Hyperacute stroke management: New prehospital models for Switzerland

Urs Fischer
University of Bern, Switzerland
Disclosures

• Principal investigator ELAN trial
• Co-Principal investigator SWITCH trial
• Co-Principal investigator SWIFT DIRECT trial
• Consultant for Covidien/Medtronic and Stryker
• Research support: SNSF, SHF, Medtronic
The Ischemic Penumbra: A Dynamic [time + space] concept
Time is brain

Volume

Penumbra

Time
Time is brain

Volume

Penumbra

Infarction

Time
Effect on mRS 0-1 by treatment delay

(ECASS, ATLANTIS, NINDS, EPITHET, IST-3)

Interaction $p=0.016$

Odds ratio (95% CI)

Time to treatment (hours)

Emerson et al. Lancet 2014
Acute stroke treatment

Shorten time to needle!

Time of symptom onset → Time to needle (IVT)
Stroke Units in CH
Endovascular stroke treatment
Acute stroke treatment

Shorten time to puncture!

- Time of symptom onset
- Time to needle (IVT)
- Time to groin puncture (EVT)
Benefit of endovascular reperfusion

Time to reperfusion:
- 20% probability for a good outcome
- 40% probability for a good outcome
- 60% probability for a good outcome
- 80% probability for a good outcome

Prabhakaran JAMA 2015; Khatri Lancet Neurology 2014; Mazhigi Circulation 2013
90 Day mRS 0-2 by TLSW to Randomization

<table>
<thead>
<tr>
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<th>Trevo</th>
<th>MM</th>
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<td>6-12h</td>
<td>55.1%</td>
<td>20.0%</td>
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<td>12-24h</td>
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Acute stroke treatment

Shorten time to reperfusion!

- Time of symptom onset
- Time to needle (IVT)
- Time to groin puncture (EVT)
- Time to reperfusion (IVT and EVT)
Impact of the collaterals
Time is brain, but collaterals set the pace!

Volume

Penumbra

Infarction

Time
Variability in infarct growth

- 2h: >460 billion neurons/min
- 2h, 5h, 11h: 650,000 neurons/min
- 1d, 7d, 12d, 17d: 9000 neurons/min
Stroke centers and units
Best candidates for…

IVT

±IVT + EVT
Stroke treatment 2018

• To treat patients as soon and effective as possible

• Patients with LVO should be immediately transferred to an endovascular stroke center

• Patients without LVO should be transferred to the nearest thrombolysing stroke unit
Proportion of patients with LVO ?
Proportion of patients with LVO

Clinical Selection Strategies to Identify Ischemic Stroke Patients With Large Anterior Vessel Occlusion
Results From SITS-ISTR (Safe Implementation of Thrombolysis in Stroke International Stroke Thrombolysis Registry)

J NEUROL Science 2016

Significance of Large Vessel Intracranial Occlusion Causing Acute Ischemic Stroke and TIA

Stroke 2009

Stroke 2016
• 16,000 stroke patients/y

• 5000 LVO
Proportion of patients eligible for EVT?
Eligibility and Predictors for Acute Revascularization Procedures in a Stroke Center

Peter Vanacker, MD, PhD; Dimitris Lambrou, PhD; Ashraf Eskandari, MD, RN; Pascal J. Mosimann, MD; Ali Maghraoui, PhD; Patrik Michel, MD

Background and Purpose—Endovascular treatment (EVT) is a new standard of care for selected, large vessel occlusive strokes. We aimed to determine frequency of potentially eligible patients for intravenous thrombolysis (IVT) and EVT in comprehensive stroke centers. In addition, predictors of EVT eligibility were derived.

Methods—Patients from a stroke center–based registry (2003–2014), admitted within 24 hours of last proof of usual health, were selected if they had all data to determine IVT and EVT eligibility according to American Heart Association/American Stroke Association (AHA/ASA) guidelines (class I–IIa recommendations). Moreover, less restrictive criteria adapted from randomized controlled trials and clinical practice were tested. Maximum onset-to-door time windows for IVT eligibility were 3.5 hours (allowing door-to-needle delay of ≤60 minutes) and 4.5 hours for EVT eligibility (door-to-groin delay ≤90 minutes). Demographic and clinical information were used in logistic regression analysis to derive variables associated with EVT eligibility.

Results—A total of 2704 patients with acute ischemic stroke were included, of which 26.8% were transfers. Of all patients with stroke arriving at our comprehensive stroke center, a total proportion of 12.4% patients was eligible for IVT. Frequency of EVT eligibility differed between AHA/ASA guidelines and less restrictive approach: 2.9% versus 4.9%, respectively, of all patients with acute ischemic stroke and 10.5% versus 17.7%, respectively, of all patients arriving within <6 hours. Predictors for AHA–EVT eligibility were younger, shorter onset-to-admission delays, higher National Institutes of Health Stroke Scale (NIHSS), decreased vigilance, hemineglect, absent cerebellar signs, atrial fibrillation, smoking, and decreasing glucose levels (area under the curve=0.86).

Conclusions—Of patients arriving within 6 hours at a comprehensive stroke center, 10.5% are EVT eligible according to AHA/ASA criteria, 17.7% according to criteria resembling randomized controlled trials, and twice as many patients are IVT eligible (36.2%). (Stroke. 2016;47:1844–1849. DOI: 10.1161/STROKEAHA.115.012577.)

Key Words: cerebral revascularization ■ cerebrovascular occlusion ■ endovascular procedure ■ intravenous thrombolysis ■ stroke
Eligibility and Predictors for Acute Revascularization Procedures in a Stroke Center

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Results—A total of 177 patients were eligible for IVT. Of all patients, 10.5% were EVT eligible, versus 4.9%.

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Key Words: cerebral revascularization, cerebrovascular occlusion, endovascular procedure, intravenous thrombolysis, stroke
Clinical prediction of LVO ?
Sensitivity and specificity of NIHSS score on admission of all patients to find a central (ICA, M1, M2, or BA) occlusion on DSA (55 of 226 patients with peripheral occlusion).

Fischer U et al. Stroke 2005;36:2121-2125
### NIHSS subitems

#### Table 3
Odds ratios of different NIHSS subitems predicting large vessel occlusion in acute anterior circulation stroke

<table>
<thead>
<tr>
<th>Subitem</th>
<th>Odds ratio</th>
<th>Univariate 95% CI</th>
<th>p</th>
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<tr>
<td>Best Gaze</td>
<td>9.60</td>
<td>6.765–13.632</td>
<td>&lt;0.0001</td>
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<td>Motor arms</td>
<td>7.60</td>
<td>5.589–10.204</td>
<td>&lt;0.0001</td>
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<tr>
<td>Aphasia/neglect</td>
<td>7.13</td>
<td>5.352–9.492</td>
<td>&lt;0.0001</td>
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<tr>
<td>Visual fields</td>
<td>7.00</td>
<td>3.981–12.370</td>
<td>&lt;0.0001</td>
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<tr>
<td>Motor legs</td>
<td>5.78</td>
<td>4.436–7.560</td>
<td>&lt;0.0001</td>
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<tr>
<td>LOC&lt;sup&gt;a&lt;/sup&gt; alterness</td>
<td>5.64</td>
<td>3.732–8.522</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Facial palsy</td>
<td>5.50</td>
<td>4.044–7.468</td>
<td>&lt;0.0001</td>
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<tr>
<td>LOC&lt;sup&gt;a&lt;/sup&gt; commands</td>
<td>4.50</td>
<td>3.287–6.157</td>
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<tr>
<td>LOC&lt;sup&gt;a&lt;/sup&gt; questions</td>
<td>4.23</td>
<td>3.248–5.503</td>
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<td>Dysarthria</td>
<td>3.20</td>
<td>2.480–4.119</td>
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<td>Sensation</td>
<td>2.40</td>
<td>1.865–3.088</td>
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<td>Limb ataxia</td>
<td>0.87</td>
<td>0.362–2.074</td>
<td>0.747</td>
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Heldner MR, …Fischer U., J Neurol 2016
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<tr>
<td>NIHSS≥8</td>
<td>2183/3505 (63.2)</td>
<td>85.0</td>
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<td>36.0</td>
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<td>2410/3505 (68.8)</td>
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<td>97.2</td>
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*False positiv rate
*False negativ rate

Stroke. 2017;48:290-297
Problem with scores

- Most scores not tested for **paramedics**
- Most scores **not** tested in the **prehospital setting** (only RACE has been validated)
- Most scores tested in patients with **ischaemic stroke only**
- If **specificity** is high **sensitivity** is low, and vice versa
- Stroke is **not** a stable disease! Clots are a moving target...
Models of prehospital stroke management
Models of prehospital patient management

1. Drip and ship
2. Ship (Mothership)
3. Drip and drive
4. Mobile stroke unit
4. Mobile stroke unit
World’s First Vehicle Based CT

Cocktail Cabinet

TeleMed Wireless Communication
Mobile stroke units for prehospital thrombolysis, triage, and beyond: benefits and challenges

Klaus Fassbender, James C Grotta, Silke Walter, Iris Q Grunwald, Andreas Radoschke-Schumm, Jeffrey L Saver

In acute stroke management, time is brain. Bringing swift treatment to the patient, instead of the conventional approach of awaiting the patient’s arrival at the hospital for treatment, is a potential strategy to improve clinical outcomes. This approach has been demonstrated to be effective in reducing ischemic stroke volumes and improving outcomes.

Figure 2: Multimodal imaging in a mobile stroke unit
Non-contrast CT (A), CT angiography (B), and ASPECTS (C) done in a mobile stroke unit of a 73-year-old woman with acute right hemiparesis. Although the parenchyma shows no signs of infarction (ASPECTS 10), CT angiography allowed prehospital diagnosis of an occlusion of the left middle cerebral artery (B, arrow). Reproduced from Grunwald et al, by permission of Cerebrovascular Diseases (Karger). ASPECTS- Alberta Stroke Program Early CT Score.
3. Drip and drive
Drip and drive

- NL sees Pat.
- CT/CTA
- Nrad MT on call
- Preparation in Angio suite
  - Evtl. sheath by General Radiologist
- Patient to Angio (Monitoring)
- Technician (prepares)
- Anaesthesia
- Porsche (Taxi)
- Imaging inclusion criteria
- Imaging incl. criteria
- Intervention
- Pat. to Stroke Unit/ICU
- Report

Brekenfeld et al., unpublished
Hamburg: „Drip-and-Drive“ vs. „Drip-and-ship“

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<tr>
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<th>Group A</th>
<th>Group B</th>
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<td>Median</td>
<td>IQR (min.)</td>
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n=15  Brekenfeld, C et al. submitted, 2017
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<td>121</td>
<td>108-134</td>
<td>&lt;0.0001</td>
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<tr>
<td>O-DSA</td>
<td>31</td>
<td>88</td>
<td>59-124</td>
<td>NS</td>
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<tr>
<td>CT-DSA</td>
<td>41</td>
<td>123</td>
<td>93-147</td>
<td>&lt;0.0001</td>
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<tr>
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<td>37</td>
<td>24-54</td>
<td>NS</td>
</tr>
<tr>
<td>O-R</td>
<td>22</td>
<td>270</td>
<td>249-319</td>
<td>&lt;0.001</td>
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</table>

Brekenfeld, C et al. submitted, 2017

Hamburg: „Drip-and-Drive“ vs. „Drip-and-ship“

„Drip and drive“ saves 2h (in Hamburg)
Models of prehospital patient management

1. Drip and ship
2. Ship (Mothership)
3. Drip and drive
4. Mobile stroke unit
Female

55 years

144 called 45 minutes after symptom onset

NIHSS 16
Female
55 years
144 called 45 minutes after symptom onset
NIHSS 16
Female
55 years
144 called
45 minutes after symptom onset
NIHSS 16
Female

55 years

144 called after symptom onset

NIHSS 16
Arguments

Drip and ship

Advantages
• Earlier initiation of IVT
• Improved patient selection
• Higher proportion of IVT
• Preinterventional recanalisation

Disadvantages
• Delayed time to reperfusion
• Resources

Mothership
Arguments

Drip and ship

Advantages
• Earlier initiation of IVT
• Improved patient selection
• Higher proportion of IVT
• Preinterventional recanalisation

Disadvantages
• Delayed time to reperfusion
• Resources

Mothership

Advantages
• Earlier initiation of EVT
• Shorter time to reperfusion
• Higher proportion of EVT

Disadvantages
• Delay (or even deny) of IVT
• Transfer of ineligible EVT patients (futile transports)
• Resources
Prioritize IVT?  Prioritize EVT?
Intention to bridge (319 patients)

Relevant recanalization

- **Mother ship paradigm**
  - ICA (n MS=52, n DNS=41): 3.8
  - M1 (n MS=101, n DNS=47): 5.9
  - M2 (n MS=34, n DNS=13): 12.8
  - BA (n MS=20, n DNS=24): 10

- **Drip and ship paradigm**
  - ICA (n MS=52, n DNS=41): 7.3
  - M1 (n MS=101, n DNS=47): 12.8
  - M2 (n MS=34, n DNS=13): 30.8
  - BA (n MS=20, n DNS=24): 16.7

S. Jung et al. EJoN
Delay by Non-Endovascular-capable center?

- Direct to ECC (n=126):
  - 65 minutes
  - 17.5 hours
  - 10 hours
  - 37 minutes
  - 23 minutes
  - 24 minutes
  - 7 minutes

- Arrival at Non-ECC First (n=66):
  - 214.5 hours
  - 14 minutes
  - 7 minutes
  - 22.5 minutes
  - 17 minutes
  - 23.5 minutes
  - 9 minutes

- Median Time (Minutes):
  - 2:30 h

- Graph:
  - % Functional independence at 90 days
  - Solitaire repurposed (n=70)
  - Time from onset to reperfusion (min)
  - 150, 180, 210, 240, 270, 300, 330, 360, 390

Goyal, M et al. Radiology 2016 ePub
STRATIS: Systems of care study

• **Hypothesis:** Interhospital transfer from a community hospital to an endovascular-capable center may result in treatment delays and worse clinical outcomes compared to direct presentation.

• **We assessed:**
  1. real-world time metrics of stroke care delivery
  2. outcome differences between direct and transfer patients undergoing mechanical thrombectomy based on 90d mRS
  3. the potential impact of local hospital bypass

© Michael Froehler
Median Times from Stroke Onset to Revascularization

- Stroke Onset to 911 call
- 911 call to EMS Scene Arrival
- EMS Scene Arrival to Door [Initial Hospital]
- Door to Picture [Initial Hospital]
- Picture to IV t-PA [Initial Hospital]
- IV t-PA to Departure [Initial hospital]
- Transfer time (Departure initial hospital to Door Enrolling Hospital)
- EMS Scene Arrival to Door [Enrolling Hospital]
- Door to Picture [Enrolling Hospital]
- Picture to IV t-PA [Enrolling Hospital]
- Picture to Puncture [Enrolling Hospital]
- IV t-PA to Puncture [Enrolling Hospital]

Direct:
- 16 minutes
- 8 minutes
- 29 minutes
- 13 minutes
- 23 minutes
- 48 minutes
- 34 minutes
- 268 minutes
- P < 0.0001

Transfer:
- 118 minutes
- 23 minutes
- 14 minutes
- 42 minutes
- 47 minutes
- 35 minutes
- 15 minutes
- 42 minutes
- 37 minutes
- 169 minutes
Outcome at 90 days

mRS 0-2:
- 60.0% direct
- 52.2% transfer
- OR 1.38 (1.06-1.79)

mRS 0-1:
- 47.4% direct
- 38.0% transfer
- OR 1.47 (1.13-1.92)

Mortality:
- 15.0% direct
- 13.7% transfer
- p=0.56

Shift analysis favored direct presentation (p=0.012 by Cochran-Mantel-Haenszel test).
STRATIS conclusions

- Interhospital transfer was associated with
  - significant delays to treatment, and
  - significantly lower chance of good outcome.

- Strategies to facilitate more rapid identification of LVO and direct routing to endovascular centers for some severe stroke patients may help to improve outcomes.
Drip and ship
or
mothership?
Randomized controlled trial!

Stroke Center

Stroke Unit

RACECAT
Randomized controlled trial!

Stroke Center

Stroke Unit

RACECAT
**RACECAT** *(NCT02795962)*

A Trial Comparing TRAtransfer to the Closest Local Stroke Center vs Direct Transfer to Endovascular Stroke Center of Acute Stroke Patients with Suspected Large Vessel Occlusion in the Catalan Territory.

- Prospective, multicenter, academic trial (unrestricted grant from Medtronic)
- Cluster randomized, controlled (pre-established temporal sequence)
- Acute stroke patients with suspected acute large vessel occlusion identified by EMS
- Two strategies will be compared:

![Diagram showing two strategies: Local Stroke Center (+/- iv tPA) and EVT Stroke Center (+/- iv tPA).](image)

Perez de la Ossa N, Ribó M, Abilleira S. 2016

Niaz Ahmed¹,², Thorsten Steiner³,⁴, Valeria Caso⁵ and Nils Wahlgren²; for the ESO-KSU session participants*
B. Mechanical thrombectomy: ‘Drip and ship’ or ‘load and go’?

For patients with a suspected LAO based on current clinical tools on field, there is uncertainty about the equipoise between drip and ship (that prioritizes early IVT and other standard of care therapies) and mother-ship (that prioritizes early endovascular thrombectomy) models. Data based on randomized controlled trials are needed to determine the most beneficial model for each particular patient (eligible or not for iv-tPA) in different geographical regions and to establish isochrones where a particular model may be beneficial (Grade C).
B. Mechanical thrombectomy: ‘Drip and ship’ or ‘load and go’?

In the absence of evidence, for patients considered eligible to IVT in the field, if estimated transfer time to the nearest primary stroke centre is considerably shorter than time to a comprehensive stroke centre (approximately more than 30–45 min), the drip and ship model should be considered (Grade C).
B. Mechanical thrombectomy: ‘Drip and ship’ or ‘load and go’?

In the absence of evidence, in a scenario where a primary stroke centre and comprehensive stroke centre are equidistant (approximately not more than 30–45 min apart) or when contraindications to IVT are known in the field, patients with suspected LAO in the field, should be considered for transfer directly to a comprehensive stroke centre, bypassing any closer primary stroke centres (Grade C).
B. Mechanical thrombectomy: ‘Drip and ship’ or ‘load and go’?

In case of primary admission to a primary stroke centre, evaluation and treatment for patients with a possible LAO must be expeditious, to ensure a rapid secondary transfer to a comprehensive stroke centre, avoiding any sources of delay such as complex neuroimaging studies (i.e. perfusion studies) or waiting for effect of IVT. First picture to puncture time should be less than 90 min (Grade A).
What should we do in Switzerland?
Score to identify LVO

<table>
<thead>
<tr>
<th>Gaze deviation</th>
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<tbody>
<tr>
<td>Face weakness</td>
<td>1</td>
</tr>
<tr>
<td>Arm weakness</td>
<td>1</td>
</tr>
<tr>
<td>Speech / language problem</td>
<td>1</td>
</tr>
</tbody>
</table>
Ideal candidates for direct transport

- High suspicion of LVO
- Time from symptom onset >4h and <24 hours
- Contraindications for IVT
  - Unknown time of symptom onset
  - Wake-up and siesta stroke
  - (N)OAC therapy
  - Prior surgery
  - Etc.
Conclusions

• No randomised evidence which prehospital model should be preferred
• Time is brain: shorten time to reperfusion
  • Stroke patients should be transferred as fast as possible (also after 4.5 hours!)
• Scores can help to identify patients with LVO
• Future:
  • Prehospital identification of LVO (ambulance)
  • Evidence needed for individualised treatment decisions
Thanks to

- Patrik Michel
- Simon Jung
- Marcel Arnold
- Heini Mattle
- Johannes Kaesmacher
- Mirjam Heldner
- Jan Gralla
- Jens Fiehler, Caspar Brekenfeld, Michael Froehler, Tudor Jovin, etc.
Mark Your Calendar

4th European Stroke Organisation Conference
16-18 May 2018 | Gothenburg, Sweden

ESO - The Voice of Stroke in Europe

www.eso-conference.org