated anterior circulation or mixed circulation) to evaluate the robustness of study findings in different situations.

3. Results

3.1. Selection process and study characteristics

In our systematic search of electronic databases supplemented with the manual search, we retrieved 368 records, narrowed down to 49 after deduplication and title/abstract screening. After a full-text review, 14 studies met the eligibility criteria for the meta-analysis (18-31). A flow diagram describing the article selection process is shown in Figure 1 (PRISMA).

All of the studies (8 in the U.S., 1 each in Canada, Germany, Hungary, Switzerland, and Finland) were cohort studies, 12 retrospective and 2 prospective. Seven studies assessed CPSS for LVO detection across three cut-off points. Data were available for CPSS≥1 in 9 articles, CPSS≥2 in 12, and CPSS≥3 in 10. The 14 studies included 20,776 participants. Ten reported CPSS for suspected stroke, 4 exclusively for confirmed stroke. Five studies (2,620 participants) focused on ischemic stroke; 9 (18,156 participants) included both hemorrhagic and ischemic strokes. Clinical data came from in-hospital records and NIHSS assessment carried out by emergency physicians or neurologists (9 studies) or pre-hospital CPSS values by EMS providers, paramedics, or nurses (5 studies; 3,164 patients).

As for LVO definition, studies were not uniform with respect to constituted vascular segments. The majority of studies evaluated the occlusion of specific large vessel segments from both anterior and posterior cerebral circulations as their outcome. In contrast, two studies restricted the LVO to involved segments in anterior circulation only. The characteristics of the studies included are listed in Table 1.

3.2. Meta-analysis

3.2.1. Diagnostic value of CPSS in the detection of LVO

The CPSS showed the highest sensitivity of 97% (95% CI: 87%–99%) and the lowest specificity of 17% (95% CI: 4%–54%) at the cut-off point of ≥1, resulting in an AUC of 0.83 (95% CI: 0.80–0.86) and a DOR of 7.59 (95% CI: 3.09–18.61). When the cut-off point was set at ≥2, the CPSS showed 82% (95% CI: 74%–88%) sensitivity and 62% (95% CI: 48%–74%) specificity, with an AUC of 0.81 (95% CI: 0.77–0.84) and a DOR of 7.52 (95% CI: 5.76–9.81).

Finally, at the highest cut-off point of ≥3, the CPSS had the lowest sensitivity of 60% (95% CI: 51%–69%) and the highest specificity of 81% (95% CI: 71%–88%), along with an AUC of 0.75 (95% CI: 0.71–0.78) and a DOR of 6.39 (95% CI: 4.72–8.65) (Figure 2–5). The results of the three stratified analyses based on the cut-off point used exhibited significant heterogeneity (I2 = 100%). Additional information on the performance of CPSS at various cut-off points is provided in Table 2.

3.2.2. Sensitivity analysis

Table 3 depicts the results of sensitivity analyses on in-hospital setting, suspected stroke patients, studies on population of ischemic and hemorrhagic stroke, and studies defining LVO by main arteries of both anterior and posterior circulation. The sensitivity analysis on studies utilizing CPSS in hospital, revealed unremarkable changes at all cut-off points. This finding demonstrates the robustness of our analyses at both pre-hospital and in-hospital settings. The sensitivity analysis was executed with a restriction on participating patients who were suspected of experiencing a stroke rather than patients who had confirmed stroke diagnoses. The outcomes indicated unremarkable alterations in sensitivity and specificity at ≥2 and ≥3 cut-offs. However, a considerable rise of specificity (68% vs 17%) was observed at ≥1 cut-off, resulting in an AUC of 0.98 (95% CI: 0.97-0.99). Similarly, sensitivity analysis on studies with patients of both ischemic and hemorrhagic stroke, revealed neglectable changes of results at ≥2 and ≥3 cut-offs, but resulted in a higher specificity (68% vs 17%) and AUC of 0.97 (95% CI: 0.96-0.99). Ultimately, the same pattern happed with mixed circulation studies. There were no significant changes of results at ≥2 and ≥3 cut-offs. Even so, at CPSS≥1, we observed substantially higher specificity (59% vs 17%) and AUC of 0.96 (95% CI: 0.12-0.94) in those studies.

3.3. Risk of bias assessment

Table 4 presents a comprehensive overview of the methodological quality of the 14 studies that were included in the analysis. As per the risk of bias assessment conducted using the QUADAS-2 tool, five studies were identified to have low risk of bias across all domains (22, 24, 27, 28, 30). Within the patient selection domain, four studies were deemed to have a high risk of bias, as their sample solely consisted of patients with confirmed acute ischemic stroke (18, 19, 21, 31). Additionally, one study had an unclear risk of bias due to the inclusion of patients referred from a community hospital (29).

In the second domain, the index test, only one study had a high risk of bias because CPSS was not calculated without knowledge of the results of the imaging (23). As to the third domain, reference standard, also one study had a high risk of bias due to implementing transcranial doppler ultrasound (TCD) as a reference standard (25).

In the fourth domain, which is flow and timing, two studies

were found to have a high risk of bias. In one of the studies, imaging was done routinely only after administering IVT, which was often hours after the patient's arrival at the ED (19). This raised concerns that some patients with negative vessel imaging studies in this study may have actually been positive for LVO if the patient had been imaged before IVT administration. In the other study, patients without CT angiography were assumed to not have an LVO stroke, which goes against the principle of all patients receiving the reference standard. Therefore, this study also scored a high risk of bias for the flow and timing domain (26).

In the applicability items, two studies had a high risk of bias in the patient selection domain; one of them did not include occlusions in the posterior circulation in the primary outcome (26), and the other one did not include the M2 branch of the middle cerebral artery (20). There was also a study with unclear concern situation regarding applicability in the patient selection domain because the definition of the large vessel is unknown in their study (29).

3.4. Publication bias

Figure 6 demonstrates the results of Deek's funnel asymmetry test, which suggests no evidence of publication bias at cut-off points ≥1 (P = 0.39), ≥2 (P = 0.42), and ≥3 (P = 0.65).

3.5. Certainty of evidence

The evidence level of the articles that were included in the study was evaluated using the GRADE guidelines, which provide instructions for grading the level of evidence for diagnostic tests (32). All of the studies included in the analysis were designed as cohort studies of patients with diagnostic uncertainty, where a direct comparison between the index test (CPSS in this case) and an established reference standard was made. Hence, despite the observational nature of the studies, the level of evidence started off as high.

However, the included studies had a serious risk of bias, inconsistency, and indirectness, which rated down the overall quality of evidence by three levels. Significant limitations in the above-mentioned two criteria made us hesitant to rate up for a large magnitude of effect.

Consequently, the certainty of evidence for the predictive value of the CPSS scale in LVO detection was determined as very low (Table 5).

4. Discussion

Our systematic review found that CPSS's accuracy in detecting Large Vessel Occlusion (LVO) varies with different thresholds, with a trend of lower sensitivity and higher specificity as the cut-off point increased. At a threshold of ≥1, the same used for screening stroke, CPSS showed the highest sensitivity (97%) for LVO detection. This sensitivity is notably higher than the 75% reported by Baratloo et al. in their umbrella review on CPSS performance for diagnosing suspected stroke patients (33). However, this finding is consistent with the fact that LVO patients exhibit more frequent and severe signs and symptoms.

Despite the high sensitivity of CPSS≥1 benefiting LVO detection and transferring potential EVT candidates to CSC, the low specificity (16%) raises concerns. Maintaining high specificity is crucial to avoid unnecessary transport of non-eligible patients to CSC, preventing increased costs, extended EMS out-of-service time, and oversaturation of CSC facilities. Additionally, questions arise about potential delays in IVT for non-LVO stroke patients when bypassing the nearest PSC (12, 34). Therefore, in cases where a CSC has a faster door-to-needle time than a PSC, bypassing the PSC may not cause a significant delay in IVT delivery. A Danish study, despite a considerable distance between PSC and CSC, demonstrated no significant delay after implementing a triage destination score (35).

To achieve a lower false positive rate, a CPSS≥3 provides the highest specificity (81%). However, this cut-off excludes 40% of LVO patients needing immediate transfer to the nearest CSC. Quick transfer to a PSC ensures an on time IVT, but delays in inter-hospital transportation impact EVT timing. Local regulations and PSC-CSC distance influence these delays. Striking a balance between sensitivity (82%) and specificity (62%), a CPSS cut-off of ≥2 proves optimal, considering the importance of lower false negative and false positive rates.

Stroke scales' accuracy in predicting LVO is heavily influenced by the adopted LVO definition. Studies in our analysis varied in LVO definition, with recent ones adopting a broader definition covering more distal segments. Angiographic findings suggest that prehospital stroke scales may struggle to detect these distal segments due to milder manifestations (26). Therefore, although broadening the definition of LVO may increase outcome prevalence in the population and subsequently augment the PPV of the score, its sensitivity is likely to be compromised.

In the 2018 American Heart Association and the American Stroke Association (AHA/ASA) guidelines, EVT is recommended for LVO strokes in both anterior and posterior circulation within 24 hours, given fulfillment of other eligibility criteria (36). With advancement in EVT, we can foresee the expansion of eligibility criteria. This makes it even more important to improve stroke scale performance to identify LVO patients. One practical suggestion is to incorporate known risk factors for LVO, such as atrial fibrillation, into the CPSS assessment, which can be assessed quickly and easily in a prehospital setting (18, 37, 38). This would provide a more comprehensive understanding of a patient's risk beyond their clinical presentation.

Various tools can be employed to diagnose LVO stroke beyond the use of CPSS. Numerous stroke severity assessment scales exist, including but not limited to RACE, LAMS, and 3ISS, which are utilized to identify LVO stroke (39-42). However, this review doesn't compare CPSS to other tools. Just comparing performance might not be enough for practical use. When evaluating a clinical tool, consider end users' perspectives, including factors like education, training, re-

producibility, and adherence. Crowe et al. found that EMS personnel favored CPSS in prehospital medical record evaluations (28). This could be due to immediate use, binary scoring, and exclusion of complex parameters, reducing challenges for novice paramedics and enhancing inter-rater reliability. (43). Concordantly, our sensitivity analysis demonstrated that CPSS scoring by EMS and ED physicians is comparably sensitive, affirming its simplicity and user-friendliness.

Although our review presented a comprehensive audit of the performance of CPSS to detect LVO, we acknowledge some limitations that necessitate exercising caution in the interpretation of our results. First, we used LVO as a proxy for detecting those who were eligible candidates for bypassing PSC and direct transportation to CSC. However, it should be remembered that even some non-LVO patients, such as severe hemorrhagic stroke patients, are routinely referred to CSC, and their primary divert to these sophisticated centers is encouraged (24).

Hence, if intended to be utilized as a tool for the triage destination of stroke patients to top-notch centers, simply relying on this review findings may underestimate the efficacy of CPSS for this purpose. Second, studies varied upon their inclusion criteria, with some restricting patients to those with confirmed acute ischemic stroke; meanwhile, other studies recruited suspected stroke patients who were ultimately diagnosed with ischemic stroke, TIA, ICH, or stroke mimics. Confining the administration of CPSS to those with confirmed stroke may underrate the false negatives and yield higher sensitivity. Even so, the sensitivity analysis showed that this limitation could not have a clinically significant effect on the diagnostic yield of CPSS at the optimal threshold. Third, we observed differences among patients across studies in terms of the duration since they experienced a stroke or were last known to be well. Some studies reviewed patients who were admitted up to 24 hours after stroke incidence and didn't expound on the exact timing of CPSS administration. This could lead to bias since partial recanalization of LVO can improve some stroke symptoms over time, significantly impacting stroke scale scoring performance.

5. Conclusions

In summary, our research demonstrated that CPSS, with a threshold set at ≥2, is a useful tool for identifying LVO stroke and directing patients to CSCs, both in prehospital and in-hospital settings. However, it's important to note that the effectiveness of CPSS depends on several factors, such as the prevalence of LVO in stroke cases, the distribution of PSCs and CSCs, workload, and local policies. In addition, we recommend that CPSS be updated as EVT eligibility criteria for LVO patients evolve, which will require further prospective studies.

6. Declarations

6.1. Acknowledgments

None.

6.2. Competing interest

None.

6.3. Funding and supports

None

6.4. Using artificial intelligence chatbots

None

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Table 1: Characteristics of included studies

Author	Setting	Assessor	Design	Population	Cut-off point	Sample size	Male (n)	Mean age	References	LVO definition
Crowe, 2021, USA	In-hospital	Nurse	RCS	SS	1, 2, 3	11319	4972	71	CTA/MRA	ICA, MCA, BA
Dowbiggin, 2022, USA	Pre-hospital	Paramedic	PCS	SS	1, 2, 3	1359	608	69.35	CTA	ICA, MCA (M1, M2), BA
Duvekot, 2021, Netherlands	Pre-hospital	Paramedic	PCS	SS	1, 2, 3	1039	560	72	CTA	ICA, MCA (M1, M2), ACA (A1, A2)
Frank, 2021, Germany	In-hospital	Neurologist	RCS	SS	1, 2	2815	NR	NR	CTA/TCD	ICA, MCA (M1, M2), BA
Heldner, 2016, Switzerland	In-hospital	Neurologist	RCS	SS	2	1085	658	67.7	CTA/MRA	ICA, MCA (M1, M2, M3, M4), ACA
Keenan, 2019, USA	In-hospital	Neurologist and ED physician	RCS	SS	2	735	NR	NR	CTA	ICA, MCA (M1, M2), BA
Keenan, 2021, USA	In-hospital	Neurologist	RCS	SS	1, 3	68	36	66	CTA	ICA, MCA (M1, M2), BA
Keenan, 2022, USA	In-hospital	Neurologist	RCS	SS	2, 3	184	94	70	CTA/MRA	ICA, MCA (M1, M2), BA
Krebs, 2021, Germany	In-hospital	Neurologist	RCS	CS	1, 2, 3	741	389	72.1	CTA/MRA	CCA, ICA, MCA (M1, M2), ACA (A1), PCA (P1), BA
Lawner, 2020, USA	Pre-hospital	EMS providers	RCS	SS	2	255	NR	NR	CTA/MRA	ICA, MCA, ACA, PCA, VA, BA
Navalkele, 2020, USA	In-hospital	Physician	RCS	CS	3	244	119	66	CTA/MRA	ICA, MCA, ACA, PCA, VA, BA
Nehme, 2019, Canada	Pre-hospital	Paramedic	RCS	SS	1, 2, 3	376	NR	NR	CTA/MRA	ICA, MCA (M1), BA
Richards, 2018, USA	Pre-hospital	Paramedic	RCS	CS	1, 2, 3	135	70	68.39	CTA/MRA	ICA, MCA (M1, M2), ACA (A1, A2), PCA (P1, P2), VA, BA
Tarkanyi, 2020, Hungary	In-hospital	Neurologist	RCS	CS	1, 2, 3	421	216	67.2	CTA	ICA, MCA (M1, M2, M3), ACA, PCA, VA, BA

ACA: Anterior cerebral artery; BA: Basilar artery; CCA: Common carotid artery; CS: Confirmed stroke; CTA: Computed tomography angiography; ED: Emergency department; EMS: Emergency medical service; ICA: Internal carotid artery; LVO: Large vessel occlusion; MCA: Middle cerebral artery; MRA: Magnetic resonance angiography; NR: Not reported; PCA: Posterior cerebral artery; VA: Vertebral artery; PCS: Prospective cohort study; RCS: Retrospective cohort study; SS: suspected stroke; TCD: Transcranial Doppler ultrasound.

Table 2: Characteristic performance of CPSS for detection of LVO in different cut-off points

Cut-off	No. studies	AUC [95% CI]	Sensitivity [95% CI]	Specificity [95% CI]	PLR [95% CI]	NLR [95% CI]	DOR [95% CI]	Inconsistency (I^2)
≥1	9	0.83 [0.80–0.86]	0.97 [0.87–0.99]	0.17 [0.04–0.054]	1.17 [0.91–1.52]	0.15 [0.07–0.35]	7.59 [3.09–18.61]	100% [100-100]
≥2	12	0.81 [0.77–0.84]	0.82 [0.74–0.88]	0.62 [0.48–0.74]	2.15 [1.62–2.85]	0.29 [0.23–0.36]	7.52 [5.76–9.81]	100% [100-100]
≥3	10	0.75 [0.71–0.78]	0.60 [0.51–0.69]	0.81 [0.71–0.88]	3.14 [2.27–4.36]	0.49 [0.42–0.57]	6.39 [4.72–8.65]	100% [99-100]

AUC: Area under the receiver operating characteristic (ROC) curve; CI: Confidence interval; DOR: Diagnostic odds ratio; NLR: Negative likelihood ratio; PLR: Positive likelihood ratio; CPSS: Cincinnati Prehospital Stroke Scale; LVO: large vessel occlusion.

Table 3: The sensitivity analyses at all cut-off points.

Cut-off	Parameter	No. studies	AUC [95% CI]	Sensitivity [95% CI]	Specificity [95% CI]	PLR [95% CI]	NLR [95% CI]	DOR [95% CI]
	Suspected to stroke	6	0.98 [0.97, 0.99]	0.99 [0.89, 1.00]	0.68 [0.09, 0.98]	3.1 [0.4, 26.7]	0.02 [0.00, 0.27]	151 [2, 10905]
≥1	Ischemic and hemorrhagic	7	0.97 [0.96, 0.99]	0.98 [0.87, 1.00]	0.68 [0.14, 0.97]	3.1 [0.5, 18.1]	0.03 [0.00, 0.29]	94 [3, 3204]
	In-hospital	5	0.86 [0.83, 0.89]	0.94 [0.83, 0.98]	0.39 [0.14, 0.71]	1.5 [1.0, 2.5]	0.16 [0.10, 0.26]	10 [5, 18]
	Anterior and posterior	8	0.96 [0.96, 0.97]	0.97 [0.85, 0.99]	0.59 [0.12, 0.94]	2.4 [0.6, 9.6]	0.05 [0.01, 0.42]	46 [2, 1114]
	Confirmed stroke	9	0.82 [0.78, 0.85]	0.84 [0.77, 0.89]	0.60 [0.46, 0.72]	2.1 [1.6, 2.7]	0.26 [0.21, 0.33]	8 [6, 11]
	Ischemic and hemorrhagic	8	0.83 [0.80, 0.86]	0.84 [0.74, 0.91]	0.64 [0.47, 0.79]	2.3 [1.6, 3.4]	0.25 [0.18, 0.34]	9 [7, 13]
≥2	In-hospital	7	0.80 [0.77, 0.84]	0.79 [0.69, 0.87]	0.65 [0.46, 0.80]	2.3 [1.5, 3.4]	0.32 [0.26, 0.38]	7 [5, 10]
	Anterior and posterior	10	0.81 [0.77, 0.84]	0.83 [0.73, 0.89]	0.61 [0.44, 0.75]	2.1 [1.5, 2.9]	0.28 [0.22, 0.36]	7 [5, 10]
	Confirmed stroke	6	0.78 [0.74, 0.82]	0.68 [0.55, 0.79]	0.76 [0.64, 0.85]	2.8 [2.1, 3.8]	0.42 [0.33, 0.54]	7 [5, 8]
	Ischemic and hemorrhagic	7	0.78 [0.74, 0.81]	0.64 [0.52, 0.75]	0.80 [0.68, 0.88]	3.2 [2.2, 4.6]	0.45 [0.36, 0.55]	7 [5, 9]
≥3	In-hospital	6	0.66 [0.62, 0.70]	0.53 [0.47, 0.60]	0.84 [0.72, 0.91]	3.3 [2.1, 5.1]	0.56 [0.52, 0.60]	6 [4, 9]
	Anterior and posterior	9	0.75 [0.71, 0.79]	0.61 [0.50, 0.70]	0.80 [0.69, 0.88]	3.1 [2.2, 4.4]	0.49 [0.41, 0.58]	6 [4, 9]

☺:Low Risk; ☹: High Risk; ?: Unclear Risk.

Table 4: Risk of bias assessment of included studies using the QUADAS-2 tool

Study	Risk of bias				Applicability		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Crowe, 2021	☺	☺	☺	☺	☺	☺	☺
Dowbiggin, 2022	☺	☺	☺	☺	☺	☺	☺
Duvekot, 2021	☺	☺	☺	☹	☹	☺	☺
Frank, 2021	☺	☺	☹	☺	☺	☺	☺
Heldner, 2016	☺	☺	☺	☺	☺	☺	☺
Keenan, 2019	☺	☺	☺	☺	☺	☺	☺
Keenan, 2021	☺	☹	☺	☺	☺	☺	☺
Keenan, 2022	☺	☺	☺	☺	☺	☺	☺
Krebs, 2021	☹	☺	☺	☺	☺	☺	☺
Lawner, 2020	?	☺	☺	☺	?	☺	☺
Navalkele, 2020	☹	☺	☺	☺	☺	☺	☺
Nehme, 2019	☺	☺	☺	☺	☹	☺	☺
Richards, 2018	☹	☺	☺	☹	☺	☺	☺
Tarkanyi, 2020	☹	☺	☺	☺	☺	☺	☺

☺:Low Risk; ☹: High Risk; ?: Unclear Risk.

Table 5: Certainty of evidence for the performance of CPSS

Outcome	No. of studies	Design	Risk of bias	Heterogeneity (I2 value)	Indirectness	Imprecision	Publication bias	Quality of evidence
LVO detection	14 studies (20776 patients)	Cohort studies	Serious (1)	Serious	Serious (2)	None	None	Very Low

(1) Several studies included in the meta-analysis utilized Cincinnati Prehospital Stroke Scale (CPSS) on patients with confirmed stroke, which differs from our intended population of patients with suspected stroke. (2) In 9 out of 14 studies ED physicians and/or neurologists had calculated the CPSS score during in-hospital assessments, which differs from the setting the test intended to be used (prehospital assessment by EMS providers). LVO: Large Vessels Occlusion.

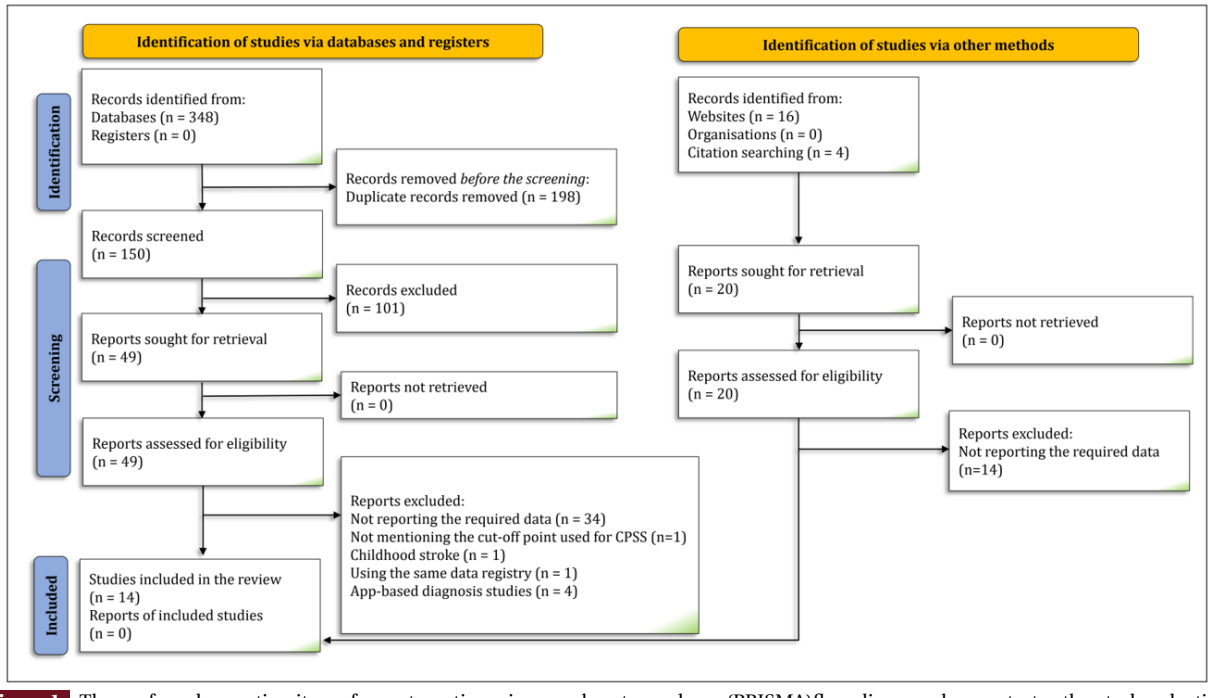

Figure 1: The preferred reporting items for systematic reviews and meta-analyses (PRISMA)flow diagram demonstrates the study selection process. CPSS: Cincinnati Prehospital Stroke Scale.

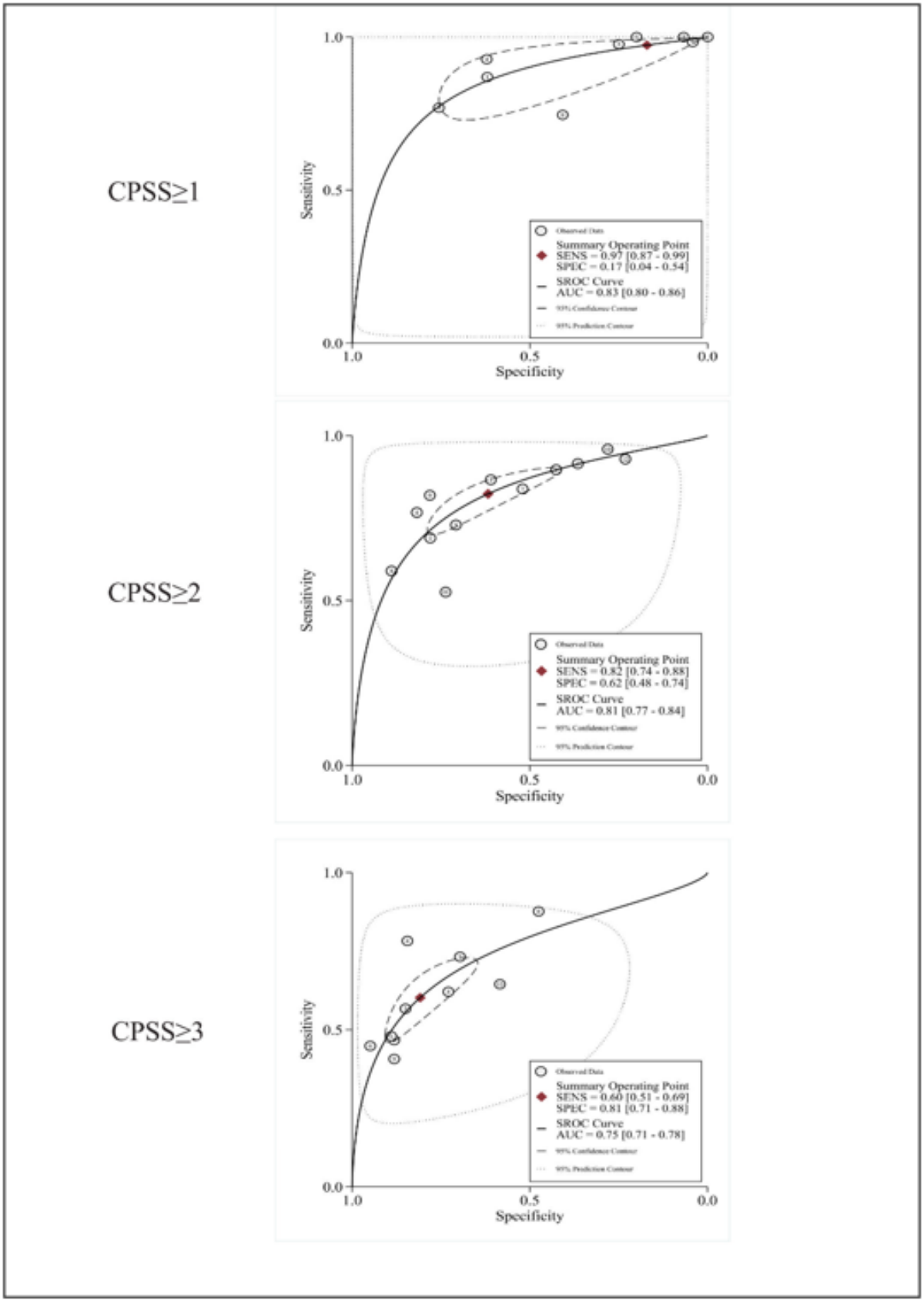

Figure 2: Summary Receiver Operating Characteristic Curve (SROC) of Cincinnati Prehospital Stroke Scale (CPSS) with different cut-off points in detecting large vessel occlusion. SENS: sensitivity; SPEC: specificity; AUC: area under the curve.