

# Prehospital care delivery and triage of stroke with emergent large vessel occlusion (ELVO): report of the Standards and Guidelines Committee of the Society of Neurointerventional Surgery

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## INTRODUCTION

Recent randomized clinical trials<sup>1–5</sup> established the superiority of endovascular recanalization techniques, specifically mechanical embolectomy, compared with best medical therapy alone for the treatment of patients with emergent large vessel occlusion (ELVO) stroke. ELVO stroke is defined as a stroke secondary to anterior circulation large vessel occlusion (LVO) of the internal carotid, middle cerebral (M1 segments) arteries documented by imaging, without large completed infarct and presenting within 6 hours of symptom onset.<sup>6</sup> Given the overwhelming clinical evidence provided by these trials, recent American Heart Association (AHA) guidelines concluded that “embolectomy needs to be performed as rapidly as possible for the greatest clinical benefit, and is best when performed within 6 h from onset of symptoms” (AHA class I, level of evidence A).<sup>6</sup> In addition, cost modeling derived from trial outcomes data and claims databases in the USA strongly suggests that cost-effectiveness and an overall societal benefit is associated with investment in access to these endovascular techniques.<sup>7</sup> Rapid access to endovascular services depends upon optimization of pre-hospital stroke care and transport within stroke systems of care, focusing on the unique needs of patients with ELVO through their diagnostic investigation and treatment pathway. The Society of NeuroInterventional Surgery (SNIS) proposed process time metrics for ELVO stroke treatment, including door to IV tissue plasminogen activator (t-PA) of <30 min, comprehensive stroke center (CSC) door to puncture of <60 min, CSC door to recanalization of <90 min and primary stroke certification (PSC) picture to CSC puncture of <90 min.<sup>8</sup> Early team awareness of the patient with potential ELVO, coupled with efficient interdisciplinary communication, triage and transport assist in meeting these ideal time metrics, and also contribute to improved clinical outcomes through

efficiency gains and maximization of endovascular care delivery.

## MATERIALS AND METHODS

The Standards and Guidelines Committee of the SNIS, a multidisciplinary society representing leaders in the field of endovascular therapy for neurovascular disease, prepared this document based upon a comprehensive review of English language literature relating to the topic. The strength of evidence supporting each recommendation was summarized using levels of evidence as defined by the AHA.

## OUTCOMES AND TIME TO REVASCULARIZATION IN ELVO STROKE

The dependence of good clinical outcome on time to revascularization in ELVO stroke is well established.<sup>9–10</sup> Reperfusion therapy is effective at preserving penumbral tissue, the volume of which diminishes with time.<sup>11</sup> Data from the endovascular cohort in the Interventional Management of Stroke (IMS) III trial demonstrated that shorter time to reperfusion was associated with improved outcome (modified Rankin Scale score  $\leq 2$  at 90 days).<sup>10</sup> A relative risk reduction of a good outcome of approximately 12–15% was associated with each 30-min delay in time to reperfusion (unadjusted RR with 30-min delay: 0.85, 95% CI 0.77 to 0.94). Dramatic recovery in ELVO, defined as National Institutes of Health Stroke Scale (NIHSS) score  $\leq 3$  at 24 hours, or a decrease of the NIHSS score of  $\geq 10$  points in 24 hours, was shown to be a powerful predictor of excellent outcome (OR of modified Rankin Scale score  $\leq 1$  at 90 days: 23.82, 95% CI 10.85 to 53.25;  $p < 0.001$ ),<sup>12</sup> and was also independently associated with time to recanalization, being significantly more likely with each 30-min reduction in time (OR of dramatic recovery: 1.24, 95% CI 1.04 to 1.48;  $p = 0.016$ ).<sup>12</sup>



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The SPEED study, which evaluated a newer technique/catheter against older data from the PIVOTAL study<sup>13</sup> suggests that faster reperfusion times improve outcome.<sup>14</sup> A smaller study of patients who underwent rapid imaging to reperfusion with embolectomy found that faster treatment led to high rates of excellent clinical outcomes (82% of patients).<sup>15</sup> Evaluation of the databases from the SWIFT and STAR trials determining mechanical embolectomy with stent retrievers, focusing on 202 patients in whom embolectomy was technically successful, showed that shorter times from symptom onset to recanalization were associated with significantly improved 90-day clinical outcomes.<sup>16</sup> The authors noted that, for every 15-min reduction in time from onset to recanalization, 34 of every 1000 treated patients had an improved disability outcome.<sup>16</sup>

The recently published randomized controlled trials mentioned above provide further confirmation of the benefit of time (table 1). The MR CLEAN trial,<sup>1</sup> compared with IMS III,<sup>17</sup> which previously showed no significant added benefits of endovascular management to standard medical therapy, demonstrated clinical benefits of endovascular treatment with mechanical embolectomy without initiating an improvement in time to treatment, suggesting that the benefits shown in the study were probably related to better patient selection using imaging confirmation of LVO and better revascularization techniques employing modern devices in the endovascular group.<sup>18</sup> Subgroup analyses from the MR CLEAN trial presented at the International Stroke Conference 2015 showed an approximately 7% decreased probability of good outcome for each hour delay in revascularization.<sup>19</sup> For patients revascularized within 2 hours of stroke onset, the absolute difference in good outcomes between the endovascular and control groups was 33%, decreasing to 6.5% at 6 hours.<sup>19</sup>

Subsequently published trials, with similar design to MR CLEAN but faster treatment times, also suggest a widening absolute treatment effect difference between the control and treatment groups with decreasing time to endovascular treatment (table 1). In two trials, particular emphasis was placed upon efficiency with monitored time goals of qualifying imaging to groin of 70 min in SWIFT PRIME<sup>4</sup> and goals of CT to groin and CT to reperfusion of 60 and 90 min, respectively, in ESCAPE.<sup>3</sup> Analyses of efficiency data from these trials show clear benefits of reduced time to reperfusion, with 8.3% reduction in good outcome for every 30-min delay from imaging to reperfusion in ESCAPE<sup>20</sup> and a 91% probability of good outcome for those in SWIFT PRIME reperfused within 150 min of symptom onset, decreasing by 10% for an initial hour of delay and 20% for each subsequent hour of delay.<sup>21</sup>

These studies provide models for efficiency that will probably strongly influence future recommended time metrics for ELVO stroke. Clearly, time to reperfusion has a profound effect on outcome.

## TIMING AND EFFICIENCY IN ELVO STROKE

Most of the time-related outcome gains realized in recently reported studies result from improvements in techniques and hospital processes involving the treatment link along the American Stroke Association (ASA)-defined 'stroke chain of survival' connecting recognition, dispatch, transport, and treatment (<http://www.strokeassociation.org>). Since time until treatment is a continuous variable with a non-linear effect on outcome, time savings achieved along each earlier link of recognition, dispatch, and transport may likewise significantly affect outcome in ELVO stroke. Analysis of pooled data from embolectomy trials including the multi-MERCI, TREVO, and TREVO-2 trials involving 1248 patients over a 10-year period showed that significant improvement occurred in procedure times, without corresponding improvements in last known normal (LKN) to puncture times. Prolonged LKN to puncture times were significantly associated with a decreased chance of good outcome (OR=0.84, 95% CI 0.76 to 0.92;  $p=0.0004$ ).<sup>22</sup> Thus, rapid recognition and triage of patients with stroke has become paramount.

Liebeskind *et al*<sup>23</sup> analyzed data from the SWIFT trial (which compared different techniques in embolectomy for stroke) and found that a time >3 hours was the only predictor of extensive infarct on imaging ( $p=0.003$ ). In that study, shorter times from symptom onset to hospital arrival were associated with smaller infarcts, better collateral vessels, and improved clinical outcome from embolectomy.<sup>23</sup> To that end, the AHA/ASA 2015 guidelines recently found that "Patients should be transported rapidly to the closest available certified primary stroke center or comprehensive stroke center or, if no such centers exist, the most appropriate institution that provides emergency stroke care"<sup>24</sup> A variety of legislative efforts also support this approach. Evaluation of the endovascular cohort in the IMS III trial showed that transfer of patients between centers resulted in longer stroke onset to reperfusion times than for those treated at the same center,<sup>25</sup> providing impetus for consideration of primary transport to endovascular-capable centers. Indeed, although local systems of care may vary, the importance of rapid recognition of diagnosis and transport to appropriate centers is consistently paramount.

## STROKE SYSTEMS OF CARE AND ELVO STROKE

Systems of care for stroke are rapidly gaining importance in acute stroke intervention. As the pivotal roles of early recognition and rapid treatment have become clear, protocols for care and real-time data collection are now vital. In the 1990s and early 2000s, several organizations and healthcare bodies recognized the uneven distribution of stroke care, and the need to standardize approaches.<sup>26</sup> Born from the efforts of the Brain Attack Coalition (BAC) with certification offered through the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), PSC began in 2004.<sup>27</sup> Later partnership with the AHA/ASA led to widespread adoption and by 2011, there were over 800 PSC hospitals.<sup>26</sup>

The maintenance of PSC requires practice of stroke care to standardized guidelines, and reporting of metrics (core measures) as a marker of success. For example, primary stroke centers must report their door-to-needle time that marks the average time interval from the moment a patient with stroke enters the hospital to the administration of IV t-PA. Primary

**Table 1** Endovascular stroke trials and treatment time

Study	Time to groin (median) (min)	Time to reperfusion (median) (min)	mRS 0–2 Endovascular (%)	mRS 0–2 Medical (%)	Absolute difference (%)
IMS III	208	325	40.8	38.7	2.1
MR CLEAN	260	332	32.6	19.1	13.5
REVASCAT	269	355	43.7	28.2	15.5
SWIFT PRIME	224	252	60.2	35.5	24.7
EXTEND IA	210	248	71	40	31
ESCAPE	185	241	53	29.3	23.7

IMS, Interventional Management of Stroke; mRS, modified Rankin Scale.

stroke centers are also involved in developing stroke networks, providing education to providers, and guiding emergency medical services (EMS) protocols for stroke recognition and care. Such certification carries some benefits—improving adherence to standards of care in thrombolysis for ischemic stroke, and reducing overall mortality.<sup>28–30</sup>

However, recognizing that some hospitals were needed that could reliably offer more complex stroke care, the Joint Commission launched certification for CSCs in 2012. Although somewhat controversial, these centers, with reliable 24/7 availability of endovascular services, are ideal destinations for patients with ELVO stroke. The new certification process aligns with earlier recommendations from the BAC in 2005 for advanced centers.<sup>31</sup> CSCs must meet requirements for PSC, but also have a minimum case volume of patients with complex ischemic and hemorrhagic stroke. Furthermore, they must have cerebrovascular imaging capabilities on site, 24/7 neurosurgical services, and a dedicated intensive care service that manages patients with complex stroke. They must also have peer-review mechanisms to discuss complex cases, participate in stroke-related research, and report additional core measures above those required by primary stroke centers. They must also be staffed sufficiently to be able to care for simultaneous complex stroke patients.<sup>32</sup>

Early data suggest that care in a CSC is associated with improved survival at 90 days for patients with hemorrhagic stroke, who typically require more complex care.<sup>33</sup> A review of patients with hemorrhagic stroke in the Myocardial Infarction Data Acquisition System (MIDAS) database,<sup>33</sup> demonstrated that patients admitted to CSCs were more likely to have neurosurgical or endovascular interventions than those admitted to a primary stroke center/non-stroke center (18.9% vs 4.7%;  $p < 0.0001$ ). Furthermore, CSC admission was associated with lower adjusted 90-day mortality (35.0% vs 40.3%; 0.93; 95% CI –0.89 to 0.97). Thus, appropriate transfer of patients with suspected or confirmed complex stroke (such as hemorrhagic stroke or ELVO) to a CSC is important within a stroke system of care.

Three levels of certification are defined by JCAHO and the AHA/ASA: acute stroke ready hospitals, primary stroke centers, and CSCs.<sup>32</sup> Certification of centers in the USA occurs through JCAHO, and other CMS authorized certification organizations such as Det Norske Veritas/Germanischer Lloyd (DNV-GL) and the Healthcare Facilities Accreditation Program (HFAP). Additionally, individual approval of stroke centers has been organized at state levels, including through the Agency for Health Care Administration (AHCA) in Florida and the Department of State Health Services (DSHS) in Texas. Although there are some subtle differences in the requirements of these different organizations, they all adhere to the structure outlined by JCAHO, the AHA/ASA, and the BAC.

Through a ‘hub and spoke’ model,<sup>34–35</sup> with the CSC serving as the hub, stroke networks can recognize and treat patients with stroke quickly, while diverting patients with complex, severe stroke to the most appropriate hospital. Ultimately, the CSCs are responsible for reporting complex metrics for all avenues of stroke treatment, including such measures as time to endovascular therapy and appropriate reversal of anticoagulation in hemorrhagic stroke.<sup>36</sup> Certification of centers provides reliable verification of effective comprehensive services for planners of stroke systems of care at local, state, and national levels. With these levels of certification, the routing of patients by EMS becomes crucial to stroke systems of care. Indeed, routing protocols for patients with stroke can help concentrate them quickly

in equipped and certified hospitals,<sup>37</sup> enabling them to receive the optimized level of care. Several opportunities exist for interaction between EMS and stroke systems of care, which could improve efficiency and, potentially, improve outcomes for patients with ELVO stroke.

## PREHOSPITAL EFFICIENCY OPPORTUNITIES IN ELVO STROKE

Prehospital efficiency improvement should focus on the two treatments with proven benefit for the patient with ELVO stroke—IV t-PA and endovascular therapy. IV t-PA should be delivered as quickly as possible to eligible patients. Randomized controlled trials have proved it to be efficacious,<sup>38–39</sup> and safe to administer in the setting of potential endovascular treatment.<sup>1–5 17</sup> A significant majority of the patients treated endovascularly in SWIFT PRIME, MR CLEAN, EXTEND-IA, ESCAPE and REVASCAT received IV-t-PA before, or at the same time as, endovascular treatment (459/634 (72.4%) patients).<sup>1–5</sup> Rapid access to endovascular treatment should be a goal for all patients suspected of having, or proved with imaging to have, ELVO.

## Public education

Two aspects of public education are of particular importance for the patient with ELVO. First, efforts to raise awareness of ELVO stroke as a distinct subtype of stroke requiring treatment at comprehensive centers with endovascular capability may prove important. Considerable success in educating the public about stroke symptoms was achieved with the introduction in the UK of the Face/Arm/Speech Time (FAST) scale,<sup>40</sup> first to EMS and primary caregivers, later to the public. This scale was derived from earlier stroke recognition scales developed and validated in the 1990s and early 2000s—namely, the Cincinnati Prehospital Stroke Scale (CPSS),<sup>41</sup> and the Los Angeles Prehospital Stroke Screen (LAPSS).<sup>42–43</sup> FAST correctly identified stroke symptoms in 88.9% of patients in one study.<sup>44</sup> Its simplicity promotes retention, with studies showing significantly increased awareness of stroke symptoms,<sup>45–47</sup> and objective improvement in delays in seeking and receiving treatment.<sup>48</sup> Similar education of the public about ELVO stroke could be carried out, providing recognition tools, and a comprehensive center with endovascular services as the appropriate treatment endpoint. Although the educational tools have yet to be defined, the accumulated evidence supporting improved outcomes with endovascular treatment suggests the importance of separately identifying ELVO stroke with its increased complexity of its treatment.

Second, as with stroke in general, public awareness about the benefits of EMS transport should be raised, with patients, families and the public being encouraged to use the 911 response system instead of self-transport for suspected ELVO stroke. Rapid transport to highly specialized centers, such as primary stroke centers or CSCs, is greatly facilitated by EMS networks. In one study involving 158 hospitals in northwestern Germany, EMS transport was independently associated with faster times of hospital arrival, shorter times to brain imaging, and higher probability of treatment with thrombolysis than self-transport.<sup>49</sup> It was estimated, based upon 2011 US demographic data and Medicare endovascular treatment rates, that 56% and 85% of the US population had ground or air access, respectively, to endovascular-capable hospitals within 60 min.<sup>50</sup> When the time interval was extended to 120 min, 99% of the US population had such access. Maximization of timely access requires sustained coordination of public and EMS educational efforts about ELVO stroke, organization of EMS and stroke care networks, and ongoing assessment of process improvement.

### EMS initial contact

On initial contact with the EMS, important information, which might affect the efficiency of treatment, should be obtained and recorded. A family or next of kin contact is critically important for history gathering or obtaining treatment consent. Preferably, this should be a consistent contact number, such as a cell phone number. Many treatment decisions related to acute stroke depend upon an accurate time of onset or LKN time, and this knowledge is critical in evaluation of the patient with ELVO stroke. Agreement between EMS-determined time of onset and hospital neurologist LKN times has been shown when personnel are appropriately trained.<sup>51</sup> Factors associated with incongruence were older patient age and wake-up strokes. A history of anticoagulant use should be obtained, as this information is useful in determining eligibility for IV t-PA.

### Early identification

Strategies for streamlining stroke care include the use of EMS field screening tools that can be administered quickly and easily by EMS personnel. Most tools employed by EMS are designed for stroke recognition rather than stroke classification or severity assessment. These recognition scales include the CPSS, FAST, LAPSS, Melbourne Ambulance Stroke Screen (MASS),<sup>52</sup> Medic Prehospital Assessment for Code Stroke (Med PACS),<sup>53</sup> and Recognition of Stroke in the Emergency Room (ROSIER) scale.<sup>54</sup> Tools used vary by region, but employment of some tool for stroke recognition is recommended in clinical guidelines.<sup>55</sup>

In North Carolina, retrospective comparison of hospitals with EMS databases for the diagnosis of stroke and the accuracy of CPSS and LAPSS stroke recognition tools in large numbers of patients (2442) showed sensitivity of 80% and 74%, respectively, but with relatively low specificity of 48% for both scales.<sup>56</sup> This low specificity was corroborated by another study from Michigan,<sup>57</sup> where EMS screening had a false-positive rate of nearly 50%. Factors in that study associated with increased accuracy of EMS stroke diagnosis included documentation of administration of the CPSS, higher NIHSS (more severe strokes; OR=1.09 for each one point increase), and early presentation (OR=2.22). Another study showed an overall low sensitivity of 62.4% for EMS recognition of stroke, but no patients with strokes presenting with unilateral weakness, facial weakness, or speech problems were missed.<sup>58</sup> Despite the relatively low overall specificity and sensitivity in these studies, these associations support use of prehospital screening scales to identify patients with stroke and suggest that EMS accuracy is higher for patients with severe strokes at early time intervals, exactly the population most likely to have IVOs that might benefit from endovascular treatment.

Early identification of patients with suspected ELVO stroke can focus the entire team on facilitating delivery of endovascular care at a CSC as early as possible either through direct transport or through later interfacility transfer. EMS can be instrumental in this regard, administering recognition tools to direct appropriate triage.<sup>59</sup> Standardization and evaluation of field clinical assessment tools for ELVO stroke have been in development for several years, with several tools described in the literature<sup>60–63</sup> sharing some common themes. Higher stroke severity and the presence of cortical signs have been associated with a higher likelihood of IVO in patients with acute stroke undergoing vascular imaging with angiography, MR angiography (MRA), or CT angiography (CTA).<sup>64, 65</sup> NIHSS scores  $\geq 12$  were associated with a 91% positive predictive value (PPV) for central IVO.<sup>64</sup> A

degree of time dependence was also demonstrated, with a NIHSS score  $\geq 9$  associated with a PPV for IVO of 86.4% within 3 hours of onset, but a lower NIHSS score  $\geq 7$  associated with a similar PPV for IVO of 84.4% between 3 and 6 hours of stroke onset,<sup>65</sup> so absolute NIHSS score cut-off points are problematic. Additional independent associations with IVO included motor function of the leg and portions of the NIHSS concerned with assessment of cortical functions, including gaze, level of consciousness questions, and neglect.<sup>64</sup> The lengthy NIHSS is not well suited to application in the field by EMS, compelling the development of simpler scales that can be more rapidly evaluated. Severe hemiparesis or hemiplegia was associated with a cerebrovascular etiology in 84.5% of 45 patients transported to a single CSC by helicopter over a period of 6 months, including 60% ischemic stroke, 13.3% intracerebral hemorrhage, 15.5% transient ischemic attack, and 2.2% subarachnoid hemorrhage.<sup>66</sup> Of the transported patients, 26.7% underwent mechanical thrombectomy for ELVO and 33% underwent an endovascular procedure for either ischemic or hemorrhagic stroke, suggesting that this clinical finding alone may indicate the potential for improved outcomes by transport to facilities with endovascular services.

Stroke field severity scales associated with a high probability of ELVO, either directly or through association with high NIHSS scores, include the 3-Item Stroke Scale (3I-SS),<sup>60</sup> the Los Angeles Motor Scale (LAMS),<sup>61</sup> the Rapid Arterial occlusion Evaluation (RACE) scale,<sup>63</sup> the Cincinnati Prehospital Stroke Severity Scale (CPSSS),<sup>62</sup> the LEGS score,<sup>67</sup> the VAN (vision, aphasia, neglect) screening tool,<sup>68</sup> and several shortened variations of the NIHSS.<sup>69–70</sup>

The 3I-SS is a simple scale derived from the NIHSS evaluating gaze and head deviation, level of consciousness, and motor function.<sup>60</sup> It is strongly associated with the NIHSS for assessing stroke severity, and correlated with ELVO in prospectively evaluated patients undergoing MRA, with a high degree of interobserver reliability (intraclass correlation coefficient 0.947). The optimal level of severity to predict ELVO was a score  $\geq 4$ , with an overall accuracy of 0.86 (table 2). More intracranial hemorrhages were associated with both a higher 3I-SS and NIHSS scores.

The LAMS incorporates three motor components of the LAPSS stroke recognition scale and is relatively quickly administered, taking about 20–30 s,<sup>61</sup> concurrent with the LAPSS. At

**Table 2** The 3-Item Stroke Scale (3I-SS)<sup>60</sup>

Item	Points
Consciousness disturbance	
None	0
Mild	1
Severe	2
Gaze and head deviation	
Absent	0
Incomplete	1
Complete	2
Hemiparesis	
Absent	0
Moderate	1
Severe	2
Total score	0–6

3I-SS  $\geq 4$ : 67% sensitivity, 92% specificity, 0.36 negative likelihood ratio for large vessel occlusion.



## Standards

the optimal threshold of  $\geq 4$  points, this scale showed an overall accuracy of 0.85 for the presence of ELVO in retrospective score derivations from trial and registry anterior circulation stroke databases (table 3). Although the LAMS does not incorporate an assessment of cortical function, a sevenfold increased incidence of ELVO was found with LAMS  $\geq 4$  points.

The RACE scale likewise incorporates motor function, but adds assessment of cortical function of each hemisphere, with aphasia assessment for the left hemisphere and agnosia assessment for the right hemisphere.<sup>63</sup> It was derived from retrospective analysis of a large Spanish stroke cohort to identify portions of the NIHSS most highly correlated with ELVO. Prospective validation in the field by EMS yielded an accuracy for prediction of ELVO of 0.72 at the optimal score of  $\geq 5$  points (table 4).<sup>63</sup> Higher RACE scores correlated strongly with the presence of ELVO and of hemorrhagic stroke and correlated less well with stroke mimics.

The CPSSS is a relatively simple scale incorporating gaze, level of consciousness, and motor components of the NIHSS.<sup>62</sup> These were derived using classification and regression tree analysis of NINDS t-PA trial data to identify NIHSS components that correlated best with NIHSS stroke severity  $\geq 15$ . Advantages associated with this scale include its brevity, use of less subjective dichotomous responses, and incorporation of gaze abnormalities. CPSSS scores of  $\geq 2$  points were associated with an accuracy of 0.89 for the detection of severe stroke with a NIHSS score  $\geq 15$ . Validation with the IMS III dataset for the presence of ELVO on CTA yielded an accuracy of 0.67 for CPSSS scale scores  $\geq 2$  points (table 5).

The VAN screening tool incorporates assessment of vision, aphasia, and neglect with motor assessment of arm strength.<sup>68</sup> It is a dichotomous tool rather than a numeric scale with the overall screen considered positive for weakness combined with any positive vision, aphasia, or neglect screen. Prospective single-center correlation with ELVO when administered by trained emergency room nurses yielded an accuracy of 0.92 (table 6).

From the above discussion, it is clear that several similar pre-hospital stroke severity/ELVO identification scales are available with similar reported accuracy. Scales such as the 3I-SS, CPSSS, LAMS, and the VAN screening tool have the advantage of being simple and easy to administer by EMS, but have not yet undergone prospective validation. The RACE scale, although more complicated to administer, has undergone prospective field EMS

validation. Given the overwhelming data supporting endovascular treatment, further studies of these tools in the field are needed. There is insufficient evidence to state which scale or field tool is optimal, but we recommend that EMS use one of them to identify patients with ELVO in the field. Direct transport to comprehensive centers with endovascular capability for severe strokes with a high probability of ELVO maximizes time savings for potential endovascular treatment, and ensures that appropriate neurosurgical and neurointensive care is readily available for those patients with hemorrhagic strokes and severe strokes identified by higher scores on these scales. Indeed, patients with hemorrhagic strokes treated at CSCs have improved survival.<sup>33</sup>

Perhaps the most accurate means of identifying a patient with ELVO requires imaging equipment or other testing being brought to the patient. Transcranial ultrasound has been used in the prehospital setting with adequate personnel and training.<sup>71 72–74</sup> This modality can diagnose middle cerebral artery (MCA) occlusion with a reasonably high degree of accuracy. In one German study, transcranial ultrasound used in a prehospital setting demonstrated a sensitivity of 78% and specificity of 98% for the diagnosis of MCA or internal carotid artery occlusion in comparison with CTA/MRA performed at receiving hospitals.<sup>74</sup> In addition, investigations are continuing into the use of ultrasound, with or without microbubble contrast administration, to assist in mechanical clot dissolution or aid the cerebral microcirculation, potentially providing some degree of prehospital clot ‘conditioning’ or neuroprotection before definitive treatment.<sup>73</sup> An advantage of transcranial ultrasound includes its portability,

**Table 3** Los Angeles Motor Scale (LAMS)<sup>61</sup>

Item	Points
Facial droop	
Absent	0
Present	1
Arm drift	
Absent	0
Drifts down	1
Falls rapidly	2
Grip strength	
Normal	0
Weak grip	1
No grip	2
Total score	0–5

LAMS  $\geq 4$ : 81% sensitivity, 89% specificity, 0.21 negative likelihood ratio for large vessel occlusion.

**Table 4** Rapid Arterial occlusion Evaluation scale (RACE)<sup>63</sup>

Item	Race score	NIHSS equivalent
Facial palsy		
Absent	0	0
Mild	1	1
Moderate to severe	2	2–3
Arm motor function		
Normal to mild	0	0–1
Moderate	1	2
Severe	2	3–4
Leg motor function		
Normal to mild	0	0–1
Moderate	1	2
Severe	2	3–4
Head and gaze deviation		
Absent	0	0
Present	1	1–2
Aphasia* (if R hemiparesis)		
Performs both tasks correctly	0	0
Performs one task correctly	1	1
Performs neither task	2	2
Agnosia† (if L hemiparesis)		
Recognizes both paretic arm and impairment	0	0
Does not recognize paretic arm or impairment	1	1
Does not recognize paretic arm and impairment	2	2
Total score	0–9	

\*Aphasia: (1) ‘close your eyes’; (2) ‘make a fist’.

†Agnosia: (1) ‘whose arm is this?’; (2) ‘raise both hands and clap’.

RACE  $\geq 5$ : 85% sensitivity, 68% specificity, 0.22 negative likelihood ratio for large vessel occlusion.

NIHSS, National Institutes of Health Stroke Scale.

**Table 5** Cincinnati Prehospital Stroke Severity Scale (CPSSS)<sup>62</sup>

Item	Points
Gaze	
Conjugate gaze deviation ( $\geq 1$ NIHSS gaze)	2
Consciousness/commands	
Incorrectly answers one LOC question and one command on NIHSS (age, current month, close eyes, open and close hand) ( $\geq 1$ on NIHSS)	1
Motor arm	
Cannot hold arm up (left, right or both) for 10 s before it falls to bed ( $\geq 2$ on NIHSS)	1
Total score	0–4
CPSSS $\geq 2$ : 83% sensitivity, 40% specificity, 0.4 negative likelihood ratio for large vessel occlusion.	
CPSSS $\geq 2$ : 92% sensitivity, 51% specificity, 0.15 negative likelihood ratio for NIHSS score $\geq 15$ .	
LOC, level of consciousness; NIHSS, National Institutes of Health Stroke Scale.	

**Table 6** Vision, Aphasia, Neglect (VAN) screening tool<sup>68</sup>

Item	Responses
Motor arm	
Raise both arms	Mild—minor drift Moderate—severe drift Severe—flaccid or no antigravity No weakness—VAN negative
Vision	
Assessment of visual fields, vision, diplopia	Field cut Double vision New blindness None
Aphasia	
Repeat and name two objects	Expressive Receptive
Open and close eyes and fist	Mixed None
Neglect	
Gaze preference, tactile or spatial neglect	Forced gaze or inability to track to one side Unable to feel both sides at the same time or unable to identify own arm Ignores one side None
VAN+, motor involvement plus any VAN.	
VAN+, 100% sensitivity, 90% specificity, 0.0 negative likelihood ratio for large vessel occlusion.	

allowing application in air- and ground-based transport.<sup>73</sup> Disadvantages include a requirement for intensive personnel training, with direct physician supervision either physically or electronically, and the limitations imposed by cranial bony imaging windows and the inability to diagnose hemorrhage.

Improvements in diagnosis and treatment have been achieved through mobile stroke evaluation/treatment units (STEMO (stroke emergency mobile), MSU (mobile stroke unit), MSTU (mobile stroke treatment unit))<sup>75</sup> incorporating portable CT scanners, point of care testing, medication delivery, and direct or remote neurological expertise in a customized ambulance, first in Germany,<sup>76</sup> subsequently in several centers in the USA.<sup>77–79</sup> This enables accurate diagnosis in the field, and medical therapy to be delivered to higher percentages of patients at earlier times. In the German experience, higher rates of IV t-PA administration (32% vs 22%,  $p < 0.001$ ), higher

treatment rates within 1 hour of symptom onset (31% vs 4.9%,  $p < 0.01$ ), and an improved likelihood of treated patients being discharged home (adjusted OR=1.93,  $p = 0.02$ ) were achieved with the use of STEMO compared with standard, conventional care.<sup>80</sup> Early experience with MSU in Houston demonstrated reduced times from stroke onset to groin access (average 171 min) compared with published time metrics in patients receiving endovascular care after MSTU transport.<sup>78</sup> A similar experience in Cleveland showed substantial reduction in time metrics (door to CT 12 min vs 32 min, CT to IA therapy 82 min vs 165 min) for MSTU-transported patients undergoing ultimate endovascular treatment compared with those who underwent such treatment after standard EMS transport.<sup>81</sup> These efficiency gains highlight the time savings associated with MSTU evaluation/treatment, which should translate to improved outcomes. Economic evaluation suggested that MSUs are cost-efficient when used in an operating distance of greater than 9.99 miles and a population density of 202 inhabitants per square mile or greater.<sup>82</sup> Whether the promise of these mobile units will be fulfilled on a larger scale remains to be seen.

### Prehospital notification

Prehospital notification of transport is an important efficiency improvement strategy. EMS transport and prehospital notification of patients with suspected stroke reduces stroke time metrics and increases the proportion of patients receiving IV t-PA,<sup>83–87</sup> but has yet to be proved to improve patient outcomes. McKinney *et al*<sup>84</sup> found that this notification was associated with twice as many patients receiving IV t-PA. EMS transport to, or primary presentation at, stroke centers is associated with better treatment outcomes than primary presentation at community hospitals.<sup>88</sup> Once patients with suspected ELVO have been identified, important elements to include in the notification are the LKN time, hemodynamic parameters, family contact information, and anticoagulation status. Stroke networks should integrate primary and associated comprehensive center notification to maximize transfer efficiency when transfer protocols dictate initial transport of patients with suspected ELVO to centers without endovascular services. This PSC/CSC pair integration<sup>8</sup> would allow the comprehensive center to prepare for patient arrival and facilitate early communication between primary and comprehensive centers. The effect of prehospital notification may be magnified for ELVO stroke given the non-linear decay in treatment effect. The complex endovascular team, including radiologic technologists, neurointerventionalists, anesthesiologists, and trained nursing staff, takes some time to assemble it, particularly after hours when the team has to reach the treating center.

### ELVO stroke transport

Prehospital delays can affect outcomes by causing endovascular treatment delays, and by making patients with ELVO ineligible for treatment according to the length of time or other defined clinical criteria. The treatment effect of mechanical embolectomy for patients with ELVO is substantial, with one of three to four patients benefiting in several large trials.<sup>2–4</sup> In a Spanish study of futile transfer between facilities for endovascular therapy with a median transfer time of 60 min, 32% of the patients excluded from endovascular treatment were found to be ineligible at the receiving facility based upon the imaging progression of stroke.<sup>89</sup> EMS transport protocols for patients with ELVO, based on best evidence, must ensure equitable population access to this effective therapy. These protocols should consider patient preference, time from symptom onset

or LKN, overall clinical stability, transport distance, stroke severity/ELVO probability, and the capabilities of regional centers.<sup>35 90</sup>

The primary transport requirement for the patient with suspected ELVO is prompt endovascular treatment. Ideally, the secondary transfer of patients between centers before therapy should be avoided. Protocols should only diverge from comprehensive, endovascular-capable centers for closer centers in the event of unstable patients, hypoglycemia or perhaps IV t-PA eligible patients who might miss their treatment opportunity at the closer facility by being transported directly to a more distant comprehensive center. These transport differences represent major and potentially catastrophic sources of delay for the patient with ELVO, with a median delay of 104 min in one urban study having a relatively short median hospital transfer distance of 14.7 miles between the primary and comprehensive centers.<sup>91</sup> The odds of receiving endovascular treatment were reduced in that study by 2.5% for each minute of transfer delay. In another study,<sup>92</sup> transfer times to a single comprehensive center were consistently longer than expected driving times, highlighting these delays. Formal studies of stroke systems of care interventions relating to ELVO are being organized and should inform recommendations in an area of rapid development.

Although stroke practitioners disagree about the priority of transport,<sup>93</sup> protocols prioritizing direct transport of patients with suspected ELVO to facilities with endovascular services are used and becoming more refined. They include bypassing closer facilities without endovascular services if transport time differences are not too great. The optimal transport time difference between centers is not firmly established, but it is generally accepted that a bypass of closer facilities should be considered if the transport time difference is 15–20 min for higher level stroke centers. This time has been recommended partially based upon the time required to mobilize the acute stroke team at the receiving hospital,<sup>35</sup> particularly when no in-house team is available. This seems reasonable for IV t-PA eligible patients with suspected ELVO given the benefit afforded them by the receipt of IV t-PA as early as possible.<sup>94</sup> Bypass of closer facilities for more capable distant facilities has been advocated for transport time differences as long as 30 min in cases of major trauma or ST-segment elevation myocardial infarction (STEMI).<sup>95 96</sup> For patients with suspected ELVO who are ineligible for IV t-PA on clinical or time grounds (last known well >3.5 hours), strong consideration for direct transport to a comprehensive center with endovascular capability should be given, regardless of transport time differences. Implementation of statewide protocols for direct transport of patients with suspected ELVO to facilities with endovascular services is currently occurring locally.<sup>97</sup>

Bypassing centers incapable of providing endovascular services has been evaluated for acute coronary syndromes with STEMI. In North Carolina, the RACE program encouraging bypass of non-percutaneous coronary intervention (PCI)-capable centers, even though they were closer, allowed evaluation of performance through a retrospective registry review published in 2013 in *Circulation*.<sup>98</sup> They evaluated bypass of closer non-PCI capable facilities for direct transport to PCI-capable facilities and reported statistically significant reductions in time to PCI and better adherence to time guidelines for PCI in those patients taken directly to PCI centers. Trends for better outcomes were also seen, although not statistically significant after adjusting for cases of cardiac arrest. In addition, better outcomes have been demonstrated in patients with STEMI randomized to

be transferred for PCI versus local thrombolysis at non-PCI capable facilities.<sup>99</sup>

For patients with suspected ELVO transported to primary facilities without endovascular services, rapid stabilization, evaluation, and transfer maximize the opportunity for effective endovascular treatment at the receiving comprehensive facility. Identification and labeling of the patient with suspected ELVO by prehospital screening may focus the entire team on time and facilitation of transfer. Although primary facilities should be able to perform vascular evaluation non-invasively to identify LVO,<sup>8</sup> this testing is not mandatory if it cannot be performed and interpreted expeditiously. Indeed, advanced imaging at the primary facility before transfer may contribute to delays (111 min, IQR 73–179, compared with 54 min, IQR 32–76, for non-contrast CT alone;  $p < 0.001$ ).<sup>100</sup> Imaging should be expeditious and directed towards excluding hemorrhage and evaluating candidacy for IV t-PA. For patients with suspected ELVO, protocols expediting evaluation may include performing imaging before formal emergency room evaluation based upon prehospital screening. Strategies to improve efficiency should involve ‘drip and ship’ paradigms<sup>101</sup> to allow t-PA infusion immediately before or during transport to endovascular-capable centers,<sup>102</sup> this requires tight coordination with EMS teams.

Time metrics for process improvement in ELVO stroke have assumed importance, many of which are correlated with outcome. Since significant delays can be introduced in the primary evaluation hospital before transfer to an endovascular-capable facility, a time metric to assess and improve delays seems helpful. For STEMI, emergency department (ED) arrival to ED discharge—‘door in–door out’ times<sup>103</sup>—at the primary, non-PCI capable facility as well as ‘door 1–door 2’ times<sup>104</sup> between hospitals, have been proposed as metrics to assess the interhospital transfer processes. However, the usefulness of these measures in stroke systems of care has been questioned since <50% of the continuum of care from patient presentation to reperfusion is accounted for by these metrics.

The ‘picture to puncture’ (P2P) metric assessing time from primary hospital CT to groin puncture at the recipient comprehensive center has been advanced as a better metric, encompassing about 74% of the continuum of processes involved in transfers of patients, as well as distance.<sup>100</sup> Outside transfers were shown to have substantially longer P2P times (205 min, IQR 162–274 compared with 89 min, IQR 70–119;  $p < 0.001$ ) than those for patients with ELVO transported directly to a comprehensive facility. This longer time correlated with worse Alberta Stroke Program Early CT (ASPECT) scores on receiving hospital CT and worse clinical outcomes. The P2P time was also independently correlated with outcome (OR=0.994, 95% CI 0.990 to 0.999;  $p = 0.009$ ).<sup>100</sup> For every 10 min delay in P2P, there was a 6% decrease in the probability of a good outcome. A time metric proposed as a goal for P2P is <90 min.<sup>8 100</sup>

Methods of transport from the field or primary facility to comprehensive facilities differ based upon distance and rural versus urban settings. Air transport shortens transport time,<sup>105</sup> improves survival in patients with trauma,<sup>106</sup> and may lower the incidence of infarction, stroke, or death in patients with STEMI.<sup>107</sup> Similar benefits to patients with stroke include providing access to IV t-PA or interventional stroke care in rural settings.<sup>108 109</sup> Urban areas with airspace restrictions, heavy road traffic, and multiple geographically concentrated facilities create a different set of transport challenges. In this setting with an increased density of comprehensive endovascular-capable facilities, strategies requiring transport of interventional teams to multiple different facilities may be warranted (Fifi J, *et al.* SNIS

presentation July 2015, San Francisco, California, USA). Regardless of the transport mechanism, EMS providers must be given tools for delineation of facility competence, such as certification status and license to transport across state lines or outside of established networks to the most appropriate facilities.

### Interdisciplinary communication

Interdisciplinary communication between members of stroke networks is vitally important. Electronic communication brings expertise to the field through 'telestroke'—that is, telemedical outreach for acute stroke evaluation and management.<sup>110</sup> Additionally, mobile technology aids can be used to facilitate communication between caregivers. Efforts should be made in the organization and delivery of care, and in the communication of outcome to remote members of the care team to stimulate team cohesion. Since efficient acute treatment of patients with ELVO stroke may involve transport outside of home communities and care networks, return home at appropriate times after treatment may facilitate recovery and foster partnerships.

### SUMMARY AND RECOMMENDATIONS

1. Patients with ELVO with anterior circulation stroke secondary to occlusion of the internal carotid artery or M1 segment of the MCA and a corresponding clinical deficit benefit from efficient endovascular embolectomy. Embolectomy needs to be *performed as rapidly as possible* for the greatest clinical benefit, and is best when performed within 6 hours from onset of symptoms.  
(AHA class I, level of evidence A)
2. EMS systems within stroke systems of care should have pre-hospital *protocols specific to patients with a high likelihood of ELVO*, including identification, transport prioritization, and efficient delivery to comprehensive centers capable of endovascular treatment to *minimize treatment delays* that can profoundly affect outcome.  
(AHA class I, level of evidence A)
  - A. IDENTIFICATION. EMS systems should adopt the use of a *field stroke severity scale* associated with ELVO (such as 3I-SS, LAMS, RACE, CPSSS, VAN) to identify patients with suspected ELVO and prioritize transport. Further experience and study to determine the optimal field scale should continue.  
(AHA class I, level of evidence B)
  - B. IDENTIFICATION/POINT OF CARE TREATMENT. *Transcranial ultrasound* is a diagnostic and therapeutic method that may identify ELVO in the field and facilitate definitive treatment through prehospital thrombus 'conditioning' or neuroprotection. This strategy will benefit from further experience and study.  
(AHA class II, level of evidence C)
  - C. IDENTIFICATION/POINT OF CARE TREATMENT. The *mobile stroke unit* (STEMO, MSU, MSTU) strategy reduces transport delays and times to treatment for patients with ELVO and may improve outcomes. This strategy will benefit from further experience and study.  
(AHA class II, level of evidence C)
  - D. TRANSPORT PRIORITIZATION. Patients with suspected ELVO based on field testing (3I-SS $\geq$ 4, LAMS $\geq$ 4, RACE $\geq$ 5, CPSSS $\geq$ 2, or VAN positive) who are *eligible for IV t-PA* (LKN <3.5 hours) should be considered for *direct* transport to a comprehensive center with endovascular treatment capability, bypassing closer facilities without this capability, if the transport difference to the

closer facility is less than or equal to 15–30 min.

(AHA class I, level of evidence B)

- E. TRANSPORT PRIORITIZATION. Patients with suspected ELVO based on field testing (3I-SS $\geq$ 4, LAMS $\geq$ 4, RACE $\geq$ 5, CPSSS $\geq$ 2, or VAN positive) who are *ineligible for IV t-PA* (LKN >3.5 hours) should be *transported directly* to a comprehensive center with endovascular treatment capability, bypassing closer facilities without this capability, if feasible.  
(AHA class I, level of evidence C)
- F. EFFICIENT DELIVERY. Patients with suspected ELVO primarily transported to non-endovascular-capable centers owing to large transport time differences or clinical instability should undergo expeditious evaluation and treatment, including non-contrast head CT, possible vessel imaging immediately upon arrival, and administration of IV t-PA (if eligible). Vessel imaging should not delay patient transfer. Rapid transfer to a comprehensive center with endovascular capability to minimize inter-hospital transfer delays is a priority. A metric proposed to assess transfer processes is the picture to puncture (P2P) time. A P2P of <90 min should be a goal.  
(AHA class I, level of evidence C)

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