Perioperative Stroke and Neuroprotection

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Disclosures

♦ Consulting:
  • Claret Medical, Inc, Sentinel TAVR embolic protection device
  • Keystone Health Inc, Clinical Events Committee, REFLECT Trial

♦ Research:
  • Local Principal Investigator, Gore REDUCE PFO Closure Trial
  • Local Principal Investigator, Bayer NAVIGATE-ESUS Trial
  • Local Principal Investigator, Novartis BAF ICH Trial
  • Local Principal Investigator, Biogen CHARM Study for large hemispheric infarction
  • Principal Investigator, Mallinkrodt Diffusion Optical Monitoring of Inhaled Nitric Oxide (DOMINO) study
  • Co-Principal Investigator, Gore Proximal Aortic Disease Outcome Study
  • NIH:
    – U01-DK060990 (Prospective renal insufficiency cohort, stroke endpoint adjudication committee)
    – U01 NS07442504 (iDEF study of desferoxamine for ICH, local PI)
    – UM1 HL088957-06 NIH/NHLBI (CT Surgery Network, sub-investigator)
Overview

- Perioperative stroke incidence and outcomes
- Embolic protection and neuroprotection
- Neurologic “clearance”
- Antithrombotic management
- Post-operative stroke interventions
“Next, an example of the very same procedure when done correctly.”
Actor Bill Paxton’s stroke during heart surgery: What were the odds?

Updated: FEBRUARY 27, 2017 — 1:05 PM EST
Periprocedural Ischemic Neurologic Injury Is Common

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Ischemic Neurologic Complication Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic CEA or stenting</td>
<td>Stroke in 3 – 10%</td>
</tr>
<tr>
<td>Asymptomatic CEA or stenting</td>
<td>Stroke in 1 – 3%</td>
</tr>
<tr>
<td>CABG</td>
<td>Stroke in 1 – 4%</td>
</tr>
<tr>
<td>Cardiac Valve Replacement</td>
<td>Stroke in 1 – 10%</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>Stroke in 0.3 – 0.5%</td>
</tr>
<tr>
<td>Heart Transplant and LVAD</td>
<td>Stroke in 3 – 10%</td>
</tr>
<tr>
<td>Cerebral aneurysm clipping or coiling</td>
<td>Stroke in 3 – 10%</td>
</tr>
<tr>
<td>Descending thoracic aorta and thoracoabdominal aorta repair</td>
<td>Stroke in 1 – 9%</td>
</tr>
<tr>
<td></td>
<td>Spinal infarct in 4 – 23%</td>
</tr>
</tbody>
</table>
## Periprocedural Ischemic Neurologic Injury Is Common

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Annual # of procedures</th>
<th>Risk of stroke</th>
<th>Estimated # of events</th>
</tr>
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<tbody>
<tr>
<td>Symptomatic CEA or stenting</td>
<td>70,000</td>
<td>6%</td>
<td>4,200</td>
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<tr>
<td>Asymptomatic CEA or stenting</td>
<td>100,000</td>
<td>2%</td>
<td>2,000</td>
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<tr>
<td>CABG</td>
<td>450,000</td>
<td>3%</td>
<td>13,500</td>
</tr>
<tr>
<td>Cardiac Valve Replacement</td>
<td>100,000</td>
<td>5%</td>
<td>5,000</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>2,000,000</td>
<td>0.4%</td>
<td>8,000</td>
</tr>
<tr>
<td>Heart Transplant and LVAD</td>
<td>4,000</td>
<td>7%</td>
<td>300</td>
</tr>
<tr>
<td>Cerebral aneurysm clipping and coiling</td>
<td>30,000</td>
<td>5%</td>
<td>1,500</td>
</tr>
<tr>
<td>Descending thoracic aorta and thoracoabdominal aorta repair</td>
<td>20,000</td>
<td>10%</td>
<td>2,000</td>
</tr>
</tbody>
</table>

Periprocedural stroke accounts for ~5% of ALL strokes in the US
Reality Worse Than Literature

- Risk estimates come from trials, case series, and QI databases
  - Clinical practice vs. the trial environment
  - Case series by individual surgeons or centers would not be published if the outcomes were not positive
  - Self reported quality databases of ? reliability

- Most studies do not include active ascertainment or systematic evaluation of patients by neurologists

<table>
<thead>
<tr>
<th>Risk of Stroke at Follow-up, d</th>
<th>Passive Ascertainment, % (95% CI)</th>
<th>Active Ascertainment, % (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>3.1 (1.7-4.6)</td>
<td>9.9 (4.9-14.9)</td>
<td>.02</td>
</tr>
<tr>
<td>30</td>
<td>6.4 (4.2-8.5)</td>
<td>13.4 (9.8-17.1)</td>
<td>.004</td>
</tr>
<tr>
<td>90</td>
<td>8.7 (6.3-11.1)</td>
<td>17.3 (9.3-25.3)</td>
<td>.11</td>
</tr>
</tbody>
</table>

Anyanwu et al. Journal of Thoracic and Cardiovascular Surgery, 2002
Cost of Procedural Stroke Is High

- Stroke after cardiac surgery
  - doubles the duration and cost of hospitalization
  - portends a 5-10-fold increase in early mortality
  - >2/3 of survivors suffer major disability

Messe et al, Circulation, 2014
Perioperative Stroke Rates in Clinical Practice?
Neurologic Complications of Thoracic Aortic Procedures
Neurologic Complications of Thoracic Aortic Procedures

- **Review of 224 open high risk DTA/TAAA surgeries**
  - Ischemic neurologic complications occurred in 85 (38%)
    - 63 (28%) had spinal ischemia
    - 13 (6%) had a stroke
    - 9 (4%) had both

- **Thirty day in-hospital mortality was 40/224 (18%)**
  - 64% with a stroke died vs 17% without (P<0.001)
  - 39% with spinal ischemia died vs 14% without (P<0.001).
  - Mortality was 90% among those with permanent paraplegia
Aortic Valve Replacement

- Aortic valve replacement is one of the most common cardiac surgical procedures
- Incidence is increasing
- Stroke risk reported to be 1 - 10%
Determining Neurologic Outcomes from Valve Operations (DeNOVO) Study

- Prospective cohort of patients undergoing aortic valve surgery and non-surgical controls
- Subjects receive preoperative and postoperative MRI and neurologic/cognitive assessments
- Post operative in hospital evaluations performed by neurologists

NIH/NHLBI RO1 HL084375-01 (PI: Thomas Floyd)
DeNOVO Results

- 196 patients underwent AVR
  - age 75.8 ± 6.2 years
  - 36% female
  - 6% non-white
- 10 (5%) died in hospital
- 34 (17%) had a clinical stroke
  - 32 ischemic strokes
  - 2 hemorrhages
- Most strokes were mild
  - Median NIHSS 3 (IQR 1-9)

Impact of Stroke

- **Stroke was associated with increased length of stay in the ICU and total length of stay**
  - ICU days median 3 days (IQR 2 - 5) vs 1 day (IQR 1 - 2), \( p=0.0006 \)
  - Total length of stay, median 12 days (IQR 9 - 15) vs 10 days (IQR 8 - 13), \( p=0.01 \)

- **Stroke was also associated with increased total hospital billing charges**
  - Median $281,012 (IQR $218,754 - $304,031) vs $209,807 (IQR $175,163 - $273,755), \( p=0.003 \).

Impact of Stroke

- Overall, stroke was not associated with mortality
  - 9% vs 4%, p=0.28
- Moderate-to-severe stroke (NIHSS>5) in 12 (6%)
  - Associated with increased mortality (25% vs 4%, p=0.02)

DeNOVO Compared to STS

- The number of patients with stroke reported in the STS database was 13 (6.6%)
- Strokes in the STS database were more severe
  - Median NIHSS 5 (IQR 3-13) vs 1 (IQR 1-8), p=0.14
MRI Results

- Post-procedure MRI was performed on 129 subjects (66%).

- DWI lesions were seen in 79 patients (61%)
  - Lesions per patient ranged from 0 – 34
  - Mean number of lesions per patient was 2.3 (SD 4.6) and the median was 1 (IQR 0-3)
  - The total volume of DWI lesions ranged from 16 – 56,000 mm³

- Clinically silent infarcts were seen in 59 of 109 patients without stroke (54%)
  - Not associated with LOS, billing, mortality
Volume of infarcts
Acute infarcts were classified by two neurologists, blinded to clinical information as watershed or embolic using pre-specified criteria.

There was excellent interrater agreement on assessment of infarct type ($\kappa = 0.93$).

Embolic strokes identified in 60 (46%), watershed only strokes in 2 (2%), and both types in 17 (13%).

Conclusions

- **Stroke is a more prevalent complication of SAVR than prior series (STS) suggest**
  - Most strokes are mild
  - Strokes are associated with increased LOS, increase ICU LOS, increased billing charges
  - Moderate-to-severe strokes are strongly associated with mortality
  - Silent infarct on MRI is highly prevalent but does not appear to have short or long term consequences
Effect of Cerebral Embolic Protection Devices on CNS Infarction in Surgical Aortic Valve Replacement: A Randomized Clinical Trial

The **CardioGard** embolic protection cannula

The **Embol-X** intra-aortic filtration device

Neuro outcomes assessed day 1, 3, and 7
MRI on day 7
Disability and cognitive outcomes at day 90

Trial Endpoints

- **PRIMARY**
  - Freedom from clinical or radiographic CNS infarction at 7 (± 3) days post procedure

- **SECONDARY**
  - Composite: 1) clinical ischemic stroke, 2) acute kidney injury (AKI), 3) death ≤30 days after surgery
  - Volume and number of radiographic brain lesions
  - Mortality at 30 days
  - Serious AEs and readmissions within 90 days
  - Delirium 7 days post-operatively
  - Neurocognition at 90 days
Debris Captured

- CardioGard filter – captured debris in 76%
- Embol-X filter – captured debris in 99%
Primary Endpoint*

Freedom From Clinical or Radiographic CNS infarction

**OR of CNS Infarct:**
- **CardioGard Control:** 1.06 (95% CI: 0.60, 1.87)  
  **P = 0.84**
- **Embol-X Control:** 1.40 (95% CI: 0.81, 2.40)  
  **P = 0.22**

<table>
<thead>
<tr>
<th>Group</th>
<th>% of Patients w/ No Infarcts</th>
</tr>
</thead>
<tbody>
<tr>
<td>CardioGard</td>
<td>32.7 %</td>
</tr>
<tr>
<td>Control</td>
<td>34.8 %</td>
</tr>
<tr>
<td>Embol-X</td>
<td>27.1 %</td>
</tr>
<tr>
<td>Control</td>
<td>34.8 %</td>
</tr>
</tbody>
</table>
Clinical Stroke – Overall 6.6%

- Severe (>20)
- Moderate (5-15)
- Mild (0-4)

P-values:
- P=0.61
- P=0.49
- P=0.77
- P=0.99

Percentage of Patients:
- ≤7 Days
- ≤3 Days
MRI in ~90% - Volumetric Analysis
MRI Infarcts and Stroke

- Clinical stroke was strongly associated with volume of infarct
  - Mean 1688mm$^3$ vs 236mm$^3$, between group difference 1452mm$^3$, 95%CI 883 – 2021mm$^3$, p=0.001
Infarct volumes above 191 mm³ are uniformly more likely to be observed among controls (i.e. RR <1 in favor of CardioGard device)

Infarct volumes above 496 mm³ are uniformly more likely to be observed among controls (i.e. RR <1 in favor of Embol-X device)
Delirium at 7 Days

CardioGard vs. Control

Emboli-X vs Control

Active  Control

P=0.03  P=0.07
Neurocognitive Decline at 90 Days

**Verbal Memory**
- CardioGard: P=0.14
- Control: P=0.65
- P=0.82

**Executive Function**
- CardioGard: P=0.40
- Control: P=0.05
- P=0.54

**Overall Cognition**
- CardioGard: P=0.05
- Control: P=0.54

% of Patients w/ Decline

CardioGard vs. Control

Perelman School of Medicine
University of Pennsylvania
In patients undergoing SAVR, the use of 2 different embolic protection device was NOT associated with an improvement in:

- Freedom from clinical or radiographic infarction
- Clinical stroke
- Overall volume of CNS infarcts by MRI
- Neurocognitive outcomes at 90 days
Completed CTSN Neuroprotection Trial

- In patients undergoing SAVR, the use of 2 different embolic protection devices WAS associated with:
  - Capture of embolic debris in majority of patients
  - Numerically fewer early (<3d) severe strokes (1 vs 6)
  - A reduction in prolonged delirium
  - An observed difference in infarct size distribution with fewer large volume infarcts

Does Periop Stroke Matter??

- Perioperative stroke, seen in 7% overall, associated with:
  - Longer length of stay in ICU (6 vs 3) and overall (11 vs 8)
  - Much higher rate of cognitive decline at day 90 (71% vs 28%), p=0.0009
  - Lower QoL at day 90 (SF12 physical health 39 vs 44, p=0.08 and geriatric depression scale >10 in 24% vs 7%, p=0.006)
  - Increased disability at day 90 (modified Rankin score>2 in 17% vs 3%, p=0.01)
Does Periop Delirium Matter??

- Patients with delirium at day 7, present in ~10% overall, associated with:
  - Numerically longer length of stay in ICU (4 vs 3) and overall (10 vs 7)
  - Numerically higher rate of readmission (12% vs 8%, p=0.24)
  - Numerically higher rate of cognitive decline at day 90 (42% vs 29%, p=0.15)
  - Lower QoL at day 90 (SF12 physical health 38 vs 45, p=0.01 and geriatric depression scale >10 in 19% vs 7%, p=0.09)

Stroke and delirium matter!!!
SENTINEL Trial

- Randomized trial of an embolic protection device in 363 TAVR patients

- No difference in DWI lesion volume, 178.0 mm³ in control subjects and 102.8 mm³ in the device arm (p = 0.33)
- No difference in stroke at 30 days, 9.1% in control subjects and 5.6% in patients with devices (p = 0.25)
- Neurocognitive function was similar in control subjects and patients with devices, but there was a correlation between lesion volume and neurocognitive decline (p = 0.0022)
Ischemic Neuroprotection

The holy grail of vascular neurology

© Monty Python
Neuroprotection Studies Failed In Acute Stroke

- Pre-treatment preclinical studies versus post-treatment clinical studies
- Time window too long
- Inadequate concentration of medication reaching tissue at risk
Neuroprotection in the OR

- **Medication or treatment can be given prior to the procedure**
  - Neuroprotectant in tissue when ischemia occurs
  - Can provide proof-of-concept

- **Challenges remain**
  - Most patients do not have clinically meaningful endpoints
  - Safety is paramount
Not a Novel Concept

- **Multiple prior RCTs of pharmacologic agents**
  - Studies included 100 – 350 patients
  - No benefit on primary clinical endpoints
  - All severely underpowered as neurologic events were relatively uncommon

- **Recent studies of remote ischemic preconditioning**
  - Adequately powered
  - No benefit

ENACT Study

- 185 subjects randomized to NA-1 or placebo at completion of aneurysm embolization
- No difference in volume of lesions by DWI MRI (adjusted p value=0.120)
- Fewer infarcts on MRI in the NA-1 group compared to the placebo group, (adjusted incidence rate ratio 0.53, 95% CI 0.38–0.74)

ENACT Results

A

Frequency (%)

B

Lesion count (n)

Placebo

NA-1

0-1 lesion  2-15 lesions  >15 lesions

41%  43%  16%

50%  47%  3%
## ENACT Results

<table>
<thead>
<tr>
<th></th>
<th>NA-1 group</th>
<th>Control group</th>
<th>Relative risk (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>92</td>
<td>93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIHSS score of 0-1</td>
<td>86 (94%)</td>
<td>83 (89%)</td>
<td>1.0 (0.9-1.1)</td>
<td>0.43</td>
</tr>
<tr>
<td>mRS score of 0-2</td>
<td>86 (94%)</td>
<td>87 (94%)</td>
<td>1.0 (0.9-1.1)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Patients with unruptured aneurysms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>74</td>
<td>74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIHSS score of 0-1</td>
<td>68 (92%)</td>
<td>70 (95%)</td>
<td>1.0 (0.9-1.1)</td>
<td>0.75</td>
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<tr>
<td>mRS score of 0-2</td>
<td>69 (93%)</td>
<td>73 (99%)</td>
<td>0.9 (0.88-1.0)</td>
<td>0.21</td>
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<tr>
<td><strong>Patients with ruptured aneurysms</strong></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Number of patients</td>
<td>18</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIHSS score of 0-1</td>
<td>18 (100%)</td>
<td>13 (68%)</td>
<td>1.5 (1.1-2.0)</td>
<td>0.02</td>
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<tr>
<td>mRS score of 0-2</td>
<td>17 (94%)</td>
<td>14 (74%)</td>
<td>1.3 (0.95-1.7)</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Patients with strokes &lt;10 mL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>89</td>
<td>93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIHSS score of 0-1</td>
<td>85 (96%)</td>
<td>83 (89%)</td>
<td>1.1 (0.98-1.2)</td>
<td>0.16</td>
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<tr>
<td>mRS score of 0-2</td>
<td>84 (94%)</td>
<td>87 (94%)</td>
<td>1.0 (0.9-1.1)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

NIHSS—National Institutes of Health stroke scale. mRS—modified Rankin scale. *We detected statistical evidence of effect modification by aneurysm status on the treatment effect (p=0.0073, likelihood ratio test, comparing a logistic regression model with and without a multiplicative interaction term—aneurysm status by treatment, using NIHSS 0-1 at 30 days as the binary outcome).

**Table 4: Pre-specified neurological outcomes at 30 days**
Neurologic “Clearance”
Case

66 year old man with a history of hypertension, diabetes, and prior ischemic stroke (left pontine lacune 3 months prior, on clopidogrel) has stable angina and is diagnosed with triple vessel coronary artery disease.

A CABG is planned.

You are asked to provide “neurologic clearance” for surgery.

What can you tell the patient? What can you tell the surgeon? Should you order any tests?
“Neurologic Clearance”

- There is no formal approach, but we try
- Two important factors - the procedure and the patient

Hoque et al. Circulation.2001; 103: 2133-2137
Procedural Risks for Perioperative Stroke

- High risk surgeries include carotid revascularization, intracranial vascular procedures, cardiac valve surgery (SAVR/TAVR), aortic procedures, and CABG
  - Combined procedures are higher risk
- Other surgical features that may influence stroke risk:
  - General anesthesia > local anesthesia
  - Longer duration of cardiac bypass
  - Lower intra-op BP
  - BP variability/drops in MAP
  - On-pump > off-pump CABG?

Mullen & Messé “Stroke Related to Surgery and Other Procedures” in Stroke: Pathophysiology, Diagnosis, and Management. 6th Ed.
Patient Risks for Perioperative Stroke

● Patient risk factors are similar to predictors of stroke in the general population
  - Advanced age
  - History of CAD, PVD
  - Atrial fibrillation
  - Female sex
  - Prior stroke/TIA.

● CHADS<sub>2</sub>VASc
  - Score < 2 = “Low Risk” (<1%)
  - Score ≥ 4 = “High Risk” (>3%)

### CHADS<sub>2</sub>VASc Score

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>C - Congestive heart failure</td>
<td>+1</td>
</tr>
<tr>
<td>H - Hypertension</td>
<td>+1</td>
</tr>
<tr>
<td>A&lt;sub&gt;2&lt;/sub&gt; - Age ≥ 75</td>
<td>+2</td>
</tr>
<tr>
<td>D - Diabetes</td>
<td>+1</td>
</tr>
<tr>
<td>S&lt;sub&gt;2&lt;/sub&gt; - Prior Stroke/TIA</td>
<td>+2</td>
</tr>
<tr>
<td>V - Vascular Disease</td>
<td>+1</td>
</tr>
<tr>
<td>A - Age 65-74</td>
<td>+1</td>
</tr>
<tr>
<td>S - Sex (Female)</td>
<td>+1</td>
</tr>
</tbody>
</table>
Patient Risks for Perioperative Stroke

- Prior stroke – important questions
  - How big?
  - How recent?

2 weeks
3-6 months
1 year

Patient Risks for Perioperative Stroke

Prior stroke – important questions

- What was the etiology?
  - Large vessel*
  - Cardioembolic
  - Small vessel

66 year old man with a history of hypertension, diabetes, and prior ischemic stroke (left pontine lacune 3 months prior, on clopidogrel) has stable angina and is diagnosed with triple vessel coronary artery disease.

A CABG is planned.

What should we tell the patient and the surgeon?
Case

What do we know:

- High risk surgery
- High risk patient
  - $\text{CHA}_2\text{DS}_2\text{VASc}=6$
- Prior stroke
  - Mechanism is relatively low risk
  - Time period is moderate

- Can the CABG wait?
- Continue the antiplatelet medication
- Avoid hypotension and swings in BP if possible
The most common question we are asked…

Continuing antithrombotics may increase bleeding risk, while stopping antithrombotics may increase stroke risk

- A primary care database including 39,512 patients receiving aspirin for secondary prevention found that stroke risk was higher within 1–15 days after the last dose, with a RR of 1.97 (95% CI 1.24 to 3.12)

Most stroke patients undergoing dental, dermatological, and spinal/epidural procedures should probably continue aspirin (Level B).

Some patients undergoing retrobulbar/peribulbar block, electromyography, transbronchial lung biopsy, colonoscopic polypectomy, upper endoscopy and biopsy, and sphincterotomy should possibly continue aspirin (Level C).

Other procedures lacked the statistical precision to exclude clinically important bleeding risks with aspirin continuation (Level U). Aspirin possibly increases transfusion risks during orthopedic hip procedures (Level C).

Most stroke patients should continue warfarin when undergoing dental (Level A) or dermatologic (Level B) procedures.

Warfarin is possibly associated with no increase in clinically important bleeding with electromyography and inguinal herniorrhaphy (Level C).

Other procedures lacked statistical precision to rule out clinically important bleeding.
Anticoagulation – Role of Bridging Therapy

**Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation**

- 1884 subject randomized trial
- Halt warfarin 5 days pre-op
- Given LMWH or Placebo from 3 days pre-op to 5-10 days post-op
  - LMWH stopped 24 hours before procedure and restarted 24-72 hours after based on presumed bleeding risk

*Douketis et al. NEJM. 2015. 373;9:823.*
“God, this is going to be all over YouTube.”
What Can Be Done Once a Stroke is Identified After a Procedure?
Only One Proven Therapeutic Approach

- **Vessel Recanalization**
  - Intravenous thrombolysis
  - Intra-arterial
    - Thrombolysis
    - Mechanical
Case Example

- 66 year-old man POD 2 from CABG, found to have left facial droop, left field cut, slurred speech, right gaze preference and left arm and leg weakness at 7:30 am, last seen normal by the nurses at 7:00 am
Avalanche of Positive IA Trials
<table>
<thead>
<tr>
<th>TRIAL</th>
<th>MR CLEAN</th>
<th>ESCAPE</th>
<th>SWIFT PRIME</th>
<th>EXTEND IA</th>
<th>REVASCAT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Netherlands</td>
<td>Calgary, international</td>
<td>US, international</td>
<td>Australia/NZ</td>
<td>Spain</td>
</tr>
<tr>
<td>Window</td>
<td>6 hours</td>
<td>12 hours</td>
<td>6 hours</td>
<td>6 hours</td>
<td>8 hours</td>
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<tr>
<td># pts</td>
<td>500</td>
<td>314</td>
<td>196</td>
<td>70</td>
<td>206</td>
</tr>
<tr>
<td>NIHSS (median)</td>
<td>17,18</td>
<td>16,17</td>
<td>17,17</td>
<td>17,13</td>
<td>17,17</td>
</tr>
<tr>
<td>tPA use</td>
<td>89%</td>
<td>73%, 79%</td>
<td>Required</td>
<td>Required</td>
<td>68, 77%</td>
</tr>
<tr>
<td>Stroke Onset Time to groin puncture (min)</td>
<td>260</td>
<td>185</td>
<td>184</td>
<td>210</td>
<td>269</td>
</tr>
<tr>
<td>Stroke Onset Time to mTICI 2b/3 (min)</td>
<td>241</td>
<td>252 (first deployment of stent retriever)</td>
<td>248</td>
<td>355</td>
<td></td>
</tr>
<tr>
<td>mTICI 2b/3 flow</td>
<td>58.7%</td>
<td>72.4%</td>
<td>88%</td>
<td>86%</td>
<td>65.7%</td>
</tr>
<tr>
<td>mRS shift</td>
<td>OR 1.67</td>
<td>OR 2.6</td>
<td>P=.0002 (CMH)</td>
<td>OR 2</td>
<td>OR 1.7</td>
</tr>
<tr>
<td>mRS 0-2</td>
<td>32.6 vs 19.1% (13.5%)</td>
<td>53 vs 29.3% (23.8%)</td>
<td>60.2 vs 35.5% (24.7%)</td>
<td>71 vs 40% (31%)</td>
<td>43.7 vs 28.2% (15.5%)</td>
</tr>
<tr>
<td>NTT</td>
<td>7</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>6-7</td>
</tr>
</tbody>
</table>

**HERMES Meta-analysis: NNT 2.6 for less disability on mRS**

R MCA Occlusion, Treated with Stentreiver
Case Continued

At discharge, he had mild left sided weakness (~5-/5)
Does Time Matter?

- Likelihood of good outcome is strongly associated with time from imaging to reperfusion

Tsai et al.  Stroke. 2018;49
In Hospital Stroke

- ~2/3 are post-operative patients
- More severe and worse outcome
- Often identified in a delayed fashion and less likely to be treated with an intervention
- Nursing and physician education is paramount
- Education and frequent neuro checks!!!
Summary

- Perioperative stroke is common and has a profoundly negative impact on outcomes
- Stroke risk depends on the surgery and the patient
- Risk factors for stroke are generally non-modifiable
  - Age, vascular disease, prior stroke
  - CHA₂DS₂-VASc ≥ 4 is HIGH RISK
- Recent stroke is a strong risk factor
  - Wait at least 3mo for elective procedures
  - Wait > 6mo if possible
- Antithrombotic therapy
  - Continue when possible
    - Reasonable to stop aspirin for major non-CV open procedures, definite stop when a small amount of bleeding would be devastating
    - Bridging anticoagulation is associated with increased risk of bleeding
- Stroke is treatable!!!
  - Frequent neuro checks for high risk patients
Questions?

"Yee-ouch! That's gotta hurt."
Carotid Stenosis
Carotid Stenosis

- Screening carotid imaging not recommended for non-cardiac surgeries
- What about cardiac surgery?

  - Reasonable to screen **high risk** patients:
    - ≥65 years old, concomitant left main coronary disease, peripheral vascular disease, history of prior stroke/TIA, or a carotid bruit

  - HOWEVER, if asymptomatic carotid stenosis is identified, it is uncertain:
    - Whether it should be fixed
    - How to fix it
    - When to fix it

References:

Hillis et al. ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. 2011
Naylor AR et al. Eur J Vasc Endovasc Surg. 2011;41:607-624
Mahmoudi et al. Stroke. 2011;42:2801-2805
Carotid Stenosis?

- The data is poor but generally indicates that a unilateral asymptomatic stenosis should not be intervened upon
  - A 2011 meta-analysis demonstrated that the risk of perioperative stroke after cardiac surgery was only increased for patients with prior stroke/TIA or complete occlusion of the carotid artery
  - A retrospective study of 117 patients with severe asymptomatic carotid stenosis (≥75 percent) compared to 761 patients without severe carotid stenosis had similar rates of stroke (3.4 versus 3.6 percent) and mortality (3.4 versus 4.2)
Guidelines on Carotid Stenosis

- Carotid screening prior to high risk surgeries, including coronary artery bypass grafting, should be limited to selected high risk patients
  - ≥65 years old, concomitant left main coronary disease, peripheral vascular disease, history of prior stroke/TIA, or a carotid bruit

- The utility of pre-operative or simultaneous carotid revascularization is uncertain, but is not likely to be beneficial unless the patient is recently symptomatic or has severe bilateral asymptomatic disease.

Hillis et al ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. 2011
If the patient requires CABG, it may be best to perform carotid stenting, and do it first...

Pre-CABG Asymptomatic Carotid Stenosis

Carotid Stenosis Present

Unilateral disease (50-99%)
- Carotid revascularization NOT required
- Maintain Mean Arterial Pressure during surgery

Bilateral disease (70-100%)
- Fix 1 of the arteries (dominant preferred)
- CABG Urgent?
  - YES! Combined CEA-CABG
  - NO! Consider CAS-CABG