

# Recent developments in pre-hospital and in-hospital triage for endovascular stroke treatment

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## ABSTRACT

Triage describes the assignment of resources based on where they can be best used, are most needed, or are most likely to achieve success. Triage is of particular importance in time-critical conditions such as acute ischemic stroke. In this setting, one of the goals of triage is to minimize the delay to endovascular thrombectomy (EVT), without delaying intravenous thrombolysis or other time-critical treatments including patients who cannot benefit from EVT. EVT triage is highly context-specific, and depends on availability of financial resources, staff resources, local infrastructure, and geography. Furthermore, the EVT triage landscape is constantly changing, as EVT indications evolve and new neuroimaging methods, EVT technologies, and adjunctive medical treatments are developed and refined. This review provides an overview of recent developments in EVT triage at both the pre-hospital and in-hospital stages. We discuss pre-hospital large vessel occlusion detection tools, transport paradigms, in-hospital workflows, acute stroke neuroimaging protocols, and angiography suite workflows. The most important factor in EVT triage, however, is teamwork. Irrespective of any new technology, EVT triage will only reach optimal performance if all team members, including paramedics, nurses, technologists, emergency physicians, neurologists, radiologists, neurosurgeons, and anesthesiologists, are involved and engaged. Thus, building sustainable relationships through continuous efforts and hands-on training forms an integral part in ensuring rapid and efficient EVT triage.

## INTRODUCTION

In medicine, the term ‘triage’ describes the assignment of resources based on where they can be best used, are most needed, or are most likely to achieve success.<sup>1</sup> Rapid and accurate patient triage and transport is of particular importance in time-critical conditions such as acute ischemic stroke (AIS). The average AIS patient with a large vessel occlusion (LVO) loses 1.9 million neurons per minute,<sup>2</sup> and every 30 min delay in recanalization decreases the chance of good functional outcome by approximately 10%.<sup>3</sup> Although endovascular thrombectomy (EVT) constitutes a highly effective treatment for AIS, its benefit decreases rapidly as time to treatment increases.<sup>4</sup> Thus, improving patient triage and transport is central to improving patient outcomes.

The goal of EVT triage is to direct AIS patients who can benefit from EVT to an EVT-capable hospital as fast as possible. While there are excellent policy statements outlining general guiding principles for the establishment of stroke systems of care,<sup>5,6</sup> there is likely no universal ‘right way’ of triaging patients for EVT, since EVT triage is highly context-specific, and depends on the local infrastructure and geography (eg, widespread rural geography with low hospital density vs urban area with high hospital density).<sup>7</sup> Furthermore, although financial and staff resources should ideally not influence EVT triage, in reality they often do. Regardless of the triage paradigm, optimization of its diagnostic accuracy and speed are central to successful performance.

In this review, we discuss key principles in evaluating and optimizing EVT triage and summarize recent promising developments and novel technologies that have the potential to improve both triage accuracy and speed. We performed a scoping review on MEDLINE/PubMed and Ovid using the search terms ‘stroke’, ‘ischemic stroke’, ‘cerebrovascular accident’, ‘mechanical thrombectomy’, ‘endovascular procedures’, ‘endovascular surgery’, ‘pre-hospital’, ‘triage’, ‘emergency medical services’, ‘emergency health service’, and ‘neuroimaging’, with a focus on randomized trials and large, prospective cohort studies. After outlining general principles on how to measure EVT triage performance and the importance thereof, we review different strategies for detecting LVO candidates in the field, measures to optimize communication between pre- and in-hospital teams such as pre-notification tools, different stroke transport paradigms and evidence behind them, and lastly strategies to optimize in-hospital workflows including stroke imaging paradigms.

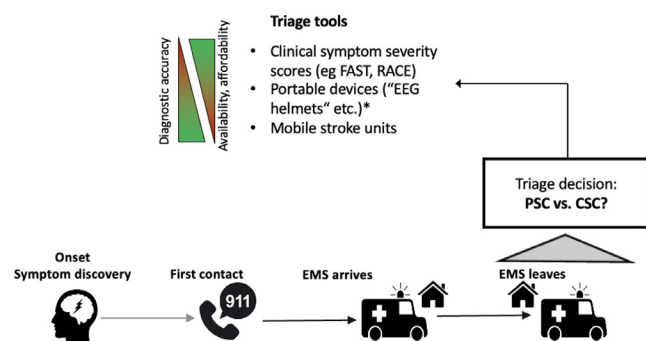
## PRE-HOSPITAL TRIAGE: DETECTING EVT CANDIDATES IN THE FIELD

After symptom onset, the initial call for help, and the arrival of the emergency medical services (EMS) on the scene, the EMS team assesses the patient. This assessment forms the basis for the triage decision and determines whether the patient is directed to the closest primary stroke center (PSC), capable of administering intravenous (IV) thrombolysis (figure 1). Several tools are available that can aid the EMS team in this decision, ranging from simple



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**Figure 1** Pre-hospital triage from symptom onset to the initial triage decision in a ground-bound transport scenario. After symptom onset and symptom discovery, the initial call for help is initiated, either by the patient themselves or a witness. Upon ambulance arrival, the emergency medical services (EMS) team assesses the patient and, in case of suspected acute ischemic stroke, makes a triage decision—that is, the team decides whether they will target the nearest primary stroke center (PSC) or the nearest comprehensive stroke center (CSC). Numerous triage tools can aid the EMS team in making this decision, and differ in their costs, availability, ease of use and diagnostic accuracy. \*See table 1 for a detailed overview. EEG, electroencephalography; FAST, Face-Arms-Speech-Time; RACE, Rapid Arterial Occlusion Evaluation.

clinical stroke severity scales to highly specialized mobile stroke units (table 1)

### Clinical stroke severity scales

Clinical stroke severity scales such as Face-Arm-Speech-Time (FAST) or Rapid Arterial Occlusion Evaluation (RACE) are the simplest pre-hospital triage tools as they do not require any specialized equipment and entail no added cost to the system beyond basic training of personnel,<sup>8</sup> while at the same time improving pre-hospital management and shortening EVT preparation times.<sup>9</sup> While some pre-hospital stroke severity scales are dichotomous,<sup>10</sup> most provide a score in the form of points rather than a binary (LVO yes/no) output, which is more complex than a dichotomous output but allows for different cut-off choices with varying sensitivity and specificity, which can be advantageous in settings in which one has to be optimized over the other. For a detailed overview of the performance metrics of the various stroke severity scales, we refer the reader to the pre-hospital triage of patients with suspected stroke (PRESTO) study,<sup>11</sup> in which scales detected LVO in the anterior circulation with acceptable accuracy. RACE, G-FAST (Gaze-Face-Arm-Speech-Time) and CG-FAST (Conveniently-Grasped Field Assessment Stroke Triage) performed best, with an accuracy similar to clinician-assessed NIHSS (National Institutes of Health Stroke Scale).<sup>11</sup> That being said, the performance of all pre-hospital scales varies substantially across the spectrum of deficit severity. They generally perform best at both ends of the severity spectrum, which is of limited value since, in these patients, paramedics may often be able to make the diagnosis purely based on their clinical experience.<sup>7</sup> In patients with intermediate symptom severity, where diagnostic uncertainty is greatest, performance of clinical symptom severity scales is poorest. In some situations, certain pre-hospital triage scales may even be misleading and, in extreme cases, may sway an EMS team from the correct diagnosis.<sup>12</sup> Furthermore, since they purely rely on symptom severity (having been derived from the NIHSS), clinical stroke severity scales will naturally fail to detect LVO strokes with mild symptoms, and their performance in medium vessel occlusion (MeVO)

strokes is also limited. This is particularly noteworthy given that several ongoing trials aim to expand EVT indications to these two patient subgroups.<sup>13 14</sup> Perhaps even more important than the performance of a particular stroke scale itself is the need for the local EMS personnel to be familiar with it and comfortable using it. Several apps that have been designed to aid EMS specifically with pre-hospital stroke severity assessment and risk stratification can help to facilitate this task.<sup>15</sup>

### Mobile stroke units

Mobile stroke units (MSUs)—that is, ambulances that are equipped with CT (and often CT angiography) capabilities—are arguably the most sophisticated and specialized pre-hospital triage tool. By ruling out intracranial hemorrhage using on-board non-contrast head CT, they allow for administration of IV thrombolysis in the field, and, if on-board, CT angiography (CTA) capabilities are available so LVOs and MeVOs can be diagnosed with high certainty, meaning EVT candidates are accurately identified and directed to the nearest EVT-capable hospital. The North American BEST-MSU and German B-PROUD trials have shown that the use of MSUs in pre-hospital stroke triage leads to improved functional outcomes.<sup>16 17</sup> The main disadvantage of MSUs is their high cost. For example, in the USA one MSU had annual operating costs of approximately \$1.2 million and initial set-up costs can range between \$600 000 to \$1 million.<sup>18</sup> However, some studies support their cost effectiveness, and these added costs may very well meet the willingness-to-pay threshold for certain healthcare systems.<sup>19–21</sup> The usefulness of MSUs is also highly dependent on local geography and the distance between the MSU base, the patient location, and the hospital location. In a recent modeling study, MSU utilization was most beneficial when low dispatch thresholds were used and at a travel time to the MSU between 180–200 min.<sup>22</sup> That being said, in the BEST-MSU trial, MSUs were shown to be beneficial when travel times were shorter as well.<sup>17</sup> Some regions may benefit from creative combinations of MSU and conventional ambulance resources to optimize pre-hospital triage and treatment times.<sup>23 24</sup>

### Emerging, alternative pre-hospital triage devices

Several smaller, portable pre-hospital triage devices are currently under development, including microwave-based, ultrasound-based, and electroencephalography (EEG)-based tools (table 1). In theory, these would be more practical and affordable than MSUs, as they could be installed in regular ambulances. Needless to say, each of those tools has its own set of challenges. Performing transcranial Doppler sonography is often difficult due to an insufficient acoustic window,<sup>25</sup> and EEG technologies may not be able to identify EVT candidates with mild clinical deficits, since the relative preservation of brain function in these patients may not lead to signal abnormalities that are conspicuous enough to be detected. Of note, none of these portable devices is used in clinical routine, yet they still have to prove their robustness, reliability, and usefulness in the clinical setting.

### PRE-NOTIFICATION: BRIDGING THE GAP BETWEEN THE PRE-HOSPITAL TEAM AND THE IN-HOSPITAL TEAM

Pre-notification of the in-hospital team, and particularly the angio team, for instance through a phone-call or an app, allows the in-hospital team to optimally prepare for patient arrival, for example, by preparing an EVT kit, clearing the angio suite, etc (figure 2). Pre-notification has been proven to reduce treatment delays, especially during off-hours, when the angio team is not

**Table 1** Tools and technologies for the pre-hospital triage of acute ischemic stroke

Pre-hospital tool	Potential indication	Examples	Advantages	Disadvantages
Clinical prediction scales	Identify patients who are likely to have large vessel occlusion based on clinical symptoms	Los Angeles Motor Scale (LAMS), Rapid Arterial occlusion Evaluation (RACE) scale	<ul style="list-style-type: none"> <li>Simple, fast, easy to use with brief training</li> <li>Reasonably high specificity for LVO for instruments like LAMS/RACE</li> </ul>	<ul style="list-style-type: none"> <li>Overall limited sensitivity for LVO, risk of missing out many patients who stand to benefit from EVT</li> <li>Stroke represents only a minority of EMS calls; continuous maintenance of training may be required</li> </ul>
Mobile stroke units (MSU), on-board CT scan	Distinguish ischemic stroke from hemorrhagic stroke by ambulance-based neuroimaging	Mostly in Germany and the USA	<ul style="list-style-type: none"> <li>The only system that currently allows safe pre-hospital thrombolysis by definitively ruling out hemorrhage</li> <li>Can detect LVO with on-board angiography<sup>90 91</sup></li> </ul>	<ul style="list-style-type: none"> <li>Expensive investment in equipment and personnel (on-board CT tech and physician or similar provider for giving thrombolysis)</li> </ul>
Transcranial Doppler ultrasonography (TCD)	Identifying LVO via high vessel velocities and emboli detection	Lucid Robotic System	<ul style="list-style-type: none"> <li>Sensitivity 91% and specificity 85% for identifying LVO per conference presentation<sup>92</sup></li> </ul>	<ul style="list-style-type: none"> <li>Cumbersome</li> <li>Operator-dependent when not robotic</li> <li>Some patients do not have an adequate bone window</li> </ul>
Electroencephalography (EEG)	Identify major strokes by confirming substantial loss of neuronal activity ipsilaterally	AlphaStroke, BrainScope One	<ul style="list-style-type: none"> <li>Amenable to rapid quantitative interpretation at point-of-care</li> <li>Brainscope studied in traumatic brain injury with 92% sensitivity for abnormal CT<sup>93</sup></li> </ul>	<ul style="list-style-type: none"> <li>Can have high background noise especially in an ambulance</li> <li>Non-specific findings are common in various pathologies; Brainscope specificity 51% for abnormal CT in TBI<sup>93</sup></li> </ul>
Brain accelerometry	Identifying LVO <sup>94</sup>	BrainPulse	<ul style="list-style-type: none"> <li>Has been studied in vasospasm (81% sensitivity) and traumatic brain injury<sup>95</sup></li> </ul>	<ul style="list-style-type: none"> <li>High background noise may interfere with detection of LVO signal</li> </ul>
Microwaves	Rule out hemorrhage	EMTensor, EMvision, Strokefinder	<ul style="list-style-type: none"> <li>Useful in ruling out large hemorrhagic strokes<sup>96</sup></li> </ul>	<ul style="list-style-type: none"> <li>Cannot rule out small bleeds</li> <li>Application limited by poor penetration of microwaves into brain</li> </ul>
Near-infrared spectroscopy	Identifying severe stroke by visualizing brain tissue oxygenation	Infrascanner 2000	<ul style="list-style-type: none"> <li>Can detect large ischemia, hemorrhage</li> <li>Sensitivity of 88% and specificity of 91% for detecting hematomas &gt;3.5 mL within 2.5 cm of the brain surface<sup>97</sup></li> </ul>	<ul style="list-style-type: none"> <li>Limited field or depth of penetration</li> </ul>
Radiofrequency pulses	Potential to identify hemorrhage	Sense Diagnostics	<ul style="list-style-type: none"> <li>Can detect ICH expansion (pre-clinical studies)<sup>98 99</sup></li> </ul>	<ul style="list-style-type: none"> <li>Maturing technology, unclear application</li> </ul>
Volumetric impedance phase-shift spectroscopy (VIPS)	Identify severe stroke by detecting small changes and asymmetries in electrical properties	Cerebrotech Visor	<ul style="list-style-type: none"> <li>Wireless visor on the head</li> <li>Sensitivity 93% and specificity 87% to identify severe stroke<sup>100</sup> (broadly defined as LVO or NIHSS &gt;6 or ICH &gt;60 mL or large established stroke)</li> </ul>	<ul style="list-style-type: none"> <li>Data have come from a derivation study to create the VIPS selection algorithm—validation is required in pre-hospital settings</li> <li>Technology relies on sending/receiving radio waves which can be modified by implants like plates/screws or metallic hair extensions</li> </ul>

EMS, emergency medical services; EVT, endovascular thrombectomy; ICH, intracerebral hemorrhage; LVO, large vessel occlusion; NIHSS, National Institutes of Health Stroke Scale; TBI, traumatic brain injury.

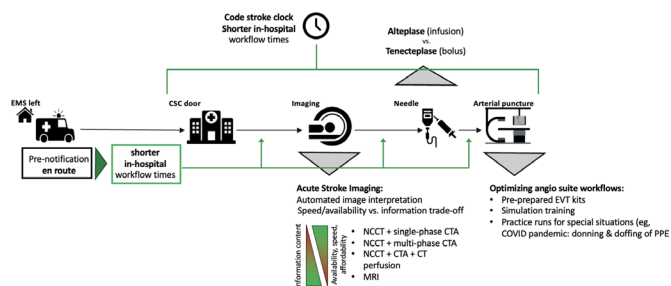
in-house and has to travel to the hospital.<sup>26</sup> This step is a critical component of integrated systems of stroke care, permitting a coordinated approach to transport and treatment of stroke patients; such integration was associated with a sustained decrease in in-hospital stroke mortality in Canada.<sup>27</sup> However, a large North American registry study and a recent international survey suggest that pre-notification tools are only used in 60–70% of EVT-capable hospitals, with large regional variations,<sup>28 29</sup> highlighting substantial potential for improvement. By using novel technologies such as natural language processing algorithms,<sup>30</sup> it may soon be possible to fully automate pre-notification, thereby obviating the need for manual texting/calling, which may further facilitate adoption of pre-notification in clinical practice.

### TRANSPORT PARADIGMS: BALANCING THE TIME TO IV THROMBOLYSIS VERSUS TIME TO EVT

One of the main goals of pre-hospital EVT triage, besides recognizing AIS, is to direct patients who are likely to be EVT candidates to an EVT and IV thrombolysis-capable hospital (comprehensive stroke center, CSC) to minimize time to EVT and

prevent further infarct progression.<sup>31</sup> At the same time, patients who are unlikely to be EVT candidates should be directed to the closest PSC, to minimize time to IV thrombolysis (ie, onset to needle time). With regard to IV thrombolysis at the CSC in EVT candidates, several recently published randomized controlled trials<sup>32–36</sup> have investigated the question whether IV thrombolysis could be forgone in EVT candidates presenting directly to the CSC; overall, the current evidence from these trials does not support withholding IV thrombolysis in these patients, although there are some subgroups in which the added benefit of IV thrombolysis should be further investigated. The only randomized controlled trial on the drip-and-ship versus mother-ship transport question (Direct Transfer to an Endovascular Center Compared with Transfer to the Closest Stroke Center in Acute Stroke Patients With Suspected LVO—RACECAT) found no difference in outcomes between the two transport paradigms, although the very well-organized stroke transfer system in which the trial was conducted (with its short door-in-door-out times in the participating PSCs) may not be representative for PSCs in other jurisdictions.<sup>37</sup> Besides these two traditional transport





**Figure 2** Pre- and in-hospital triage from the time of emergency medical services (EMS) leaving the scene to arterial puncture in a direct-to-mothership scenario. Once EMS leaves the scene, a pre-notification is sent to the comprehensive stroke center, so that the in-hospital team can get prepared before patient arrival (eg, during the night the angio team may have to travel to the hospital, the angio suite can be cleared in advance, etc). This helps to shorten in-hospital workflows. A code stroke clock keeps track of the overall in-hospital workflow time, serves as an internal quality control tool, and identifies potential time delays that can be avoided. Various imaging protocols can be used for treatment decision-making, ranging from simple protocols that include only non-contrast CT (NCCT) of the head and CT angiography (CTA) to more complex protocols that include CT perfusion imaging or MR imaging (MRI). While information content is greater in the latter, availability and speed are generally better in the former. In case of intravenous thrombolysis, either alteplase, which is administered as an infusion over 1 hour, or tenecteplase, which can be administered as a bolus, is given. In the angio suite, workflows can be streamlined by using pre-prepared endovascular thrombectomy (EVT) kits that shorten preparation time by avoiding assembling the required EVT materials. Simulation training and practice runs can improve workflows as well, especially in exceptional circumstances such as the COVID-19 pandemic, in which donning and doffing of personal protection equipment (PPE) and airway management add an additional layer of complexity to patient management in the angio suite.

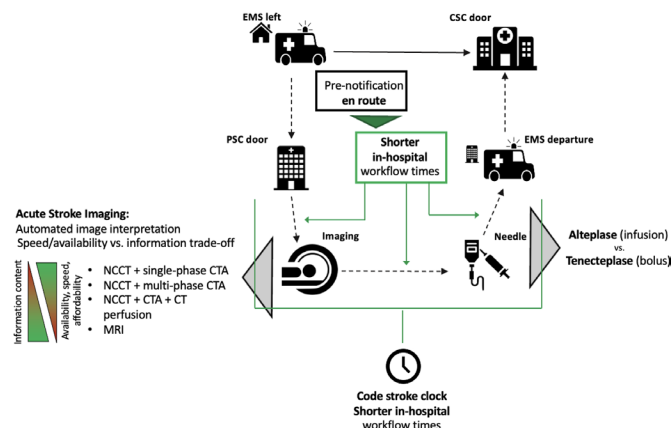
paradigms, several additional innovative transport paradigms have emerged over the last years.

As noted previously, MSUs allow for IV thrombolysis in the field, and, if equipped with CTA capabilities, for accurate identification of LVO stroke, which has been shown to improve functional outcomes.<sup>16 17</sup> Use of mobile interventional stroke teams, in which the angio team travels from the mothership to a smaller thrombectomy-capable hospital closer to the patient, are another promising alternative that has been shown to reduce workflow times and improve short-term neurological outcomes, with a trend towards better long-term functional outcomes.<sup>38</sup>

Since the local hospital landscape and transport resources as well as the efficacy of in-hospital teams are highly variable, the results of the aforementioned studies are unique to the environment in which they were conducted and cannot necessarily be generalized to other jurisdictions. Each local environment must find their own optimal transport paradigm based on local workflow times and available resources. Conditional probability modeling allows systems to take local geography and workflow efficacy into account while simulating different transport paradigms, and can aid in determining the best transport paradigm for a given environment or scenario.<sup>22 39</sup>

## IN-HOSPITAL PHASE: STREAMLINING WORKFLOWS AND REDUCING THE COGNITIVE LOAD OF THE TEAM

The potential for time-savings in the in-hospital phase is substantial.<sup>29</sup> As such, several concepts have been developed



**Figure 3** Pre- and in-hospital triage from the time of emergency medical services (EMS) leaving the scene to arterial puncture in a drip-and-ship scenario. Once EMS leaves the scene, a pre-notification is sent to the primary stroke center (PSC), so that the in-hospital team can get prepared before patient arrival (eg, during the night, the stroke neurology attending on call may have to travel to the hospital). This helps to shorten in-hospital workflows. A code stroke clock keeps track of the overall in-hospital workflow time, serves as an internal quality control tool, and identifies potential time delays that can be avoided. Various imaging protocols can be used for treatment decision-making, ranging from simple protocols that include only non-contrast CT (NCCT) of the head and CT angiography (CTA) to more complex protocols that include CT perfusion imaging or MR imaging (MRI). While information content is greater in the latter, availability and speed are generally better in the former. Especially in smaller PSCs with low case volumes, automated image interpretation could be of great help to guide less experienced readers through the imaging findings. In case of intravenous (IV) thrombolysis, either alteplase, which is administered as an infusion over 1 hour, or tenecteplase, which can be administered as a bolus, is given. The latter is more practical to handle and could substantially shorten door-in-door-out times in cases in which one wants to avoid transporting the patient in the ambulance with a running IV thrombolysis infusion. CSC, comprehensive stroke center.

to streamline in-hospital workflows, to shorten the time from patient arrival to reperfusion as much as possible.

## Rapid patient assessment and use of a 'code stroke clock'

On patient arrival, only absolutely necessary procedures should be performed before EVT. In many hospitals, EVT candidates still undergo chest x-rays or Foley catheter insertion before EVT, which is largely unnecessary and time-consuming.<sup>29</sup> The use of a 'code stroke clock'—a clock that measures workflow times—is a simple and easy-to-implement measure that increases the time awareness of the in-hospital team, and thereby shortens workflow times<sup>40 41</sup> (figures 2 and 3).

## Eliminating unnecessary workflow steps in the in-hospital pre-EVT phase

Saving time in the in-hospital phase can often be achieved by simple measures, such as eliminating unnecessary workflow steps. In a survey study among 248 stroke physicians and neuro-interventionalists, electrocardiograms were performed in 26% and even chest x rays were taken in 4% before EVT.<sup>29</sup> By simply foregoing or postponing those procedures to the post-EVT time period, time could be saved. Taking the patient to the CT scanner on the EMS stretcher or administering IV thrombolysis

in the CT scanner suite after the non-contrast head CT are other simple but effective measures to improve workflow times.<sup>42</sup>

### Direct-to-angio paradigms

In direct-to-angio workflows, the patient is transported directly to the angio suite for on-table imaging, rather than stopping by the CT/MR scanner for conventional cross-sectional imaging. A recent randomized controlled trial (Direct to Angiography Suite Without Stopping for CT Imaging for Patients With Acute Stroke—ANGIOCAT)<sup>43</sup> suggested that direct-to-angio workflows may decrease in-hospital workflow times and improve clinical outcomes when using a direct-to-angio paradigm.<sup>43</sup> However, another randomized trial was stopped early because of substantial delays in time to imaging and subsequently time to IV thrombolysis, in the direct-to-angio arm.<sup>44</sup> The benefit of direct-to-angio paradigms therefore still must be proven; they could constitute a promising alternative mainly for large centers with sufficient staff resources, an all-time available angio suite, and 24/7 in-house tech coverage.

### Translational simulation training

Simulation team training is another simple but highly effective tool to improve the speed of patient assessment and concerted team-work.<sup>45</sup> It has been widely adopted for health professional education and traditionally for procedural task training, communication and teamwork. Recently, in situ simulation has put the simulation into the clinical environment, facilitating transfer of knowledge and skills into real-world practice. As a relatively new concept, translational simulation allows for quality improvement by linking simulation training to identify latent quality threats with health service priorities and patient outcomes.<sup>46</sup> This is particularly helpful when the team has to adapt to new situations and practice new workflow steps, such as donning and doffing personal protection equipment and disposal of contaminated material during 'protected code stroke' protocols during the COVID-19 pandemic.<sup>47 48</sup>

### Acute stroke imaging protocols

The overarching goal in acute ischemic stroke imaging is to obtain the information that is needed for EVT decision-making as fast as possible, with minimal delays between image acquisition and interventional team notification and treatment planning.<sup>49</sup> No time should be lost by obtaining additional imaging that is not necessary to answer these questions. Most centers use CT-based imaging protocols due to the greater availability and affordability of CT compared with MRI, the relative absence of contraindications to CT in the acute stroke setting, and the faster image acquisition time with less sensitivity to motion.

At a bare minimum, non-contrast head CT is needed to rule out intracranial hemorrhage and roughly assess the extent of ischemic damage. CTA allows for visualization of an EVT target occlusion (LVO or MeVO) and visualizes the cervical vasculature and aortic arch, which allows for appropriate choice of EVT devices. Multi-phase CTA has some benefits over conventional single-phase CTA, as it improves occlusion detection, particularly for MeVOs, which are increasingly treated with EVT, and allows for a more accurate evaluation of collateral blood supply in the ischemic territory.<sup>50–52</sup>

Although for late time window patients (6–24 hours from last known well), current guidelines recommend using perfusion imaging for EVT patient selection; the increased accuracy of penumbra and core estimation with advanced imaging should be balanced against the additional time lost and the risk of 'decision

paralysis' due to unnecessary and potentially confusing or even misleading information. More recent data from a British national registry study<sup>53</sup> and the CLEAR study suggest that simpler imaging paradigms using non-contrast CT (NCCT) and single- or multiphase CTA may be equally capable of selecting patients for late time window EVT<sup>54–57</sup> compared with CT perfusion.<sup>58</sup>

In transfer patients, the additional question arises whether imaging should be repeated at the CSC before EVT. In a recent single center study, repeat imaging was associated with a median time delay of 20 min and rarely changed the treatment decision, suggesting that repeat imaging should not be routinely performed.<sup>59</sup>

### Automated image processing and analysis

Advanced visualization technologies and automation of image processing and analysis could be of particular value for stroke triage in smaller hospitals (eg, PSCs with limited neuroimaging experience), or hospitals in which trainees are the primary image readers off-hours. Examples for such (semi-)automated image analysis modules include automated hemorrhage detection,<sup>60 61</sup> ASPECTS (Alberta Stroke Program Early CT Score) scoring,<sup>62–65</sup> LVO detection,<sup>66 67</sup> and generation of perfusion maps from multiphase CTA.<sup>68–70</sup> These technologies could transform the acute stroke imaging workflow by (1) improving diagnostic accuracy (reduced risk of misdiagnosis), (2) timely 'rescue' of patients who have been missed in the earlier parts of the pre-hospital workflow (eg, patients with atypical or mild symptoms for whom no code stroke was initiated), and (3) linking automated detection of stroke imaging findings with instant notification of physicians and stroke teams, which could enable rapid concerted responses.

### IV thrombolysis

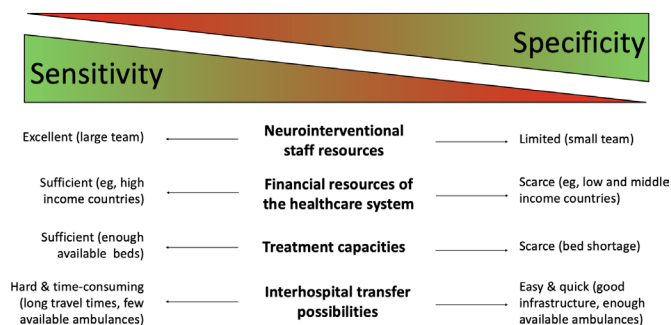
So far, combined IV thrombolysis and EVT is the standard of care for AIS with EVT target occlusion. As mentioned before, the role of IV thrombolysis in EVT candidates in the direct-to-mothership scenario has recently been questioned by several randomized controlled trials,<sup>32–36</sup> and in summary they could not show benefit of a 'dry' direct-to-EVT paradigm. The use of IV tenecteplase, which can be administered as a bolus, instead of a continuous infusion required in alteplase, could potentially decrease in-hospital workflow times, particularly in drip-and-ship settings, since the patient could be transported to the EVT-capable hospital immediately after the tenecteplase bolus has been administered without a running infusion.

### Angio suite preparation

Immediately after the in-hospital team has been informed about the arrival of a potential EVT candidate, the angio suite should be cleared and prepared for EVT. Although only used by approximately one out of two stroke teams, pre-prepared stroke kits that contain the basic equipment needed for EVT can reduce preparation time in the angio suite and thereby decrease time to arterial puncture.<sup>29 71–73</sup> The EVT procedure itself, including the equipment used, should be standardized as much as possible to reduce the cognitive load of the angio team, as this has been repeatedly shown to decrease time to reperfusion.<sup>72 73</sup>

Regarding the role of anesthesia, previous studies have shown conflicting results. While cohort studies suggest worse clinical outcomes when general anesthesia is used,<sup>74 75</sup> single-center randomized trials suggest similar outcomes.<sup>76 77</sup> In any case, suboptimal anesthesia workflow results in time delays.<sup>74</sup> Thus, the anesthesia team should be included in the pre-notification

## Sensitivity-specificity trade-off in pre-hospital triage of EVT candidates



**Figure 4** Sensitivity-specificity trade-off in pre-hospital triage of endovascular thrombectomy (EVT) candidates. Factors favoring high sensitivity at the cost of lower specificity are shown on the left. Factors favoring high specificity at the cost of lower sensitivity are shown on the right.

messages and, ideally, an anesthesiologist is available by default in the angio suite, particularly during the COVID-19 pandemic, in which intubation before EVT is often indicated in airway/breathing-compromised COVID-19 patients.<sup>47</sup>

Besides the aforementioned factors, the choice of EVT access route, devices, and techniques also influences the time from arterial puncture to reperfusion. As this article is focused on getting the right patient to the angio suite, a detailed review of EVT techniques is beyond its scope. However, irrespective of the particular technique used, simulation task training can improve operator skills and safety and thereby help to shorten the time from arterial puncture to reperfusion.<sup>45</sup>

### MEASURING EVT TRIAGE PERFORMANCE

Commonly accepted triage accuracy measures include sensitivity (the probability of transporting a patient who can benefit from EVT directly to an EVT-capable center), specificity (the probability of not transporting a patient who cannot benefit from EVT to an EVT-capable center), and the positive and negative predictive value (the proportion of true positives and true negatives among all positive and negative cases). Importantly, when considering sensitivity and specificity, one cannot be maximized without compromising on the other. In other words, increased sensitivity comes at the cost of decreased specificity and vice versa. As the goals of EVT triage are highly specific to the individual situation, the decision regarding which metrics to prioritize will also depend on specific circumstances (figure 4). In some scenarios, the priority will be to maximize specificity—that is, only treating those patients who are most likely to benefit from EVT, even at the cost of potentially withholding treatment from some patients who may be eligible. This might be the preferred strategy to gain traction for EVT adoption in a lower-resource environment such as a low- or middle-income country—the goal being to achieve success in a more highly-selected population with the highest chances of treatment effect, before support is gained to allocate resources to broader populations. In other situations, for example, in high-income countries with sufficient available resources, one may choose to maximize sensitivity—ensuring all possible EVT-eligible patients are evaluated at EVT-capable hospitals/CSCs—at the cost of potentially evaluating some patients who are ultimately deemed ineligible for EVT. Irrespective of the circumstances, EVT triage accuracy is important, and effective triage should keep time delays to EVT as short as possible in any given scenario. The speed component of EVT triage performance can in theory easily be

captured by measuring workflow times, with suggested benchmark times that have been published by the Society of Neurointerventional Surgery's standards and guidelines committee<sup>78</sup> (see online supplemental table 1) and the American Heart Association/American Stroke Association brain attack coalition.<sup>79</sup> To reliably measure workflow performance, consistent and accurate definitions of EVT triage, transport time intervals, and workflow time intervals are however needed. Although several consensus and statement papers have been published on the topic and may provide guidance,<sup>80–85</sup> no single universally accepted 'minimum reporting standard' for EVT workflows has yet emerged.

As a general principle, there is agreement that systems should aim to report broader, all-encompassing workflow times rather than fractionated time intervals to provide a more complete picture and avoid the potential for bias. Furthermore, time intervals should use automatically captured time-points (eg, DICOM (digital imaging and communications in medicine) time stamps) rather than manual data entry to avoid additional work and human errors, and describe the distribution of workflow metrics in a comprehensive way, for example, by providing the mean and standard deviation.<sup>85–86</sup> Of note, workflow performances are ideally assessed in large, multicenter registries such as the American Heart Association's 'Get with the Guidelines' registry tool,<sup>87</sup> with mechanisms that ensure all patients are included in the database, in order to avoid 'cherry-picking' and provide a realistic image of workflow performance over time.

### CONCLUSION

The landscape of EVT triage is constantly changing, and several trials are ongoing that may soon broaden EVT indications. Furthermore, new neuroimaging methods, EVT technologies, and adjunctive medical treatments are undergoing continuous development and refinement. These changes will influence EVT triage. For example, IV tenecteplase may soon replace IV alteplase as the default thrombolytic agent, making PSC-CSC interhospital transfer easier. In case neuroprotectants such as nerinetide become standard of care,<sup>88</sup> in-hospital workflows and organization will need to change to allow for timely administration of these additional adjunctive treatments. Stroke legislation, either at a regional or national level, can catalyze and guide these efforts and improve overall accessibility to stroke care at the population level.<sup>89</sup> Irrespective of these moving parts, teamwork is key to efficient EVT triage; thus, engaging paramedics and primary stroke centers is just as important as adoption of new triage technologies. Without their support, EVT triage paradigms will always lag behind the evidence and never achieve their maximum performance. Building sustainable relationships between the involved parties, and motivating and engaging all players, both at the pre- and in-hospital stage, will require continuous efforts and ongoing education and training, which should ideally include regular hands-on simulation training workshops and in-person site visits at PSCs and EMS hubs. The optimization of EVT triage is an active process requiring concerted efforts that cannot simply rely on passive flow of knowledge.

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