The strong evidence for benefits of rapid thrombectomy in patients with acute ischemic stroke (AIS) is challenging prehospital systems around the world. Although high-tech endovascular treatment (EVT) works only for a minority of patients, healthcare systems cannot afford to miss suitable candidates anymore. Recent figures show eligibility of \( \approx 25\% \) for thrombolysis and \( \approx 10\% \) for EVT in all AIS arriving at the hospital within 24 hours. Still, paramedics, local hospitals, and primary stroke centers are struggling to clinically identify the AIS patients who are likely to have intracranial large vessel occlusions (LVO) in the anterior and posterior circulation.

A similar problem was posed 20 years ago when we needed to identify stroke patients requiring immediate transfer to a thrombolyzing institution. Several prehospital schemes proved to be useful, such as the Cincinnati Prehospital Stroke Scale, the Los Angeles Prehospital Stroke Screen, or the Face-Arm-Speech-Time test (FAST). Still, today, no uniform score with a single cutoff is widely accepted. Many prehospital systems use simple descriptive terms for patient selection that include a maximal delay since last proof of good health, a potentially disabling neurological deficit, absence of a major preexisting handicap, and absence of initial seizures. Whether we use a score or a simple descriptive algorithm, most stroke-admitting hospitals accept a significant rate of overdiagnosis of AIS that are considered potentially thrombolysable in the prehospital phase. Such overdiagnosed patients may have rapidly improving and minor strokes, stroke mimics, or intracranial hemorrhages.

As for the new challenge of identifying patients eligible for EVT, that is, patients having an acute LVO and coming rapidly to the attention of the emergency medical system, there is a seemingly simple solution: get the patient to a computed tomography/computed tomographic angiography or magnetic resonance/magnetic resonance angiography as fast as possible, if needed, even in a mobile imaging facility. This rapid and widespread diagnostic option should indeed be a top priority for all acute stroke systems. Yet, geographical and financial challenges are limiting the access to such imaging. If we are adding the limited number of labor-intensive endovascular facilities, the need for effective clinical prehospital criteria to identify EVT-eligible patients will persist for a long time.

Figure shows 3 typical pathways for suspected AIS patients in the 3-level care system that currently exists in many countries and was formalized recently by the World Stroke Organization. Using this map of acute stroke care, several important considerations come to light:

- **Pathway A**: arrival at a nonthrombolyzing hospital: such patients should immediately be sent to a thrombolyzing hospital (pathway A2 or A3, ship-and-drip), without being offloaded from the ambulance. Most ideally, such non-thrombolyzing hospitals should be bypassed by patients who have the prehospital criteria, and patient should be taken directly to a thrombolyzing hospital (pathway B) or EVT-capable comprehensive stroke center (pathway C).
- **Pathway B**: admission to a thrombolyzing hospital (usually a primary stroke center): Sending patients directly to thrombolyzing hospitals is currently the preferred attitude in 2-level stroke care systems as recommended in Europe. Along this pathway, thrombolysis should be initiated immediately after radiological exclusion of intracranial bleeds. Once thrombolysis is running, arterial imaging is rapidly added to identify and transfer suitable endovascular patients (drip-and-ship, pathway B2).
- **Pathway C**: direct admission of clinically selected patients directly comprehensive stroke centers capable of EVT (termed the mother-ship approach) is likely to be quicker and therefore have more benefit for patients with LVOs, although this still needs to be proven. Also, the in-hospital delays in a streamlined one-stop imaging-to-thrombolysis-to-EVT procedure are likely less than the imaging-to-drip-and-ship approach. But again, pathway C requires important investments in the prehospital organization and EVT-capable centers willing to accept a significant rate of LVO overdiagnosis.

There are several opportunities to use clinical scales in the stroke rescue chain, as denoted by the asterisks in Figure. To identify EVT candidates, such preimaging scores should be able to do the following:

1. Avoid missing EVT-eligible patients, that is, avoid underdiagnosing these patients (also expressed as false-negative rate, ie, 1-sensitivity). We suggest aiming at an underdiagnosis rate of \( \leq 10\% \) for most geographic scenarios.
2. Avoid overdiagnosing patients not eligible for EVTs, that is, avoid overloading the endovascular EVT-institution with inadequate patients (also expressed as false-positive rate, ie, 1-specificity). An acceptable rate of overdiagnosis could be 30% to 50% or somewhat less than half of all patients directed to an endovascular center, who would not fulfill treatment criteria after arterial imaging.
authors combining FAST with gaze deviation (G-FAST) seems to perform as well as the entire National Institute of Health Stroke Scale. Still, allowing for an ≈10% rate of missed LVOs (false-negative rate of 10%), the authors confirm an important overdiagnosis rate with all scores. As the authors nicely show, choosing higher cutoffs in the scores decreases the overtriage but increases the risk of missing a LVO. It looks like we have to accept a certain proportion of over- and underdiagnosis with any prehospital criteria, as we already do with the current prehospital selection processes for thrombolysis.

Using the available data, each stroke triage system should now choose its preferred simple score for the paramedical personnel and nonstroke physicians.\(^{13}\) In addition, the moment such a score is used and its cutoffs should be adapted to local circumstances and resources. Stroke-trained physicians without access to immediate arterial imaging can increase the precision of triage by using one of the more complex LVO scores such as the National Institute of Health Stroke Scale,\(^{11}\) the RACE (Rapid Arterial Occlusion Evaluation),\(^{14}\) or the ASTRAL-occlusion score\(^{12}\) (listed in Table 1). Nevertheless, the scores should not distract us from our obligation to implement rapid arterial imaging as a standard of care in all hospitals accepting stroke and potentially in ambulances.

Where should further research go from here? First, we need to pursue the work on prehospital LVO scores that follow the challenging criteria listed in Table 2, such as external validation in prehospital settings of unselected populations with suspected AIS. Second, the impact of the real-life application of such scores has to be analyzed, as recently done by Mohamad et al.\(^{15}\) They showed, in a retrospective before-and-after study, that the combined use of 4 items to triage patients directly to EVT-capable centers reduced treatment delay after study, that the combined use of 4 items to triage patients directly to EVT-capable centers reduced treatment delay and improved outcome. Third, randomized trials of drip-and-ship versus mother-ship approaches based on a prehospital LVO score should be initiated. And last, we may need to adjust our research target: rather than aiming at LVO only, we should develop prehospital scores that identify patients with LVO who are likely to respond to EVT. Treatment response may be better in patients with fewer comorbidities, less metabolic disturbances, and a favorable TRAIT imaging

### Table 1. Overview of Several Scores Tested for LVO Prediction in AIS

<table>
<thead>
<tr>
<th>Simple Scores (Paramedics)</th>
<th>Cutoff</th>
<th>Complex Scores (Stroke Physicians or Nurses)</th>
<th>Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Cincinnati Stroke Triage Assessment Tool (C-STAT)</td>
<td>≥1</td>
<td>RACE</td>
<td>≥2</td>
</tr>
<tr>
<td>Los Angeles Motor Scale (LAMS)</td>
<td>≥4</td>
<td>Full NIHSS</td>
<td>≥7*</td>
</tr>
<tr>
<td>Prehospital Acute Stroke Severity (PASS)</td>
<td>≥2</td>
<td>ASTRAL-occlusion score</td>
<td>≥13</td>
</tr>
<tr>
<td>Gaze-Face-Arm-Speech-Time (G-FAST)</td>
<td>≥3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The cutoffs to achieve a false-negative rate are ≈10% according to current research.\(^{2,12}\) At these cutoffs, there is always a significant false-positive rate (overdiagnosis) of LVO. Most scores still need prehospital validation. AIS indicates acute ischemic stroke; ASTRAL, Acute Stroke Registry and Analysis of Lausanne; LVO, large vessel occlusion; NIHSS, National Institute of Health Stroke Scale; and RACE, Rapid Arterial Occlusion Evaluation.

*NIHSS cutoff for a low false-negative rate may be lower in certain studies and at later time windows.

### Table 2. Optimal Characteristics of a Score to Identify Endovascular Candidates (Patients With a LVO) Before Arterial Imaging

<table>
<thead>
<tr>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applicable to an unselected population with suspected acute ischemic stroke, including posterior circulation</td>
</tr>
<tr>
<td>High interrater reliability</td>
</tr>
<tr>
<td>High accuracy</td>
</tr>
<tr>
<td>To identify strokes (vs imitators)</td>
</tr>
<tr>
<td>To identify LVO (vs no LVO)</td>
</tr>
<tr>
<td>Validated</td>
</tr>
<tr>
<td>In external data sets</td>
</tr>
<tr>
<td>In the prehospital setting</td>
</tr>
<tr>
<td>Proven to improve patient outcomes</td>
</tr>
</tbody>
</table>

LVO indicates large vessel occlusion.
profile (Treatment-Related Acute Imaging Target). The latter includes good collaterals, small ischemic core, and important mismatch, factors that may be predicted on clinical grounds in the prehospital phase. The treatment response of favorable TRAIT profile patients is likely to be time independent. Therefore, future research should aim at prehospital scores identifying LVO patients ≤24 hours with moderate to high likelihood of EVT response, rather than limiting our search to identifying just LVO in short time windows, such as 0 to 6 hours.

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Disclosures
None.

References

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