Ischemic Stroke: Treatment Update

American College of Physicians
Northern California Chapter Scientific Meeting

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UC Davis Health
Objectives

• Understand the treatment of acute stroke
• Thrombectomy indications
• Differentiating stroke subtypes
• Stroke cases
• Challenges in stroke care
Globally By The Numbers

• Every year 15 million people worldwide suffer a stroke
• Globally stroke is second leading cause of death over the age of 60
• 5th leading cause of death in people aged 15 to 59
• Stroke is the second leading cause of disability, after dementia
• In China, 1.3 million have a stroke each year
  — 75% live with varying degrees of disability as a result of stroke.
• Every year, more than 795,000 people in the United States have a stroke.
• Stroke costs the United States an estimated $34 billion each year. This total includes the cost of health care services, medications to treat stroke, and missed days of work.

• Stroke is a leading cause of serious long-term disability
Brain Perfusion

- Normal brain
  - 2% of body weight but consumes 20% of cardiac output
  - CBF 50 mL per 100 g of brain tissue/minute
- Ischemia
  - 20 mL per 100 g/minute – neuronal show electrical dysfunction
  - Below 10 mL per 100g/minute – electrical failure and cell death
  - 10 to 20 mL per 100g/minute – penumbra tissues
    - “Stunned neurons”
    - Still recoverable
Why are we so aggressive with stroke?

• 1.9 million neurons each minute in which stroke is untreated
Time is Brain

- Motor function
- No treatment
- 'Plasticity'

function vs. time post stroke
Vessel Recanalization is Important

- Ischemic penumbra can be salvaged if vessel is rapidly recanalized
- Meta-analysis – strong correlation between recanalization and good outcome

<table>
<thead>
<tr>
<th></th>
<th>Functional Independence (mRS 0-2)</th>
<th>Mortality</th>
<th>Symptomatic Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recanalized</td>
<td>58.1%</td>
<td>14.4%</td>
<td>13.7%</td>
</tr>
<tr>
<td>Nonrecanalized</td>
<td>24.8%</td>
<td>41.6%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Odds Ratio:</td>
<td>4.43 (95% CI, 3.32–5.91)</td>
<td>0.24 (95% CI, 0.16 to 0.35)</td>
<td>1.11 (95% CI, 0.71 to 1.74)</td>
</tr>
</tbody>
</table>

Successful recanalization is associated with:
- 4-5 fold increase in the odds of good functional outcome
- 4-5 fold decrease in the odds of mortality

Rha et al Stroke 2007
Number Need to Treat for a Good Outcome with IV tPA (mRS < 1)

- ≤ 90 mins: NNT=4 to 5
- 90 min - 3 h: NNT=9
- 3 - 4.5 h: NNT=14
Updated Criteria for IV tPA for 3 Hour Window

**Inclusion**

- Measurable neurological deficit
- Onset of Sx < 3 hours
- Age > 18

**Exclusion**

- Head Trauma or Stroke in previous 3 mo
- SAH
- Arterial puncture at noncompressible site in previous 7D
- History of ICH
- Intracranial neoplasm, AVM, or aneurysm
- ↑ BP (SBP > 185 or SBP > 110)
- Active internal bleeding
- Platelet count < 100K
- Heparin within 48 hours with ↑PTT
- INR > 1.7 or PT > 15s
- Direct thrombin or direct Factor Xa inhibitors
- Blood glucose < 50
- CT showed hypodensity > 1/3 hemisphere

**RELATIVE EXCLUSIONS**

- Only minor or rapidly improving Sx
- Pregnancy
- Seizure at onset
- Major surgery or serious trauma in 14 d
- Recent GI or urinary tract hemorrhage in 21 d
- Recent acute MI with last 3 mo

AHA Guidelines 2015
Criteria for IV tPA for 3 to 4.5 Hour Window

**Inclusion**
- Measurable neurological deficit
- Onset of Sx < 4.5 hours
- Age 18 to 80

**Exclusion**
- Age > 80
- NIHSS > 25
- Not on any oral anticoagulants
- History of diabetes and prior stroke
- Imaging evidence of ischemic injury > 1/3 MCA territory

ECASS III 2008
Distinct Short-Term Outcomes in Patients With Mild Versus Rapidly Improving Stroke Not Treated With Thrombolytics

Jose G. Romano, MD; Eric E. Smith, MD, MPH; Li Liang, PhD; Hannah Gardener, ScD; Iszet Campo-Bustillo, MD, MPH; Pooja Khatri, MD; Deepak L. Bhatt, MD, MPH; Gregg C. Fonarow, MD; Ralph L. Sacco, MD, MS; Lee H. Schwamm, MD
• MS with NIHSS 0 to 5
• RIS with NIHSS > 5
• MS+RIS with NIHSS 0 to 5

Results

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Total (n= 42394)</th>
<th>MS (n=12464)</th>
<th>RIS (n=19734)</th>
<th>MS+RIS (n=11196)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death during admission, %</td>
<td>0.8</td>
<td>0.7</td>
<td>1.1</td>
<td>0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unable to discharge home, %</td>
<td>27</td>
<td>26.6</td>
<td>29.9</td>
<td>22.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unable to ambulate independently, %</td>
<td>27.2</td>
<td>26.7</td>
<td>30.6</td>
<td>22.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LOS ≥ 3 days</td>
<td>61.1</td>
<td>60</td>
<td>63.8</td>
<td>57.9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

• A significant proportion of patients with MS and RIS not treated with thrombolytics have suboptimal discharge outcomes.
Stroke Severity

- **Severe** strokes NIHSS > 22
  - tPA within 3 hours proven clinical benefit despite increased hemorrhagic transformation risk
- **Mild** strokes
  - No exclusion for mild but disabling stroke symptoms
  - Complete hemianopsia (≥2 on NIHSS) or severe aphasia (≥2 on NIHSS)
  - Visual or sensory extinction (≥1 on NIHSS)
  - Any weakness limiting sustained effort against gravity (≥2 on NIHSS)
  - Any deficits that lead to a total NIHSS score >5
- **Rapidly improving** strokes
  - IV tPA is reasonable for patients that demonstrate early improvement but remain impaired or disabled
Case 1

• 55 RHF with h/o HTN, hyperlipidemia, and depression presents to the ED 30 minutes after onset of severe dysarthria and unable move her right UE and LE.
  – Initial NIHSS 8 (2 dysarthria, 2 face, 2 RUE, 2 RLE)
  – After CT NIHSS 3 (1 dysarthria, 1 face, 1 RUE)

• What do you do now?
Case 1

- No tPA and NIHSS 10 at discharge, LOS 9 days
Case 2

- 38 M with h/o HTN, migraine, and depression presents to the ED 60 minutes after he was unable to produce comprehensible speech. His wife says that this has never happened before.
  - NIHSS 2 (2 severe dysarthria)
Case 2

- No change in NIHSS after CT
- What do you do?
Stroke Mimics

• Non-vascular disease that presents with stroke-like clinical picture

• Often times presentation is indistinguishable from ischemic stroke syndrome

• General Principles
  – Stroke: **NEGATIVE** symptoms
  – Stroke Mimics: **POSITIVE** symptoms
## Stroke Mimics

<table>
<thead>
<tr>
<th>Neurological Conditions</th>
<th>Cardiovascular Disorders</th>
<th>Psychiatric Disorders</th>
<th>Infectious Conditions</th>
<th>Inner Ear Conditions</th>
<th>Metabolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure with Todd’s paralysis</td>
<td>Syncope</td>
<td>Syncope</td>
<td>Viral encephalitis</td>
<td>Labyrinthitis</td>
<td>Severe hyponatremia</td>
</tr>
<tr>
<td>Brain Tumor</td>
<td>HTN Encephalopathy</td>
<td>Conversion Disorder</td>
<td>Basilar meningitis (eg TB)</td>
<td>Vestibular neuronitis</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>Demyelinating disorder (eg MS)</td>
<td></td>
<td>Malingering</td>
<td>Brain Abscess</td>
<td>BPV</td>
<td>Hypoglycemic hyperosmolar nonketotic state</td>
</tr>
<tr>
<td>Myasthenia Gravis</td>
<td></td>
<td>Factsitious Disorder</td>
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<tr>
<td>Bell’s Palsy</td>
<td></td>
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<tr>
<td>Complicated Migraines</td>
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<tr>
<td><strong>Infectious Conditions</strong></td>
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</table>

**Explanation:**

- **Neurological Conditions**
  - Seizure with Todd’s paralysis
  - Brain Tumor
  - Demyelinating disorder (eg MS)
  - Myasthenia Gravis
  - Bell’s Palsy
  - Complicated Migraines

- **Cardiovascular Disorders**
  - Syncope
  - HTN Encephalopathy

- **Psychiatric Disorders**
  - Conversion Disorder
  - Malingering
  - Factsitious Disorder

- **Infectious Conditions**
  - Viral encephalitis
  - Basilar meningitis (eg TB)
  - Brain Abscess

- **Inner Ear Conditions**
  - Labyrinthitis
  - Vestibular neuronitis
  - BPV

- **Metabolic**
  - Severe hyponatremia
  - Hypoglycemia
  - Hepatic encephalopathy
  - Hypoglycemic hyperosmolar nonketotic state
Safety of Intravenous Thrombolysis in Stroke Mimics
Prospective 5-Year Study and Comprehensive Meta-Analysis

Georgios Tsivgoulis, MD; Ramin Zand, MD; Aristeidis H. Katsanos, MD; Nitin Goyal, MD; Ken Uchino, MD; Jason Chang, MD; Eftimios Dardiotis, MD; Jukka Putaala, MD; Anne W. Alexandrov, PhD; Marc D. Malkoff, MD; Andrei V. Alexandrov, MD

A

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Stroke Mimics Events</th>
<th>Acute Ischemic Stroke Events</th>
<th>Total</th>
<th>Total Weight</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Houston</td>
<td>0</td>
<td>24</td>
<td>406</td>
<td>9.0%</td>
<td>0.12 [0.01, 1.93]</td>
</tr>
<tr>
<td>Madrid</td>
<td>0</td>
<td>18</td>
<td>606</td>
<td>9.2%</td>
<td>1.03 [0.06, 16.28]</td>
</tr>
<tr>
<td>Mannheim</td>
<td>0</td>
<td>11</td>
<td>606</td>
<td>8.9%</td>
<td>0.61 [0.04, 10.24]</td>
</tr>
<tr>
<td>Memphis</td>
<td>1</td>
<td>29</td>
<td>516</td>
<td>17.9%</td>
<td>0.24 [0.03, 1.72]</td>
</tr>
<tr>
<td>Michigan</td>
<td>0</td>
<td>8</td>
<td>151</td>
<td>9.3%</td>
<td>1.28 [0.08, 19.97]</td>
</tr>
<tr>
<td>Multicenter</td>
<td>1</td>
<td>275</td>
<td>4995</td>
<td>18.4%</td>
<td>0.18 [0.03, 1.28]</td>
</tr>
<tr>
<td>Phoenix</td>
<td>0</td>
<td>24</td>
<td>483</td>
<td>9.0%</td>
<td>0.17 [0.01, 2.81]</td>
</tr>
<tr>
<td>Pittsburgh</td>
<td>0</td>
<td>21</td>
<td>222</td>
<td>9.4%</td>
<td>0.52 [0.03, 7.96]</td>
</tr>
<tr>
<td>St. Louis</td>
<td>0</td>
<td>7</td>
<td>100</td>
<td>8.8%</td>
<td>0.32 [0.02, 5.40]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>392</td>
<td>8085</td>
<td>100.0%</td>
<td></td>
<td>0.33 [0.14, 0.77]</td>
</tr>
<tr>
<td>Total events</td>
<td>2</td>
<td>417</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.06$, $df = 8$ (P = 0.93), $I^2 = 0\%$
Test for overall effect: $Z = 2.58$ (P = 0.010)
Safety and Outcomes of Intravenous Thrombolysis in Stroke Mimics
A 6-Year, Single-Care Center Study and a Pooled Analysis of Registered Studies

Safety of Intravenous Thrombolysis within 4.5 h of Symptom Onset in Patients with Negative Post-Treatment Stroke Imaging for Cerebral Infarction

Intravenous thrombolytic therapy in patients with stroke mimics: baseline characteristics and safety profile
Y. Chen1, V. Bogosavljevic3, D. Leys2, D. Jovanovic3, L. Beslac-Bumbasirevic3, C. Lucas1

Stroke Mimics Treated with Thrombolysis: Further Evidence on Safety and Distinctive Clinical Features
Marta Guillan, Araceli Alonso-Canovas, Jaime Gonzalez-Valcarcel, Nuria Garcia Barragan, Juan Garcia Caldentey, Ignacio Hernandez-Medrano, Alicia DeFelipe-Mimbrera, Victor Sanchez-Gonzalez, Elena Terecoasa, Maria Alonso de Leciñana, Jaime Masjuan
Case 2

- Got tPA, improved in the NeuroICU
- Went home the next day with no deficits
Case 3

79 RHM with a history of CAD, hypertension, and diabetes presents to the ED 185 minutes after onset of mild dysarthria, difficulty naming and paucity in his speech and mild right hand weakness. Initial NIHSS 2 (1 dysarthria, 1 aphasia).
Criteria for IV tPA for 3 to 4.5 Hour Window

**Inclusion**
- Measurable neurological deficit
- Onset of Sx < 4.5 hours
- Age 18 to 80

**Exclusion**
- Age > 80
- NIHSS > 25
- Not on any oral anticoagulants
- History of diabetes and prior stroke
- Imaging evidence of ischemic injury > 1/3 MCA territory

ECASS III 2008
Case 3

- Got tPA, remained stable with NIHSS 2
- MRI showed small insular stroke and MRA showed resolution occlusion.
Case 4

- 61 RHM with h/o HTN, DM, and CAD presents to the ED with 2 hours of fluctuating right arm and leg weakness with occasional numbness then developed speech issues and complete hemiparesis 15 minutes after arrival
  - NIHSS 19 (2 face, 5 RUE motor, 5 RLE motor, 2 sensory, 2 dysarthria, 3 aphasia)
• What do you do here?
Large Vessel Occlusion

Scope of Problem

**Common**
- 35-40% of all AIS cases

**Severe**
- 4.5-fold increase in mortality
- 3-fold reduction in functional independence at 90 day follow-up (mRS 0-2)

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**Respond poorly to intravenous thrombolytic (IV-tPA)**
- Successful opening of occlusion by Intravenous tPA:
  - Internal Carotid Artery Terminus: 4-8%
  - Middle Cerebral Artery – M1: 24-32%
  - Middle Cerebral Artery – M2: 31-44%

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Saqqur et al Stroke 2007
Smith et al Stroke 2009
Smith et al Neurocri Care 2006
Del Zoppo et al Ann Neuro 1997
Bhatia et al Stroke 2010
Impact of Clot Burden

Overview
- 138 Patients
- Acute MCA occlusion
- All treated with IV-tPA within 3 hours of symptom onset

44.9% recanalized overall

Reidel et al Stroke 2011
Endovascular Trials
New England Journal of Medicine
2014-2015

**MR CLEAN**
A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

**EXTEND-IA**
Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

**ESCAPE**
Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

**REVASCAT**
Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

**SWIFT PRIME**
Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke
## The Setup

<table>
<thead>
<tr>
<th>Feature</th>
<th>MR CLEAN(^1) (Netherlands)</th>
<th>ESCAPE(^2) (Global)</th>
<th>EXTEND IA(^3) (AUS, NZ)</th>
<th>SWIFT PRIME(^4) (Global)</th>
<th>REVASCAT(^5) (Spain)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomization of patients to best medical care vs best medical care + Endovascular</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Time Window Studied</td>
<td>Onset to 6 hours</td>
<td>Onset to 12 hours</td>
<td>Onset to 6 hours</td>
<td>Onset to 6 hours</td>
<td>Onset to 8 hours</td>
</tr>
<tr>
<td>Number of Patients</td>
<td>500</td>
<td>316</td>
<td>70</td>
<td>196</td>
<td>206</td>
</tr>
<tr>
<td>Age</td>
<td>&gt;18</td>
<td>&gt;18</td>
<td>&gt;18</td>
<td>18-80</td>
<td>18-80</td>
</tr>
<tr>
<td>Analysis of Primary Endpoint</td>
<td>Rankin Shift</td>
<td>Rankin Shift</td>
<td>Reperfusion at 24 hrs and dramatic NIHSS improvement at 3d</td>
<td>Rankin Shift</td>
<td>Rankin Shift</td>
</tr>
<tr>
<td>Imaging Modality</td>
<td>NCCT/CTA</td>
<td>NCCT, CTA, Collateral assessment on multiphase CTA ASPECTS</td>
<td>NCCT, CTA, CTP Mismatch</td>
<td>NCCT, CTA, CTP or MRI/MRA/PWI</td>
<td>CTA or MRA, ASPECTS</td>
</tr>
<tr>
<td>Median baseline NIHSS</td>
<td>18/17</td>
<td>17/16</td>
<td>13/17</td>
<td>17/17</td>
<td>17/17</td>
</tr>
<tr>
<td>Type of Devices</td>
<td>Any Device (97.4% Stent Retrievers)</td>
<td>Any Device (86.1% Stent Retrievers)</td>
<td>100% Solitaire™ Device</td>
<td>100% Solitaire™ Device</td>
<td>100% Solitaire™ Device</td>
</tr>
<tr>
<td>Statistically Significant Benefit</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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</tbody>
</table>
Target Mismatch Profile

TMM with successful reperfusion

TMM without successful reperfusion
Outcomes Summary

<table>
<thead>
<tr>
<th>Study</th>
<th>Control</th>
<th>Endovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR CLEAN</td>
<td>19%</td>
<td>33%</td>
</tr>
<tr>
<td>REVASCAT</td>
<td>28%</td>
<td>44%</td>
</tr>
<tr>
<td>ESCAPE</td>
<td>29%</td>
<td>53%</td>
</tr>
<tr>
<td>SWIFT PRIME</td>
<td>35%</td>
<td>60%</td>
</tr>
<tr>
<td>EXTEND-IA</td>
<td>40%</td>
<td>71%</td>
</tr>
</tbody>
</table>

P-values:
- P<0.5
- P<0.05
- P<0.001
- P<0.001
- P<0.01
Number Needed to Treat to Achieve an Independent Outcome at 90 days (mRS 0-2)

MR CLEAN\(^1\)  
ESCAPE\(^2\)  
EXTEND-IA\(^3\)  
SWIFT PRIME\(^4\)  
REVASCAT\(^5\)
# Thrombectomy Meta-Analysis

**Trials:**
- SWIFT PRIME, ESCAPE, EXTEND-IA, REVASCAT

**NNT for an extra patient to achieve an independent outcome at 90 days (mRS 0-2)**
- 4.25 (95% CI 3.29-5.99)

<table>
<thead>
<tr>
<th>Outcome at 90 days</th>
<th>Intervention (n=401)</th>
<th>Control (n=386)</th>
<th>Unadjusted Effect Size Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRS 0-2</td>
<td>216 (54.0%)</td>
<td>119 (31.5%)</td>
<td>2.6 (1.9-3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Safety</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mortality</td>
<td>48 (12.0%)</td>
<td>63 (16.3%)</td>
<td>0.69 (0.43-1.1)</td>
<td>0.12</td>
</tr>
<tr>
<td>Symptomatic intracerebral hemorrhage</td>
<td>10 (2.5%)</td>
<td>11 (2.8%)</td>
<td>0.87 (0.36-2.1)</td>
<td>0.76</td>
</tr>
<tr>
<td>Parenchymal Hematoma</td>
<td>32 (8.0%)</td>
<td>31 (8.0%)</td>
<td>1.0 (0.57-1.8)</td>
<td>0.96</td>
</tr>
</tbody>
</table>
Thrombectomy Meta-Analysis

Trials:
- MR CLEAN, ESCAPE, EXTEND-IA, REVASCAT, and SWIFT PRIME

NNT for one patient to have reduced disability of at least 1 point on mRS
2.6

<table>
<thead>
<tr>
<th>Outcome at 90 days</th>
<th>Intervention</th>
<th>Control</th>
<th>Unadjusted Effect Size Odds Ratio (95% CI)</th>
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<tr>
<td>mRS 0-2</td>
<td>46.0% (291/633)</td>
<td>26.5% (171/645)</td>
<td>2.35 (1.85-2.98)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Safety</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>15.3% (97/633)</td>
<td>18.9% (122/646)</td>
<td>0.77 (0.54-1.10)</td>
<td>P=0.16</td>
</tr>
<tr>
<td>Symptomatic intracranial hemorrhage</td>
<td>4.4% (28/634)</td>
<td>4.3% (28/653)</td>
<td>1.07 (0.62-1.83)</td>
<td>P=0.81</td>
</tr>
<tr>
<td>Parenchymal Hematoma type 2</td>
<td>5.1% (32/629)</td>
<td>5.3% (34/641)</td>
<td>0.99 (0.60-1.63)</td>
<td>P=0.97</td>
</tr>
</tbody>
</table>
Patients eligible for r-tPA should receive r-tPA even if endovascular treatments are being considered. *(Class I; Level of Evidence A)*

Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria *(Class I; Level of Evidence A) (New recommendation)*:

- prestroke mRS score 0 to 1,
- acute ischemic stroke receiving intravenous r-tPA according to guidelines from professional medical societies,
- causative occlusion of the internal carotid artery or proximal middle cerebral artery (M1),
- age ≥18 years,
- NIHSS score of ≥ 6,
- ASPECTS of ≥ 6, and
- treatment can be initiated (groin puncture) within 6 hours of symptom onset
Case 4

- Received tPA and taken for a thrombectomy
- Left hospital with NIHSS 2 (1 RUE, 1 RLE)
Case 5

- 75 year right handed gentleman with a past medical history of hypertension on losartan
- April 2016 - He was normal the night before but did not wake up at his normal time
- His family had to arouse him
- When awake he was not able to talk

- EMS was called he was taken to the OSH ED
- Vitals: HR 78, BP 169/85, RR 16, 37.8C, O2 sat 98% RA
- At the hospital he had subtle right sided weakness and was not producing any speech

- He was outside an acute treatment window
- ECG – normal sinus rhythm
- Labs – Unremarkable
Transthoracic Echocardiogram

- The LV systolic function is normal. The estimated LV ejection fraction is 60%.
- Mild concentric left ventricular hypertrophy.
- The left ventricular diastolic function is abnormal. Stage I: Impaired early left ventricular relaxation (Abnormal relaxation pattern).
- The left atrium is normal in size and structure.
- The right atrium is normal in size and structure.
Case 5

- Discharged with Aspirin 81 mg daily and Atorvastatin 80 mg daily
- Physiotherapy with speech therapy
- 48 hour Holter Monitor as an outpatient

- 5/15/2017 Clinic visit
- Insertable cardiac monitor placed on 5/31/2017
Cryptogenic Stroke and Underlying Atrial Fibrillation

Tommaso Sanna, M.D., Hans-Christoph Diener, M.D., Ph.D., Rod S. Passman, M.D., M.S.C.E., Vincenzo Di Lazzaro, M.D., Richard A. Bernstein, M.D., Ph.D., Carlos A. Morillo, M.D., Marilyn Mollman Rymer, M.D., Vincent Thijs, M.D., Ph.D., Tyson Rogers, M.S., Frank Beckers, Ph.D., Kate Lindborg, Ph.D., and Johannes Brachmann, M.D., for the CRYSTAL AF Investigators*

• To assess whether a long-term cardiac monitoring strategy with an implantable cardiac monitor (ICM) is superior to standard monitoring for the detection AF in patients with Cryptogenic stroke.

• Determine the proportion of patients with cryptogenic stroke that have underlying AF.

• Determine actions taken after patient is diagnosed with AF

• **Primary endpoint:** Detection of AF at 6 months
CRYSTAL-AF

Hazard ratio, 8.8 (95% CI, 3.5 - 22.2)
P < 0.001 by log-rank test.

More AF detected at:
- 6 months: 8.9% in ICM group vs. 1.4% in control
- 12 months: 12.4% in ICM group vs. 2.0% in control
- 36 months: 30% in ICM group vs. 3.0% in control

Sanna et al. NEJM 2014
Conclusions

• ICM is superior to standard monitoring in detection of AF at 6 months (HR = 6.43), 12 months (HR=7.32), and 36 months (HR=8.78) in patients with cryptogenic stroke

• AF was detected in 8.9%, 12.4%, and 30% of patients at 6 months, 12 months, and 36 months in the ICM arm

• 92.3% of patients with AF in the ICM arm had a day with greater than 6 minutes of AF

• Detection of AF changed management to anticoagulation in 97% of patients

• Long-term continuous monitoring should be performed in patients with cryptogenic stroke

Sanna et al NEJM 2014
Case 5

• 2 months later
  – ICM detected Atrial fibrillation!

• Started on DOAC

• Currently no repeat stroke
THE NEXT
BIG
THING
• **68M** with no past medical history
  **woke up** at 6:30AM with severe aphasia, dysarthria, and right sided face/arm/leg weakness

• Enrolled patients up to 24 hours of last known well with LVO
• Presented at OSH, airlifted given ineligibility for IV t-PA. Groin Puncture @ noon.

• NIHSS=2 @ 24HR

• Normal at discharge.
Challenges

Primary Center

Comprehensive Center

Mobile Stroke Unit

Acute Stroke Ready

Basic (Level IV)
National Landscape

- 60% of US population has access to endovascular care
- 4-14% eligible to IA therapy

Adeoye et al. Stroke 2014
Zaidat et al. Neurology 2012
Challenges

• Selective triage by severity (EMS)
  — LAMS, LAG, RACE, CPSSS

• Selective Hospital triage by imaging (ED)
  — Advanced imaging quickly

• Systems of Care (EMS + ED + Hospital)
  — Planning and Coordination with EMS/ED

• Mission Creep (Everywhere)
  — Potential burden on larger centers
  — Lack of endovascular expertise
  — Growth of CSC or PSC
THANK YOU!
Key Inclusion/Exclusion Criteria

Inclusion:
• ≥40 years of age
• Cryptogenic stroke (or clinical TIA), with infarct seen on MRI or CT, within the previous 90 days; and no mechanism (including AF) determined after:
  • 12-lead ECG
  • 24-hour ECG monitoring (e.g. Holter)
  • Transesophageal echocardiography (TEE)
  • CTA or MRA of head and neck to rule out arterial source (ultrasound could be used for patients >55 if that is local practice)
  • Screening for hypercoagulable states in patients <55 years old

Exclusion:
• History of AF or Atrial Flutter
• Permanent indication or contraindication for anticoagulation
• Indication for pacemaker or implantable cardioverter defibrillator

Sanna et al NEJM 2014