Management of Acute Stroke: A Paradigm Shift

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Disclosures

• None

• Prevalence is estimated at 6.6 million Americans ≥ 20 years old
• Currently No 5 cause of death in the US

US Incidence: 795,000 per year
87% of all strokes are ischemic
Background

- >400,000 strokes each year
- Two small RCTs found no conclusive evidence of efficacy
- European large RCT of 1.1 mg IV t-PA within 6 hrs reported no benefit
- Two large RCT of IV streptokinase stopped early secondary to high rates of sICH


The 1st Revolution

- Barriers
- Diffusion of information
- Practice guidelines
- Hospital and Pre-hospital systems of care
- Infrastructure
- Economics

The 1st Revolution

2001-2002 Registry data:

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-30 minutes</td>
<td>2</td>
<td>1.9</td>
<td>46</td>
<td>0.0</td>
<td>1</td>
<td>0.0</td>
<td>1</td>
<td>0.0</td>
<td>30</td>
<td>0.3</td>
</tr>
<tr>
<td>30-60 minutes</td>
<td>11</td>
<td>10.0</td>
<td>1</td>
<td>0.0</td>
<td>1</td>
<td>0.0</td>
<td>1</td>
<td>0.0</td>
<td>1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

The 1st Revolution

- 1996 - Updated stroke guidelines
- 1998 - American Stroke Association is formed
- 1998 – ASA forms Metro Stroke Task Force (MSTF)
- 1999 – Operation Stroke
- 2000 – BAC publishes Recommendations for Establishment of Primary Stroke Centers
- 2003 – Get with the Guidelines – Stroke Program
- 2004 – TIC launches first advanced-level disease certification pathway (Primary Stroke Center)


The 1st Revolution

- 2005 – BAC publishes Recommendations for Comprehensive Stroke Centers
- 2005 – Recommendations for Establishment of Stroke Systems of Care
- 2005 – CMS creates diagnostic-related group 559 (excludes drip and ship)
- 2008 – CMS creates V code for drip and ship patients
- 2009 – Recommendations for the implementation of Telemedicine
- 2009 – Expansion of treatment time window (not FDA approved)
- 2012 – AAEM Position paper endorses IV t-PA for acute ischemic stroke
- 2013 – AHA/ASA acute ischemic stroke treatment guidelines
- 2015 – AHA/ASA Focused updated on 2013 guidelines for endovascular treatment
- 2016 – AHA/ASA Scientific rational for IV tPA inclusion / exclusion criteria

The 1st Revolution

IV tPA Treatment Rates

Figure 1: National utilization of intravenous tissue plasminogen activator in the United States.
The 1st Revolution
IV tPA door to needle time

1st Revolution Lessons

• Practice Guidelines are not enough
• Performance Measures - benchmark
• Nationwide care programs
• Hospital Accreditation & Certification
• Policy: systems of care
• Reimbursement
• Resources
• Technology

The 2nd Revolution
Positive trials

- MR CLEAN (2015)
- ESCAPE (2015)
- SWIFT PRIME (2015)
- EXTEND – IA (2015)
- REVASCAT (2015)
Impact of endovascular treatment

IV-tPA - Low recanalization rates with proximal occlusions

Logistic regression curve representing an estimate of the probability for successful recanalization of occluded vessels by intravenous thrombolysis (IVT) depending on thrombus length.
MR CLEAN

- Design: Open label, multicenter, RCT with blinded end-point evaluation between 2010 and 2014.
- Patients: 502 patients
  - NIHSS ≥ 2
  - ≥ 18 years old
  - AIS + anterior circulation LVO (ICA, M1, M2, A1, A2)
  - Initiation of IA treatment < 6 hours of sx onset
- Intervention:
  - IA (thrombolytic +/- mechanical) + usual care: N=233
    - Retrievable stents used in 81.5%
    - IV tPA in 87.1%
  - Usual care: N=267
    - IV tPA in 90.6%


MR CLEAN

- Main outcome measures: ITT
  - Primary: 90 day mRs
  - Secondary: 24 hr NIHSS, discharge NIHSS, 90 day Barthel index, 90 day EuroQoL5D
- Results:
  - Patient characteristics:
    - Mean age 65 yo (23 – 96)
    - Mean 58.4%
    - Median NIHSS (IQR): Intervention 17 (14-21). Control 18 (14-22)
    - Aspects (IQR): Intervention 8 (7-9). Control 9 (8-10)
    - Time in minutes from stroke onset to randomization (IQR): Intervention 204 (152-251). Control 196 (149-266)
    - Time in minutes from stroke onset to groin puncture (IQR): Intervention 260 (210-313)


ASPECTS Score

www.aspectsinstroke.com
Modified Ranking Scale (MRS)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms or all</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability despite symptoms able to carry out all small chores and activities</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability: unable to carry out all previous activities, but able to look after own affairs without assistance</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability: requiring some help, but able to walk without assistance</td>
</tr>
<tr>
<td>4</td>
<td>Marked disability: unable to walk without assistance and unable to attend to own bodily needs without assistance</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability: bedridden, incontinent and requiring constant nursing care and attention</td>
</tr>
<tr>
<td>6</td>
<td>Dead</td>
</tr>
</tbody>
</table>

TOTAL (0-6) _____

MR CLEAN

- Primary [90 day mRs]: Intervention 3 vs. Control 4 (OR 1.66; CI 1.21 – 2.3)
- mRs 0-2 at 90 days: Intervention 76% vs. Control 51% (OR 2.16; CI 1.39-3.38)
- Recanalization rate (24 hr CTA): 75.4% Intervention vs. 32.9% Control (OR 6.88; CI 4.34 – 10.94)
- Symptomatic ICH: 18% Intervention vs. 17% Control
- New symptomatic AIS in different vascular territory: Intervention 5.6% vs. Control 0.4%


Who qualifies?

- Prestroke mRS score 0 to 1
- Acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies
- Causative occlusion of the ICA or proximal MCA (M1)
- Age ≥18 years
- NIHSS score of ≥6
- ASPECTS of ≥6, and
- Treatment can be initiated (groin puncture) within 6 hours of symptom onset

Limitations

- Costs:
  - IV tPA: $6,749
  - Endovascular therapy: $24,154
- Little evidence of benefit > 6 hours
- Little evidence of benefit for mild to moderate strokes
- No evidence in pediatric population
- ICH risk is unchanged compared to IV tPA
- Infrastructure and resource requirement
- Benefit is time dependent


IV tPA

Mechanical thrombectomy
Conclusion / summary

- Endovascular treatment for acute ischemic stroke is highly effective and now standard of care
- For this 2nd revolution to be effective:
  - Practice Guidelines are not enough
  - Performance Measures - benchmark
  - Quality of Care programs
  - Hospital Accreditation & Certification
  - Policy: systems of care
  - Reimbursement
  - Resources
  - Technology

Thank you!