The DAWN of a New Era for Wake-up Stroke

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Objectives

- Review Epidemiology and Natural History of Large Vessel Cerebral Occlusion
- Review Recent Trials for Extended Treatment Time Window for Ischemic Stroke
- Key Criteria for Extended Time Window for Treatment of Acute Ischemic Stroke
DISCLOSURES

- None
Saving “Tissue at Risk”
Up to 24 hours
Saving “Tissue at Risk”
Up to 24 hours

UNABLE to remove the blood clot
Saving “Tissue at Risk”
Up to 24 hours

Penumbra

Infarct

TIME

REMOVE the blood clot
“reperfusion”
Saving “Tissue at Risk”
Up to 24 hours

Untreated stroke

Treated stroke

- Less disability
- Improved recovery
- Less hospital complications
Time is brain!

“2 million cells die each minute”
“One minute saved = 1 day of normal life”

BUT...

Each Stroke Evolves in Unique Manner NOT Solely Reliant Upon Time
IV tPA for Acute Ischemic Stroke
Cerebrovascular Anatomy

Carotid Artery

MCA

Carotid Terminus

Diagram showing the carotid artery and its terminus, with labels and arrows.
Large Vessel Occlusion Facts: Strokes

- Up to 46% of All **Strokes**
  - Associated 6 mo. Mortality (4.5 X) and Outcome
  - Esp. Occlusion of Basilar and Carotid T Arteries

- **RECANALIZATION** Rates from tPA Alone:
  - Prox MCA: **30%**
  - Distal MCA: **44%**
  - **IC: 6%**
  - BA: **33%**
Large Vessel Occlusion Facts: TIA

- Little Data
- ~13% of TIAs
  - Etiologies: Afib, ICAD, artery-artery
  - LVO patients present with greater disability
    (moderate vs mild stroke symptoms)
  - LVO is associated with:
    - recurrent stroke in 90 days
    - functional impairment
Advances in Brain Imaging: CT Perfusion

- “Biological Approach” vs Just Time
- New technology can identify brain tissue that is rescuable by our new treatments
- This technology (CTA/CTP) is readily available at our local hospitals and routinely used in the assessment of stroke patients
CT Angiogram

Occluded
RIGHT
Proximal
MCA
Vessel
Acute Stroke Neuroimaging
Thrombectomy Trials
Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging


A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812
JANUARY 1, 2015
VOL. 372 NO. 1

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke


Stent-Retriever Thrombectomy: t-PA vs. t-PA Alone


Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

# Stentriever Trial Summary

<table>
<thead>
<tr>
<th>Trial</th>
<th>n</th>
<th>Tx t Time (h)</th>
<th>NIHSS: IA group</th>
<th>Age</th>
<th>Imaging Selection</th>
<th>stroke to TPA</th>
<th>Stroke to puncture</th>
<th>90d mRS &lt;3</th>
<th>control</th>
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<tbody>
<tr>
<td>MRCLEAN</td>
<td>500</td>
<td>6</td>
<td>17</td>
<td>66</td>
<td>No</td>
<td>85’</td>
<td>260’</td>
<td>33%</td>
<td>19%</td>
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<tr>
<td>REVASCAT</td>
<td>206</td>
<td>8</td>
<td>17</td>
<td>66</td>
<td>Yes, CTA</td>
<td>117’</td>
<td>223’</td>
<td>44%</td>
<td>28%</td>
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<tr>
<td>ESCAPE IA</td>
<td>315</td>
<td>12</td>
<td>16</td>
<td>71</td>
<td>Yes, CTA</td>
<td>110’</td>
<td>186’</td>
<td>53%</td>
<td>29%</td>
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<tr>
<td>SWIFT-PRIME</td>
<td>196</td>
<td>4.5</td>
<td>17</td>
<td>65</td>
<td>Yes, CTP (some CTA)</td>
<td>110’</td>
<td>224’</td>
<td>60%</td>
<td>36%</td>
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<tr>
<td>Extend IA</td>
<td>70</td>
<td>6</td>
<td>17</td>
<td>69</td>
<td>Yes, CTP</td>
<td>127’</td>
<td>210’</td>
<td>71%</td>
<td>40%</td>
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Severe Deficits: Most < 4.5 hrs
2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

- **Strongest level of evidence for Endovascular:**
  - NIHSS $\geq 6$ (at least moderate disability)
  - Favorable CT (absent large infarct on 1st CT)
  - Intracranial IC or Proximal MCA
  - $< 6$ hrs from symptom onset
Acute Stroke Care Sequence

1. Spot a Stroke
   - Stroke Warning Signs and Symptoms

2. tPA
   - Thrombolytic Agent

3. CT Scan
   - Imaging of Brain

4. Angiogram
   - Imaging of Blood Vessels
Is There Anything We Can Do After 6 Hrs?

- Can we still consider Endovascular Rx?
- Is it Safe?
- Is there Data?
Hot Off The Press:
Endovascular Rx Beyond 6 Hrs

DAWN Trial
(DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo). NEJM Nov 11, 2017

DEFUSE 3 Trial
(Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3). NEJM Jan 24, 2018
Thrombectomy for AIS

DAWN Trial

Original Article

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct
Thrombectomy for AIS

DAWN Trial

- Multicenter, prospective, randomized design
- Industry sponsored (Stryker Neurovascular)
- **Eligibility:**
  - Confirmed LVO (Intracranial ICA and/or M1)
  - LKW 6-24 hrs
  - NIHSS > 10
  - Clinico-radiographic Mismatch (next slide)
  - < 1/3 MCA infarction on initial imaging
DAWN Trial

Group A
- > 80 yrs
- NIHSS >10
- Core < 21 cc

Group B
- < 80 yrs
- NIHSS >10
- Core < 31 cc

Group C (severe)
- < 80 yrs
- NIHSS >20
- Core 31-51 cc

tMax or MTT

RCB
DAWN Trial

- Additional randomization
  - Time: 6-12 hrs vs. > 12-24 hrs
- Occlusion site
  (Intracranial ICA or M1)

- Only TREVO Device
- Rescue w/ other devices or pharm NOT allowed
Outcome Measures (90 days)

- (1) Standard mRS (0-6)
- (2) *Utility-weighted mRS (0-10)
  - 0 = death
  - 10 = No symptoms
  - Performs similarly to mRS in identifying treatment effects AND valid reflection of Patient-Centered Benefit

- Several Secondary Outcomes (i.e. TICI)
Main Results

- Trial stopped early (Thrombectomy superior)
- 206 pts (NIR = 107; Control = 99)
- NIHSS = 17
- Infarct Core: NIR = 7.6 mL; Control = 8.9 mL
- LKW: NIR = ~12 hrs vs. 13 hrs (control)

Baseline characteristics well matched Except:
- Wake-up: NIR 63% vs 47%
- Afib: NIR 40% vs. 24%
- tPA: Control 13% vs. 5% (NIR)
**DAWN Trial**
*(Functional Independence)*

**mRS:** 49% vs. 13%  
*(CI 21-44)*

**Uw-mRS:** 5.5 vs. 3.4  
*(CI 1.1-3)*
Thrombectomy lead to:

- **Early Response** (improvement of deficits)
- **Less Infarct Burden**
DAWN Trial Summary

Thrombectomy within **6-24 Hrs:**

- Earlier Recovery (24 hrs-days after procedure)
- Greater Meaningful Functional Independence
- 2-3 NIR treated = 1 Functionally Independent!
- Similar Functional Independence compared to NIR < 6 hrs in pooled 5-Trial analysis (46%)

*Caveats:* DAWN controls with lower rate (13%) functional indep vs. 26% (reasons: tPA use, older, higher NIHSS)
DAWN Trial Summary

SAFETY:

- NO significant difference:
  - Stroke or All-Cause of Death
  - sICH (6 vs 3 pts)
  - Neurologic Deterioration at 24 hrs (14% vs. 26%)

A STUDY of IMAGING Assessment!!!
Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging
Thrombectomy for AIS
DEFUSE 3 Trial
Endovascular Thrombectomy Summary

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association