Review

Validated pre-hospital stroke scales to predict large vessel occlusion: a systematic review

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<https://doi.org/10.33151/ajp.16.705>

Abstract

Background

Occlusions of large cerebral vessels, including the internal carotid artery and middle cerebral artery, result in a significant burden of morbidity. Treatment was previously limited to intravenous thrombolysis, however multiple studies have shown significant improvements when patients undergo endovascular clot retrieval. Early identification and triage to centres capable of delivering this is likely to contribute to improved outcomes. This systematic review aims to compare clinical assessment tools and their performance 'in-field' to identify usability and reliability to assist pre-hospital providers with identification of this sub-group of stroke patients.

Methods

Several databases were reviewed to identify studies that have validated large vessel occlusion clinical assessment tools within the pre-hospital environment. Sensitivity, specificity and predictive value were compared along with any biases. Six studies met the study criteria and were included. A total of 1384 patients were involved in the studies with sensitivities ranging from 51.9% to 100% and specificities ranging from 68% to 90%.

Conclusion

There is significant variation among studies and the emergency medical systems they have been performed within. It is likely that no single tool will suit every system and further research is required to determine the best tool for the Australian pre-hospital environment.

Keywords:

stroke; ambulance; emergency medical service; assessment; diagnosis

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Background

Stroke is a leading cause of death and disability worldwide (1). In recent years the use of endovascular procedures to remove clots from the cerebral circulations has shown significant benefit. For a small group of acute stroke patients harbouring a large vessel occlusion (LVO), typically in the internal carotid arteries or M1 segment of the middle cerebral arteries, early removal of the clot results in improved functional outcomes. Multiple studies have shown that the earlier these interventions are provided the better the outcome for patients (2-4).

There are now six centres around Australia meeting the criteria of comprehensive stroke services, according to the 2017 National Stroke Foundation audit (5), which are defined as centres that can provide endovascular clot retrieval (ECR), stroke thrombolysis and stroke unit care 24 hours a day, 7 days a week. Specialist expertise in endovascular clot retrieval requires high volume exposure, which requires centralisation of the endovascular centre. As a result, many stroke patients with a LVO will likely attend a non-endovascular centre on initial presentation. The inherent delays associated with interfacility transfers and geographical distances result in delays to intervention compared with direct transfer to endovascular centres (6). Although the solution may seem to be transporting all stroke patients to these centres in the first instance, probability modelling has shown that depending on distances to endovascular centres and in-hospital performance metrics, bypass may result in delays to administration of intravenous thrombolysis and therefore impacts patient outcomes (7).

Pre-hospital identification of the acute stroke patient with a LVO versus a milder stroke presents an early opportunity to influence their trajectory of care. Mobile imaging solutions continue to be investigated; however the cost of mobile computer tomography (CT), the training requirements (transcranial sonography) or current lack of pre-hospital evidence (quantitative electroencephalography and biomarkers) has limited their applicability at this stage (8-12). The remaining solution is a robust clinical assessment tool combined with a decision support algorithm. Significant research has been directed at developing the ideal tool that is simplistic enough to reduce the training requirements for pre-hospital clinicians while maintaining reliability in its identification of reperfusion eligible patients. In recent years the literature has focussed on tools that have a higher specificity for acute strokes with LVO. The Rapid Arterial Occlusion Evaluation (RACE), Los Angeles Motor Score (LAMS), Cincinnati Pre-hospital Stroke Severity Score (CPSSS), Field Assessment Stroke Triage for Emergency Destination (FAST-ED), National Institute of Stroke Scale 8 (NIHSS-8) and a host of other scores have been investigated (13-28). Typically, scales are derived from retrospective data sets with very few undergoing prospective field validation.

The aim of this review was to identify an appropriate LVO clinical assessment tool for the Australian pre-hospital environment.

Methods

Information sources

A search was performed for pre-hospital large vessel occlusion stroke identification tools on the databases MEDLINE, EMBASE, CINAHL and the Cochrane Database of Systematic Reviews. Web of Science, Google Scholar and PubMed were also searched using the keywords: 'stroke', 'cerebrovascular accident', 'transient ischaemic attack', 'large vessel occlusion', 'paramedic', 'ambulance', 'allied health personal', 'identification', 'detection' and 'screening'. Dates searched were from 1 January 1985 to 3 March 2019. All relevant and included articles had their bibliographies reviewed to identify any further studies. Contact was also made with researchers who have recently published on the topic area to identify if there were any studies currently under review for publication. Titles and abstracts were initially reviewed by one author (WL) and if within the topic area were further reviewed by two authors (WL and MD) to ensure they fit the inclusion and exclusion criteria. The review process followed PRISMA guidelines to ensure consistency of reporting (29).

A systematic review protocol was registered with the international prospective register of systematic reviews (PROSPERO) and in line with Transparency and Openness Promotion (TOP) guidelines. This protocol may be used to perform an update of the review at a later date.

Inclusion and exclusion criteria

Studies were considered relevant if they included the pre-hospital validation of a clinical tool to identify LVO strokes. We included studies where the standard reference was the confirmation of a large vessel occlusion on advanced imaging. Studies were included if the tool was applied by any pre-hospital clinician in the out-of-hospital environment (paramedic, nurse, emergency medical technician [EMT] or physician). Participants were required to be more than 18 years of age and only English language studies were included. Due to the likely heterogeneity of the studies it was not expected that a meta-analysis could be performed and therefore data was not included as an inclusion criterion.

Case reports, systematic reviews, letters to the editor and poster presentations were not included, however these were reviewed to ensure capture of all relevant studies. Conference abstracts were assessed, and contact made with authors to determine the availability of published reports; studies were not included if a peer-reviewed publication was unavailable or if contact could not be made with the authors.

Study selection and data extraction

Databases were searched by one author (WL) using the text and MeSH terms agreed by all authors. Titles and abstracts were reviewed for broad relevance to the review criteria before being assessed by two authors (WL and MD) to determine if they met the inclusion/exclusion criteria. Any disagreement between the authors resulted in review of the study by a third author (AW) for final decision on inclusion/exclusion. Data was then independently extracted by two authors (WL and MD) using a standardised extraction tool adapted from the Cochrane airways randomised control trial data collection form (30). The data collection form met with Methodological Expectations for Cochrane Intervention Reviews (MECIR) standards (31).

Quality assessment

Studies meeting the inclusion criteria were then assessed by two authors (WL and MD) using the Quality Assessment of Diagnostic Accuracy Studies - 2 (QUADAS-2), which assess the quality of studies based on potential sources of bias (32). Assessments were performed independently, and disagreement was discussed with the third author (AW) to determine a consensus.

Results

Search results

Our search process yielded 431 articles: 203 from EMBASE, 125 from MEDLINE, 31 from Web of Science and 72 from CINAHL. Retrieved articles had their reference lists reviewed by one author (WL) and a further two studies were identified as possibly relevant. The study by Gupta et al (33) did not fit the inclusion criteria so was excluded, while a study by Kesinger et al (15) was identified and included in the review. Thirty-one

studies underwent full-text review after title and abstracts were screened. Studies by Gupta et al (33), Hastrup et al (20), Katz et al (21), Lima et al (34), Nazliel et al (22) Suzuki et al (23) and Taqi et al (35) were excluded as they were retrospectively derived or tested scores. Carrera et al (24) was excluded as it was a retrospectively derived score using a prospectively gathered cohort. All further studies excluded were review papers and did not directly validate any tools. Three studies were identified as conference abstracts, the authors were unsuccessful in contacting Sanchea et al (36) and a study by Purruker et al (37) was determined to not fit the inclusion criteria. Contact with authors of the third study by Zhao et al (38) was successful and it was considered for review, however the study is still ongoing at this time and only interim results were available. A study by Demeestere et al (39) involved a tool that was prospectively validated in the pre-hospital environment for stroke severity before being retrospectively analysed for LVO detection. Given the relationship between stroke severity and LVO the authors agreed to include this study for discussion but not full review. Eight studies were included for full review, the study by Andsberg et al (40) and Zaidi et al (41) were excluded by authors WL and MD as on further review they did not meet inclusion criteria. The characteristics of the six studies are shown in Table 1. Tools investigated included the RACE, C-STAT, VAN, FAST-PLUS, LAMS and NIHSS.

The studies by Zhao et al and Demeestere et al did not meet the inclusion criteria for this systematic review however given their relevance to the Australian setting and their current 'in-field' use the authors have included a discussion on their performance and relationship to other validated tools.

The PRISMA systematic review flowchart can be viewed in Figure 1 and a summary of findings can be found in Table 2.

Table 1. Study characteristics

Study	Location	Education level of participants	Training requirement	Selection criteria	Number of patients
de la Ossa et al 2014 (13) RACE	Barcelona, Spain	EMT	1 hour initial Four further sessions across 1 year	Code stroke by EMS or sending hospital	885 357 had RACE applied
Kesinger et al (15) NIHSS	Pittsburg, USA	Nurse/paramedic	Pre-existing NIHSS training	NIHSS assigned by HEMS crew	305
Teleb et al (26) VAN	Rhode Island, USA	ED nurse	2-hour session	Suspected stroke/ TIA at triage	62
McMullan et al (26) C-STAT	Cincinnati, USA	EMT/paramedic	Nil	Positive FAST assessment	131
Vaclavik et al (27) FAST PLUS	Ostrava, Czech Republic	Paramedic	Three video recordings	Suspected stroke with FAST PLUS assessed	435
Noorian et al (28) LAMS	California, USA	Paramedic	Pre-existing tool	Suspected stroke recruited into FAST-MAG trial	94

Table 2. Summary of findings for each study

Study	Tool	Study population	LVO prevalence (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
de la Ossa et al (13)	RACE	357	21	85	68	42	94
Kesinger et al (15)	NIHSS	305	68.9	51.9	87.4		
Teleb et al (26)	VAN	62	22.6	100	90	74	100
McMullan et al (26)	C-STAT	131	13	71	70		
Vaclavik et al (27)	FAST PLUS	435	28	92	44	41	94
Noorian et al (28)	LAMS	94	63	76	65	79	61

Figure 1. PRISMA systematic review flowchart

Quality assessment

Study quality was assessed using the QUADAS-2 tool and is shown in Table 3. Studies were highly variable with differing methodologies and pre-hospital systems that vary significantly. Confirmation of an LVO was also performed by differing modalities among studies, with one using transcranial Doppler ultrasound to confirm while others were confirmed using CT angiogram.

Study description

The study by McMullen et al (25) investigated the use of the Cincinnati Stroke Triage Assessment Tool (C-STAT) which is derived from the NIHSS assessing level of consciousness commands and questions along with conjugate gaze deviation and arm strength. C-STAT was performed by Cincinnati fire department EMTs over a 6-month period if there was a clinical impression of stroke or transient ischaemic attack (TIA). Patients were included if they were more than 18 years of age, had a positive FAST and calculable C-STAT and were transported to a comprehensive stroke centre or had a stroke team consult at any outlying hospital. EMTs had no formal training on the new scale beyond the scoring guide. Primary outcome was an NIHSS >15 as assessed by a physician on arrival at the emergency department, while presence of LVO was considered a secondary outcome. A C-STAT score was calculated after suspicion of stroke or TIA by the EMT and after the patient had already been screened using the FAST assessment; 158 were identified as having a suspicion of stroke with 112 having a C-STAT score calculated with a determined sensitivity of 71% and specificity of 70% (24).

The RACE scale validated by de la Ossa et al (13) was derived from a retrospective dataset based on admission NIHSS. Components included are facial palsy, arm motor, leg motor, gaze deviation and aphasia or agnosia if right or

left hemiparesis respectively. A RACE score >5 showed the greatest sensitivity (85%) and specificity (68%) with 19% of these patients receiving endovascular care versus only 2% with a RACE score <5. The RACE score was applied to patients by EMTs after completing a 1-hour initial training session and four shorter sessions over a 1-year period. Of all stroke code activations by EMS during the study period (885) only 40% had a RACE score calculated by crews, typically these were patients with more severe stroke symptoms and predictably a higher rate of LVO (24).

The VAN assessment focussed more heavily on the cortical signs of stroke requiring evidence of lateral motor weakness first before applying further assessment. Once motor deficit was determined an assessment was made of any visual disturbance (field cut, double vision or blind), aphasia (expressive or receptive) and, finally, neglect. The VAN assessment was completed by registered nurses (RNs) at the triage interface and although not strictly pre-hospital, the authors have agreed to include it. RNs already trained in the NIHSS underwent a 2-hour training package on the VAN assessment. There were 62 stroke code activations during the study period with 19 screening VAN+ with 14 having a confirmed LVO by computer tomographic angiography (sensitivity 100% and specificity 90%). In their study the authors showed VAN to have a higher specificity than the complete NIHSS (79%). The stated benefit of the VAN is its quick application (15 seconds) and minimal training requirements (26). Although the VAN appears to demonstrate excellent performance this was a tool performed only on a cohort who had already undergone stroke screening and therefore it is unlikely to achieve the same performance in a more general, unscreened population of neurologic presentations.

Table 3. Bias and applicability assessment: QUADAS-2 tool

Study	Publication year	Bias assessment				Applicability		
		Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
de la Ossa et al [13]	2014	High	Unclear	Low	Low	Low	Low	Low
Kesinger et al [15]	2015	High	Low	Unclear	High	High	High	Unclear
Teleb et al (26)	2016	Unclear	Low	Unclear	Unclear	Unclear	Low	Low
McMullan et al [26]	2017	High	Low	Low	Unclear	Low	Low	Low
Vaclavik et al (27)	2018	Low	Low	Low	Low	Low	Low	Low
Noorian et al (28)	2018	Low	Low	Unclear	Low	Low	High	Low

A study conducted in the city of Ostrava, Czech Republic was performed by Vaclavik et al (27) to determine the performance of a tool that assessed more severe hemiplegia beyond the standard Face, Arm, Speech, Time (FAST) tool. Paramedics were taught to assess for a severe leg or arm deficit (NIHSS score of 3 or 4). If the patient was deemed FAST-positive and had severe deficits to any limb then they were deemed FAST-PLUS positive. The tool was validated on a population of 637,584 people serviced by three stroke centres over a 10-month study period. The study was able to recruit 435 patients who had the FAST-PLUS tool performed with 87% having an ischaemic stroke confirmed at discharge. The mean NIHSS of this patient group was 8.3. Of the 377 ischaemic stroke patients, LVO was identified in 124 patients with 51 receiving endovascular clot retrieval. The final test performance was reported as a sensitivity of 93%, specificity of 47%, PPV of 41% and NPV of 94%.

Noorian et al (28) validated the LAMS score as an LVO stroke tool by using previously collected data from the FAST-MAG trial of magnesium for stroke therapy. During this trial paramedics had performed the LAMS along with Glasgow Coma Score (GCS) as part of the patient enrolment process and this was then linked with the NIHSS at time of arrival at the hospital. The LAMS consists of an assessment for facial droop, arm drift and grip strength with a total score out of 5 with a previous derivation study showing that a LAMS score >4 had good accuracy for LVO identification (22). The FAST-MAG data set was linked with an independently verified vessel imaging to determine the presence of LVO. The study recruited 94 patients with a median NIHSS of 9 at hospital arrival with 76% of patients having confirmed ischaemic stroke and 63% (45/71) of those harbouring an LVO. The LAMS, with a cut-off score of >4, showed a sensitivity of 76%, specificity of 65% and accuracy of 72%.

Kesinger et al (15) assessed the use of the complete NIHSS by a helicopter emergency medical service (HEMS) service staffed by a nurse/paramedic team. Crews were trained in the application of the NIHSS through the American Stroke Association. Comparison was made between HEMS and stroke team NIHSS with a sub-analysis of those presenting within 8 hours of symptoms onset and those administered thrombolysis before HEMS transport. The authors demonstrated that the HEMS teams could reliably apply the full NIHSS with a sensitivity of 51.9% and specificity of 87.4%. The population transported by the HEMS group had more severe strokes and a higher prevalence of LVO as would be expected.

The following two tools did not meet the inclusion criteria at this time. However, given their relevance to the Australian setting and the component overlap with currently validated scores they have been included for discussion.

The ACT-FAST tool was developed in Melbourne (Australia) by Zhao et al (38) and is currently undergoing pre-hospital

validation (38). ACT-FAST uses only two examination steps: arm drift followed by a speech abnormality if left hemisphere stroke is suspected or a shoulder tap if right hemisphere stroke is suspected. The authors have designed the tool to achieve high specificity for LVO detection. Interim results show that in a population of 196 (76 in ED and 120 pre-hospital) the ACT-FAST showed a sensitivity of 92% for ICA/M1 occlusion and a specificity of 83% for LVO. The authors also determined that the tool has a PPV of 83.3% when considering all patients requiring comprehensive stroke care (LVO, haemorrhage and tumour).

The original NIHSS-8 was validated by Demeestere et al to identify thrombolysis eligible acute stroke patients and as a stroke severity score (17). It consists of eight components of the full NIHSS: level of consciousness (LOC), LOC questions, LOC commands, best gaze, facial palsy, arm motor, dysarthria and neglect (Table 4). After training, the NIHSS-8 was performed by paramedics in the pre-hospital environment. Using this previously collected validation dataset NIHSS-8 scores were retrospectively calculated on a cohort of suspected stroke patients transported by ambulance (n=551). Receiver operating characteristics analysis was used to determine the accuracy of the tool in identifying LVO. Furthermore, the authors assessed for inter-rater reliability between ambulance staff and stroke team staff. Using a cut-off score of eight the authors achieved a sensitivity of 81% and specificity of 75%. They also determined that the tool could achieve substantial agreement between paramedics and the stroke team.

Discussion

It is generally accepted that any patient with clinical symptoms of stroke will require assessment at a stroke centre where advanced imaging can be used to dictate the most appropriate treatment option. However, delivery to the nearest health facility able to provide this may not result in the most timely treatment and there is mounting evidence that direct ambulance delivery of patients to ECR-capable centres is the most appropriate course of action (42,43). This is not dissimilar to the delivery of ST elevation myocardial infarction (STEMI) to a facility with primary percutaneous coronary intervention (pPCI) capabilities, however this decision is guided by the use of a technological solution in the form of a 12-lead electrocardiogram. Such a technological solution does not yet exist for those suffering a stroke and as such reliance is placed on clinical assessment tools alone.

This systematic review found that relatively few of the researched clinical assessment tools recommended for use in the pre-hospital environment have been validated 'in-field'. Those that have been validated did not have consistently high sensitivity and specificity. In an ideal system there would be no missed opportunities to deliver endovascular care and therefore a high sensitivity would be ideal however, the impact on comprehensive stroke centres receiving a large volume of

false positive stroke activations would have ramifications on the effectiveness of these systems of care. Attempts at a higher level of specificity to reduce false positives has been shown to result in greater than 10% of large vessel strokes being missed (44). It seems unlikely that a clinical assessment tool alone will provide the solution to pre-hospital triage of the reperfusion eligible stroke patient, however until mobile technologies become more cost effective and reliable there is no alternative.

The full NIHSS is too cumbersome for the pre-hospital environment and many assessment items would likely add little to the decision requirements in this setting. The use of such a tool also results in a lower sensitivity (51.9%), which may result in an unacceptable high miss rate; it does however have one of the highest specificities (87.4%). The VAN and RACE demonstrated high sensitivity (100% and 85% respectively), however both studies had methodological issues and the results need to be replicated in further validation studies. It is likely that the high specificities in these studies was a result of selective pre-screening of the populations. During the validation of the RACE scale it was preferentially applied to more severe strokes thereby inflating its specificity. The cohort of patients in the VAN study had also undergone pre-screening and was applied to already identified 'code-stroke' patients.

FAST PLUS also demonstrated a very high sensitivity, however its specificity was unacceptably poor and likely due to the exclusion of cortical signs. C-STAT showed the most

balanced sensitivity versus specificity however these remain unacceptably low. The LAMS tool is also a widely used tool in the United States and has now been validated for LVO detection and performs moderately well when compared to other tools.

On review of the available validated tools it appears apparent that none are immediately applicable to the Australian pre-hospital system, however a further two studies have identified tools currently in use by Australian ambulance services. The ACT-FAST and NIHSS-8 did not meet the inclusion criteria of this review, however due to their component crossover with validated tools the authors have deemed it pertinent to present them.

The ACT-FAST tool is simple to apply and performs well, however it must be combined with further assessment items or tools to capture non-LVO stroke, including assessments for facial palsy, handshake and speech. The NIHSS-8 has been applied to a much larger patient group, performs well, can be used in isolation for stroke detection, severity and LVO presence and has the added benefit of being useful in future research, however it is lengthier and will have greater training requirements.

In the rural and remote Australian pre-hospital environment, the clinician is faced with large geographic distances which will likely limit the opportunities to deliver the LVO patient to an

Table 4. Comparison table of LVO screening tools

	NIHSS	NIHSS-8	ACT-FAST	RACE	FAST-PLUS	VAN	C-STAT	LAMS
Facial palsy	0-3	0-3		0-2	Y/N			0-1
Arm motor	0-4	0-4	Y/N	0-2	Y/N	Y/N	0-1	0-2 + grip
Leg motor	0-4			0-2	Y/N			
Gaze deviation	0-2	0-2		0-1		0-3	0-2	
Language	0-3		Y/N (right arm)	0-2	Y/N	0-3		
Dysarthria	0-2	0-2						
Agnosia/neglect	0-2	0-2	Y/N (left arm)	0-2		0-3		
LOC	0-3	0-3					0-1	
LOC command	0-2	0-2						
LOC questions	0-2	0-2						
Visual fields	0-3							
Limb ataxia	0-2							
Sensory	0-2							
Sensitivity	51.9%	81%	92%	85%	92%	100%	71%	76%
Specificity	87.4%	75%	83%	68%	44%	90%	70%	65%
PPV		52%	57%	42%	41%	74%		79%
NPV		92%		94%	94%	100%		61%
Population	305	551	104	357	435	62	131	94

endovascular capable facility thereby making pre-hospital bypass unrealistic, however integration with aeromedical retrieval services requires clear and reliable LVO detection before resource allocation. In metropolitan and semi-rural areas the decision on road bypass needs to be made. Many primary stroke facilities or regional hospitals can deliver stroke thrombolysis while comprehensive or tertiary hospitals tend to be located within the centres of the major cities. Studies have shown the decision on bypassing a thrombolysis capable facility must be weighed against transport time, in-hospital performance metrics and patients eligibility for thrombolysis (7).

Australian EMS has high education standards, requiring a tertiary level entry into the discipline. In 2005 Bray et al (45) demonstrated that focussed stroke education resulted in much improved paramedic identification of stroke. Since this study, paramedic education has continued to evolve to support a wider skill set and level of responsibility.

Even with increased education there will always be a role for clinical assessment tools and decision support algorithms as was shown in a study by Karlinski et al (46) where, even among a cohort of emergency physicians, there was a high sensitivity for stroke diagnosis but poor accuracy when not using a clinical screening tool.

Tools with improved specificity for LVO are those that include cortical signs such as neglect and aphasia and therefore systems that are aiming to develop pre-hospital bypass protocols should include a screening tool with this capacity. Any tool chosen must identify both non-LVO (potential thrombolysis eligible candidates) as well as LVO (potential ECR eligible candidates). A summary comparison of all the tools discussed here is available in Table 4. There is significant heterogeneity among the validated studies making a recommendation difficult and the authors believe that the decision on the best tool will be system specific and should be conducted with careful consideration of all factors, which includes level of clinician education, initial and ongoing training requirements, role in bypass versus thrombolysis versus aeromedical retrieval decisions and future research opportunities.

Conclusion

Further research is required in the Australian pre-hospital environment to determine if a severity score such as NIHSS-8 or a step-wise approach such as ACT-FAST results in improved patient delivery to thrombolysis and ECR-capable facilities.

Conflict of interest

The authors declare they have no competing interests. Each author of this paper has completed the ICMJE conflict of interest statement.

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