Design and Validation of a Prehospital Scale to Predict Stroke Severity

Cincinnati Prehospital Stroke Severity Scale

Brian S. Katz, MD; Jason T. McMullan, MD; Heidi Sucharew, PhD; Opeolu Adeoye, MD, MS; Joseph P. Broderick, MD

Background and Purpose—We derived and validated the Cincinnati Prehospital Stroke Severity Scale (CPSSS) to identify patients with severe strokes and large vessel occlusion (LVO).

Methods—CPSSS was developed with regression tree analysis, objectivity, anticipated ease in administration by emergency medical services personnel and the presence of cortical signs. We derived and validated the tool using the 2 National Institute of Neurological Disorders and Stroke (NINDS) tissue-type plasminogen activator Stroke Study trials and Interventional Management of Stroke III (IMS III) Trial cohorts, respectively, to predict severe stroke (National Institutes of Health Stroke Scale [NIHSS] ≥15) and LVO. Standard test characteristics were determined and receiver operator curves were generated and summarized by the area under the curve.

Results—CPSSS score ranges from 0 to 4; composed and scored by individual NIHSS items: 2 points for presence of conjugate gaze (NIHSS ≥1); 1 point for presence of arm weakness (NIHSS ≥2); and 1 point for presence abnormal level of consciousness commands and questions (NIHSS level of consciousness ≥1 each). In the derivation set, CPSSS had an area under the curve of 0.89; score ≥2 was 89% sensitive and 73% specific in identifying NIHSS ≥15. Validation results were similar with an area under the curve of 0.83; score ≥2 was 92% sensitive, 51% specific, a positive likelihood ratio of 3.3, and a negative likelihood ratio of 0.15 in predicting severe stroke. For 222 of 303 IMS III subjects with LVO, CPSSS had an area under the curve of 0.67; a score ≥2 was 83% sensitive, 40% specific, positive likelihood ratio of 1.4, and negative likelihood ratio of 0.4 in predicting LVO.

Conclusions—CPSSS can identify stroke patients with NIHSS ≥15 and LVO. Prospective prehospital validation is warranted. (Stroke. 2015;46:1508-1512. DOI: 10.1161/STROKEAHA.115.008804.)

Key Words: acute stroke ■ NIHSS ■ prehospital emergency care ■ severe stroke ■ vessel occlusion

Currently, Primary Stroke Centers and Comprehensive Stroke Centers (CSC) form a 2-tier regionalized system of care for the efficient emergent management of patients with acute stroke.1 Although both Primary Stroke Centers and CSCs provide acute stroke care,1 CSCs are better equipped to provide state-of-the-art care for patients with severe ischemic and hemorrhagic stroke, including endovascular therapies, advanced diagnostic imaging, continuous in-hospital neurosurgical availability, and neurocritical care. These capabilities have led to improved cost-effectiveness and outcomes for ischemic stroke, intracerebral hemorrage, and subarachnoid hemorrhage at CSCs compared with non-CSCs.2-12 Large volume stroke centers provide faster treatment and improve the use of thrombolysis for patients with acute ischemic stroke (AIS).13 With the recent findings that timely endovascular therapy may improve outcomes in AIS patients with confirmed large vessel occlusions (LVO),14-16 and the greater likelihood of LVO in AIS patients with more severe AIS,17,18 there is now greater clinical need to care for patients with severe stroke at CSCs early in their clinical course.

Emergency medical services (EMS) providers are the first medical contact for half of all stroke patients19 and are responsible for triaging patients to appropriate hospitals. EMS bypass of nonstroke centers in favor of Primary Stroke Centers has been advocated,1,20,21 but the concept of bypassing a Primary Stroke Center for a CSC has been recommended for consideration but not yet been widely adopted.22 Bypass could be justified because interfacility transfer of patients introduces significant unnecessary delays in care and patient charges compared with direct EMS transport to a specialty care center.23-27 Other prehospital stroke scales28-30 have been proposed to identify patients experiencing an acute stroke or LVO,30-32
but have not been widely adopted in clinical practice because of the absence of positive LVO endovascular therapy trials.

We describe the retrospective derivation and validation of a new brief neurological scale, the Cincinnati Prehospital Stroke Severity Scale (CPSSS), in prediction of severe AIS and LVO.

Methods

Data Sets

To derive the CPSSS, we used the 2 National Institute of Neurological Disorders and Stroke (NINDS)-issue tissue plasminogen activator (tPA) Stroke Study trials data set, which is composed of a diverse cohort of patients having mild to severe strokes (National Institutes of Health Stroke Scale [NIHSS] 1–37) randomized to treatment with tPA or placebo within 3 hours of onset. The IMS-III data set served as the validation cohort. IMS-III was a prospective randomized trial comparing placebo within 3 hours of onset. The IMS-III data set served as the validation cohort. IMS-III was a prospective randomized trial comparing tPA with or without endovascular intervention. In both trials, pretreatment NIHSS scores (component and composite) were collected by NIHSS-certified study physicians at the time of enrollment. Subjects in each data set with complete pretreatment NIHSS component scores were included in the derivation or validation cohorts. Because the IMS-III cohort had higher NIHSS scores per the eligibility criteria, we chose to derive the CPSSS from the 2 NINDS tPA Stroke Study cohort to study sensitivity and specificity among a broader severity of stroke patients.

Outcome Measures

The primary outcome was the CPSSS ability to identify a severe stroke defined as NIHSS ≥15 because >95% of AIS patients with NIHSS ≥15 have a LVO by baseline imaging and is the lower limit of stroke severity for the consideration of hemicraniectomy. Secondary outcomes included CPSSS ability to identify moderate stroke severity (NIHSS ≥10) and proximal LVO (extracranial internal carotid artery, intracranial internal carotid artery, M1, tandem cervical internal carotid artery plus M2, or basilar artery occlusions [excluding M3, M4, posterior cerebral artery occlusion sites, and isolated M2]) by computed tomographic angiography before intravenous tPA therapy.

Derivation and Validation Methods

CPSSS was designed with a similar approach to that used in the development of the original Cincinnati Prehospital Stroke Scale. A classification and regression tree (CART) analysis was used to identify subsets of NIHSS items, as well as item score cut points, working together to predict severe stroke defined as NIHSS total score ≥15. Next, important candidate items identified by the classification tree were reviewed by the study clinicians (including board-certified EMS, emergency medicine, and vascular neurology physicians), and those items that are objective (eg, correctly answering questions or following commands) were chosen by expert consensus over those that are subjective (ie, degree of aphasia) to ensure ease of use by EMS personnel. Selected items were given a point score of 1 or 2 based on importance in predicting severe stroke as determined by the CART analysis. Receiver operating characteristic curves were generated to determine the accuracy of the CPSSS and to identify an optimal cut point to define an abnormal/positive screening assessment.

After derivation, the tool performance was assessed using the IMS III Trial data (validation data set), where, in addition to predicting AIS severity, the CPSSS was assessed for its accuracy in detecting LVO. Sensitivity, specificity, and positive and negative likelihood ratios were calculated for the optimal cut point.

Results

The 2 NINDS tPA Stroke Study trials data set contained 624 patients, of which there were 447 patients (71.6%) with pretreatment NIHSS ≥10 and 311 patients (49.8%) with pretreatment NIHSS ≥15. The presence of pretreatment proximal LVO was not obtained. CART analysis was used to identify potential NIHSS items for consideration by scale designers. CART analysis identified 5 NIHSS items that were important factors in predicting severe stroke (NIHSS ≥15). The most important factor, first defining split, was abnormal gaze (best gaze >0). For those with normal gaze (best gaze =0), motor function (right arm, right leg, and left leg) and language were found to be important factors. Of these, abnormal gaze and arm motor function were chosen to be included in the CPSSS, and the presence of abnormal gaze was weighted heavier on the CPSSS based on its predictive value on the CART and because of its suggestion of focal cortical dysfunction. Motor function of arm falling to bed was selected for ease of EMS providers to ascertain. Language was specifically not chosen to be included, despite being an important predictive factor, because of subjectivity of interpretation. Language was replaced with level of consciousness questions and commands because of the objective interpretation for EMS providers, yielding the CPSSS (Figure 1). A score is given for the presence of each clinical feature. The total CPSSS score is calculated as the sum of the individual scores and ranges from 0 to 4, with higher score reflecting higher stroke severity.

In the derivation set, the CPSSS score had an area under the receiver operating characteristic of 0.89 for detecting severe stroke (Figure 2). A CPSSS score ≥2 was 89% sensitive, 73% specific, positive likelihood ratio of 3.30, and negative likelihood ratio of 0.15 in identifying severe stroke (NIHSS of ≥15). For identification of stroke patients with a moderate stroke, a CPSSS score of ≥2 had a sensitivity of 75%, a specificity of 85%, positive likelihood ratio of 5.00, and negative likelihood ratio of 0.29 (Table 1).

The performance of CPSSS was validated using the IMS III data set, which was composed of 650 patients, of which 390 patients (60%) presented with an NIHSS ≥15 and 641 patients (99%) presented with an NIHSS ≥10. In the IMS III data set, the CPSSS had similar area under the receiver operating characteristic and test characteristics to the derivation set (Table 1; Figure 3).

For identifying LVO, 303 IMS III subjects had data available and were included in the analysis, of which, 222 had LVO. For LVO, CPSSS had an AUC of 0.67 and a score ≥2 was 83% sensitive, 40% specific, a positive likelihood ratio of 1.4, and negative likelihood ratio of 0.4 (Table 1).

Cincinnati Prehospital Stroke Severity Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal gaze, no motor weakness, no language difficulty</td>
</tr>
<tr>
<td>1</td>
<td>Abnormal gaze, normal motor function, normal language</td>
</tr>
<tr>
<td>2</td>
<td>Abnormal gaze, abnormal motor function, no language difficulty</td>
</tr>
<tr>
<td>3</td>
<td>Abnormal gaze, abnormal motor function, abnormal language</td>
</tr>
</tbody>
</table>

Figure 1. The Cincinnati Prehospital Stroke Severity Scale’s individual items and scoring. NIHSS indicates National Institutes of Health Stroke Scale.
A comparison of the CPSSS to other prehospital stroke scales is shown in Table 2.

**Discussion**

We found that the CPSSS has high sensitivity and acceptable specificity in detecting the presence of severe stroke, moderate stroke, and LVO among populations of patients with AIS. Specifically, the CPSSS can identify stroke patients who could be most likely to benefit from rapid triage to a CSC, including those who harbor proximal LVO that are appropriate targets for intravenous tPA and endovascular therapy. These patients may also be eventual candidates for hemircanectomy and benefit from a dedicated Neurological Intensive Care Unit (ICU). Given the time-sensitivity of the above therapies, accurate initial triage of patients to hospitals, where these therapies are available, is a key to prevent delays in care and increased costs associated with transfers.

Three screening tools to identify severe ischemic strokes have been previously proposed, but none has been widely adopted into EMS practice (Table 2). The Los Angeles Motor Scale (LAMS) is limited by the fact that a sizable proportion of the population studied to derive LAMS occurred retrospectively and included patients enrolled in clinical trials >11 years at a single institution. The Rapid Arterial Occlusion Evaluation (RACE) scale was developed to predict LVO. However, RACE scale was not evaluated in 60% of patients transferred by EMS, and patients not included had less severe strokes and less frequency of LVO than patients included in the analysis. The complexity of RACE (6 domains requiring subjective interpretation in several of the domains) further poses a significant challenge for accurate EMS implementation. It should be noted that we constructed the CPSSS before awareness of the recent RACE publication, but there are similarities between the 2 scales. The major differences are that the CPSSS is shorter, uses dichotomous answers, and rates conjugate gaze deviation more heavily. Finally, the 3-Item Stroke Scale (3ISS) is most similar to our prehospital scale given modalities that were tested. The 3ISS was limited by sample size and requires subjective grades, such as none, moderate, or severe disturbance of consciousness.

Using a prehospital scale, such as the CPSSS, as a triage tool in the field would affect the initial transport of patients in many communities in the United States and potentially other countries depending on the prehospital system. However, because almost 80% of patients with ischemic stroke have a baseline NIHSS <10 and nearly 90% have a baseline NIHSS <15, the actual number of patients with ischemic stroke triaged to CSCs would have relatively limited impact on individual community hospitals that are not comprehensive centers. The NIHSS distribution of hemorrhagic stroke within a population is unknown; as such we are unable to reliably estimate the proportion of patients with hemorrhagic stroke that may be

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Data Set</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PLR</th>
<th>NLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke severity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>Derivation</td>
<td>89%</td>
<td>73%</td>
<td>3.30</td>
<td>0.15</td>
</tr>
<tr>
<td>(NIHSS≥15)</td>
<td>Validation</td>
<td>92%</td>
<td>51%</td>
<td>1.89</td>
<td>0.16</td>
</tr>
<tr>
<td>Moderate</td>
<td>Derivation</td>
<td>75%</td>
<td>85%</td>
<td>5.00</td>
<td>0.29</td>
</tr>
<tr>
<td>(NIHSS≥10)</td>
<td>Validation</td>
<td>79%</td>
<td>89%</td>
<td>7.18</td>
<td>0.24</td>
</tr>
<tr>
<td>LVO</td>
<td>Validation</td>
<td>83%</td>
<td>40%</td>
<td>1.38</td>
<td>0.42</td>
</tr>
</tbody>
</table>

LVO defined as occlusion sites of internal carotid artery, M1, tandem cervical internal carotid artery plus M2, or basilar arteries. LVO indicates large vessel occlusion; NIHSS, National Institutes of Health Stroke Scale; NLR, negative likelihood ratio; and PLR, positive likelihood ratio.

Figure 2. The receiver operating characteristic curve for Cincinnati Prehospital Stroke Severity Scale in detecting stroke severity in the derivation data set. AUC indicates area under the curve.

Figure 3. The receiver operating characteristic curve for Cincinnati Prehospital Stroke Severity Scale in detecting stroke severity and large vessel occlusion in the validation data set. AUC indicates area under the curve.
Table 2. Comparison of CPSSS to Other Published Prehospital Stroke Severity Scales

<table>
<thead>
<tr>
<th></th>
<th>CPSSS</th>
<th>LAMS</th>
<th>RACE</th>
<th>I3SS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derivation data set (n)</td>
<td>624</td>
<td>119</td>
<td>654</td>
<td>171</td>
</tr>
<tr>
<td>Validated in independent data set (Y/N)</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>No. of items scored</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Sensitivity/specificity for severe stroke</td>
<td>89%/72%</td>
<td>NA</td>
<td>NA</td>
<td>86%/95%*</td>
</tr>
<tr>
<td>Sensitivity/specificity for LVO</td>
<td>83%/46%</td>
<td>81%/89%†</td>
<td>85%/67%‡</td>
<td>67%/92%§</td>
</tr>
<tr>
<td>Evaluated in prehospital setting (Y/N)</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
</tbody>
</table>

CPSSS indicates Cincinnati Prehospital Stroke Severity Scale; CTA, computed tomography angiography; I3SS, 3-item Stroke Scale; LAMS, Los Angeles Motor Scale; LVO, large vessel occlusion; MRA, magnetic resonance angiography; N, no; NA, not applicable; RACE, Rapid Arterial Occlusion Evaluation; and Y, yes.

*Severe stroke defined as National Institutes of Health Stroke Scale (NIHSS) ≥14.
†LVO defined as terminal intracranial carotid artery occlusion, M1 segment middle cerebral artery occlusion, M2 segment middle cerebral artery occlusion, and M3/M4 segment middle cerebral artery occlusion using catheter angiography, MRA, CT, and carotid ultrasound.
‡LVO was defined as occlusion of the terminal intracranial carotid artery, proximal middle cerebral artery (M1 segment), tandem (extracranial carotid artery plus middle cerebral artery) and basilar artery with transcranial duplex (50% of cases), CTA, and MRA.
§LVO defined as T/M1 occlusion all using MRA.

This study has some limitations. First, this was a retrospective analysis of 2 existing ischemic stroke trial cohorts; therefore, prospective evaluation by EMS providers is required. Second, there is variability of the NIHSS during the first few hours of AIS onset, and it is possible that the stroke severity at the time of EMS examination will change by the time a treatment decision for ischemic stroke is made by medical providers. Next, isolated M2 lesions were not included in the CPSSS’s LVO prediction analysis; however, only a minority of isolated M2 occlusions (2%–8% of patients) was included in recent positive endovascular trials. The CPSSS has not been tested in populations of patients with hemorrhagic stroke or in a general population of patients with potential stroke who are evaluated by EMS personnel in the field. The CPSSS is likely to be less sensitive to subarachnoid hemorrhage in which patients’ presentations are often nonfocal, unless the patient presents in coma. However, patients with sudden onset of coma are probably more likely to be preferentially triaged to tertiary centers.

In summary, the CPSSS was designed to be user-friendly and applicable for EMS providers in the field. CPSSS ≥ 2 has promising characteristics in predicting severe strokes and LVO and should be prospectively evaluated to demonstrate clinical use. This study serves as the foundation for an ongoing study assessing the feasibility of CPSSS by EMS providers in the prehospital setting among patients with potential stroke. The eventual goal is a prehospital scale that can be used as a reliable and practical method of prehospital triage of stroke patients in which the large majority of patients are transported to the location, where the best therapy can be delivered as rapidly as possible.

Sources of Funding
This study was supported by grants from the National Institute of Neurological Disorders and Stroke T-32 Cerebrovascular Fellowship Training Program for Cerebrovascular Disease.

Disclosures
Dr Broderick has received research monies to Department of Neurology from Genentech for PRISMS Trial; travel to Australian stroke Conference paid for by Boehringer Ingelheim. Study medication from Genentech for IMS III Trial and study catheters supplied during Protocol Versions 1 to 3 by Concentric Inc, EKOS Corp, and Cordis Neurovascular. The other authors report no conflicts.

References
Design and Validation of a Prehospital Scale to Predict Stroke Severity: Cincinnati Prehospital Stroke Severity Scale
Brian S. Katz, Jason T. McMullan, Heidi Sucharew, Opeolu Adeoye and Joseph P. Broderick

Stroke. 2015;46:1508-1512; originally published online April 21, 2015; doi: 10.1161/STROKEAHA.115.008804

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/46/6/1508

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/