Approaches to Common Clinical Scenarios in Hospitalized Stroke Patients

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DISCLOSURES

Medscape Neurology Editorial Advisory Board
Objectives

To review common consult questions:

• Which antiplatelet(s) to use when my patient is already on clopidogrel and has a recurrent stroke?
• Can my patient with a history of stroke stop his aspirin prior to surgery (and related questions)?
• Should I consider other approaches or is it just IV tPA now for acute stroke?

Patient Case: Antithrombotics in Recurrent Stroke

Mrs. H. has been on clopidogrel since having a TIA that occurred while she was on aspirin. A week ago she had a right frontal infarct. She has no known cardioembolic cause.

What should her treatment be?

1) Keep her on clopidogrel
2) Add aspirin to the clopidogrel
3) Switch her to Aggrenox (ER dipyridamole and aspirin)
PRoFESS Trial

- Stroke prevention trial in 20,332 patients
- Aggrenox compared to clopidogrel
  - Showed similar rates of recurrent stroke and major vascular events

*NEJM* 2008;359:1238-51

Clopidogrel vs Aggrenox

- Data don’t support switching from clopidogrel to Aggrenox except in certain cases (i.e., genetic non-responder)
**Clopidogrel Plus Aspirin: When OK ASA Guidelines 2014**

- Symptomatic high grade intracranial stenosis for 3 months as per SAMMPRIS
  - “For patients with recent stroke or TIA (within 30 days) attributable to severe stenosis (70%–99%) of a major intracranial artery, the addition of clopidogrel 75 mg/d to aspirin for 90 days might be reasonable (Class IIb; Level of Evidence B). (New recommendation)”

  *NEJM* 2011;365:993-1003; *Stroke* 2014;45:2160-2236

**Clopidogrel Plus Aspirin: When OK ASA Guidelines 2014**

- Potential benefit in TIA and minor stroke when started within 24 hours as per CHANCE
  - “…Might be considered for initiation within 24 hours of a minor ischemic stroke or TIA and for continuation for 90 days (Class IIb; Level of Evidence B). (New recommendation)

- Investigated in the US for use within 12 hours of high risk TIA or minor stroke and continued for 3 months in POINT

  *NEJM* 2013; 269:11-19; *Stroke* 2014;45:2160-2236; ClinicalTrials.gov
**Clopidogrel Plus Aspirin**
ASA Stroke Prevention Guidelines 2014

- “The combination of aspirin and clopidogrel ...increases the risk of hemorrhage... and is not recommended for routine long-term secondary prevention...”

*Stroke 2014;45:2160-2236*

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**Long-Term Clopidogrel + Aspirin Fails in Stroke**

**MATCH Trial: combination vs clopidogrel**
- No difference in stroke/MI/death or stroke outcomes
- Major bleeds and life-threatening bleeds significantly higher with combination treatment

**SPS3 Trial: combination vs aspirin in lacunes**
- Terminated early due to risks and futility
- Risk of major hemorrhage nearly doubled with dual antiplatelet therapy and mortality increased

Risk Factor Control
ASA Stroke Prevention Guidelines 2014

- Blood pressure goal <140/90
  - For recent lacunar stroke, a target systolic of <130 mm Hg may be reasonable
- Intensive lipid lowering therapy if stroke of presumed atherosclerotic origin
- Smoking cessation, no heavy alcohol use
- Moderate exercise

*Stroke 2014;45:2160-2236*

Patient Case: Patient With Previous Stroke Needs Surgery

Mr. M. needs surgery for his broken hip. However, he had a mild stroke 3 months ago and is on aspirin.

Does stopping aspirin increase his risk of stroke in the weeks following surgery?

1) Yes
2) No
Antithrombotic Medications: “Neurology” Guidelines

**Aspirin**
- Discontinuation probably is associated with increased stroke and TIA risk
  - Relative risk 1.97 if stopped for 2 weeks

**Clopidogrel, ticlopidine or aspirin/dipyridamole**
- Insufficient evidence regarding peri-procedural use

*Neurol 2013;80:2065-2069*

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Are There Markers of Increased Stroke Risk With Surgery?
## Perioperative Ischemic Stroke Risk Rates

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Stroke risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General surgery</td>
<td>0.2</td>
</tr>
<tr>
<td>General surgery with or without carotid bruit</td>
<td>0.5</td>
</tr>
<tr>
<td>General surgery after prior stroke</td>
<td>2.9</td>
</tr>
<tr>
<td>General surgery w/ carotid stenosis and bruit or prior sxs</td>
<td>3.6</td>
</tr>
<tr>
<td>CABG prospective studies</td>
<td>2.0</td>
</tr>
<tr>
<td>CABG surgery after prior stroke or TIA</td>
<td>8.5</td>
</tr>
<tr>
<td>CABG surgery + valve surgery</td>
<td>4.2-13.0</td>
</tr>
<tr>
<td>CABG surgery + unilateral &gt;50% carotid stenosis</td>
<td>3.0</td>
</tr>
<tr>
<td>CABG surgery + bilateral &gt;50% carotid stenosis</td>
<td>5.0</td>
</tr>
<tr>
<td>CABG surgery + carotid occlusion</td>
<td>7.0</td>
</tr>
<tr>
<td>Surgery with symptomatic vertebrobasilar stenosis</td>
<td>6.0</td>
</tr>
</tbody>
</table>


## Risks Specifically With Hip Surgery

**Danish study of total hip replacement  n=66,583**

- 4.7-fold risk of ischemic stroke and 4.4-fold risk of hemorrhagic stroke in the first 2 weeks after hip surgery

- Those patients that had been on an antiplatelet in the outpatient setting had a 70% decreased risk of ischemic stroke 6 weeks post surgery (no effect on ICH)

Stroke 2012;43:3225-3229
But Can Aspirin Be Continued During Surgery?

Patient Case: Patient With Previous Stroke Needs Hip Surgery

Are the bleeding risks with hip surgery low enough that he can continue the aspirin?

1) Yes
2) No
# Bleeding Risk Table: Aspirin and Warfarin

<table>
<thead>
<tr>
<th>Highly likely not to increase bleeding risk</th>
<th>Aspirin&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Warfarin&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental procedures</td>
<td>Dental procedures</td>
<td>Dental procedures</td>
</tr>
<tr>
<td>Invasive ocular anesthesia</td>
<td>Dermatologic procedures (small risk)</td>
<td>Invasive ocular anesthesia</td>
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<tr>
<td>Cataract surgery</td>
<td></td>
<td></td>
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<tr>
<td>Dermatologic procedures</td>
<td></td>
<td></td>
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<tr>
<td>TRUS-guided prostate biopsy</td>
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<td></td>
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<tr>
<td>Spinal/epidural needle procedures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carpal tunnel syndrome surgery</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Likely not to increase bleeding risk</th>
<th>Aspirin&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Warfarin&lt;sup&gt;b&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>Vitreoretinal surgery</td>
<td>EMG</td>
<td></td>
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<tr>
<td>EMG</td>
<td>Prostate procedures</td>
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<tr>
<td>Transbronchial biopsy</td>
<td>Inguinal herniorrhaphy</td>
<td></td>
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<tr>
<td>Colonoscopic polypectomy</td>
<td>Endothermal ablation of the saphenous vein</td>
<td></td>
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<tr>
<td>Upper-gastrointestinal endoscopic biopsy</td>
<td></td>
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<tr>
<td>Sphincterotomy</td>
<td></td>
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<tr>
<td>Ultrasound-guided biopsies</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Possibly does not increase bleeding risk</th>
<th>Aspirin&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Warfarin&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>TURP</td>
<td>Ophthalmologic procedures (other than anesthesia)</td>
<td></td>
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<tr>
<td>Colorectal polypectomy</td>
<td></td>
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<th>Possibly increases bleeding risk</th>
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<th>Warfarin&lt;sup&gt;b&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Orthopedic hip procedures</td>
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**Should Any Other Management Occur Prior to Surgery in a Stroke Patient?**
Patient Case: Patient With Previous Stroke Needs Hip Surgery

The patient has known asymptomatic carotid stenosis. Does the patient need carotid revascularization prior to his hip surgery?

1) Yes
2) No

Preoperative Approaches

Patients with stroke or TIA

• Evaluate for mechanism if surgery is not urgent
• Treat *symptomatic* carotid stenosis with CEA or CAS
• Allow a month to elapse if moderately large stroke

Asymptomatic carotid stenosis

• Does not require surgery with CEA or CAS before *general surgery*
• In selected patients (bilateral stenosis or contralateral occlusion) having CABG, consider CAS first

Should All Patients on Warfarin Be Bridged Before Surgery?

Antithrombotic Medications: “Neurology” Guidelines

Warfarin

- Discontinuation risk hard to assess because of varying anticoagulation indications in subjects
  - Thromboembolic risk increased if stopped for ≥7 days in one study

Non-warfarin oral anticoagulants

- Insufficient evidence regarding periprocedural use

*Neurology* 2013;80:2065-2069
Antithrombotic Medications: “CHEST” Guidelines for Warfarin Interruption

Warfarin

• “In patients with a mechanical heart valve, atrial fibrillation or VTE at high risk for thromboembolism, we suggest bridging anticoagulation instead of no bridging during interruption of VKA therapy (Grade 2C)”

• In atrial fibrillation, CHADS2 score is used for risk stratification

Chest 2012;141(2 suppl):e326S-e350S

Patient Case: Acute Stroke – tPA or More?

Mr. C., a 75 year-old, had the sudden onset of vertigo, dysconjugate gaze, right face and left body weakness on the wards 15 minutes ago. He does not have increased bleeding risks.

Which treatment should be considered?

1) IV tPA
2) IV tPA and endovascular therapy
3) Endovascular therapy alone
Intravenous Thrombolysis

- IV tPA 0-3 hours FDA approved
- IV tPA 3-4.5 hours not approved by FDA but AHA/ASA science advisory and acute stroke treatment guidelines support its use
  - Additional treatment exclusions apply

*NEJM* 2008;359:1317-29; *Stroke* 2009; 40: 2945-8; *Stroke* 2013;44:870-947

Intra-Arterial Thrombolysis

- PROACT II showed the benefit of IA pro-urokinase compared to heparin in MCA occlusions but a confirmatory trial was not done

What is the Controversy Regarding Endovascular Therapy?

**IMS III Randomized Trial**

IV tPA within 3 hrs vs. combined IV tPA + IA tx

- NIHSS ≥ 10
- Baseline CTA not required, but if done needed to show occlusion in M1, ICA or basilar
- IA treatments included either IA tPA or mechanical embolectomy: Merci Retriever, Penumbra System, Solitaire (4 cases only) or EKOS System

*NEJM* 2013; 368:893-903
**IMS III Randomized Trial**

Enrollment Stopped Early for Futility (n=656)

Similar outcomes in both groups:

- Functional independence, mRS 0-2, 40.8% with endovascular treatment versus 38.7% with IV tPA (95% CI -6.1-9.1)
  - Similar after adjustment for the NIHSS score, or those with NIHSS ≥ 20 or ≤ 19
- Mortality at 90 days, 19.1% and 21.6% (p=0.52)
- Symptomatic ICH, 6.2% and 5.9% (p=0.83)

*NEJM* 2013; 368:893-903

**IMS III: Questions**

Unknown if large vessel occlusion was present

- Baseline CTA that showed occlusion in only 43%

Old technologies used for embolectomy

- Stent retrievers only used in 4 cases

Bias in cases included by criteria or choice?

- Median baseline NIHSS of 16-17 lower than in recent embolectomy trials (NIHSS 18-19)
So When Should I Push for Endovascular Treatment in My Acute Stroke Patient?

ASA Acute Stroke Guidelines 2013

- “Intra-arterial fibrinolysis or mechanical thrombectomy is reasonable in patients who have contraindications to the use of intravenous fibrinolysis (Class IIa; Level of Evidence C).”

- “Rescue intra-arterial fibrinolysis or mechanical thrombectomy may be reasonable approaches to recanalization in patients with large-artery occlusion who have not responded to intravenous fibrinolysis. Additional randomized trial data are needed (Class IIb; Level of Evidence B). (New recommendation)”

*Stroke* 2013; 44:870-947
One Treatment Selection Paradigm

• Consider IV tPA in all eligible patients
• Patients with large vessel occlusion that are not tPA candidates are considered for embolectomy
• Vertebro-basilar occlusions are considered for both IV tPA and embolectomy since mortality is 80% without treatment
  — Certain patients with ICA or M1 occlusions also considered for both tPA and embolectomy

Use of Imaging to Select Patients for Endovascular Treatment
**Target Mismatch Pattern**

Before Treatment

After Intra-arterial Therapy

**ASPECTS Scale**
Alberta Stroke Program Early CT Score

One point is subtracted from 10 for any evidence of early ischemic change for each of the defined regions

- Score of ≤7 associated with poor functional outcome and symptomatic ICH

www.aspectsinstroke.com
One US Embolectomy Trial in Progress

**SWIFT PRIME**
- IV tPA (4.5 hrs) versus IV tPA plus embolectomy
  - Age 18-80
  - Intracranial ICA or M1 only
  - ASPECTS <6 by imaging (few early ischemic changes)

54 y/o Woman Found at 10 AM: Last Known At Baseline Previous Evening

Found by family at 10 AM sitting dressed in chair
- Had spoken with husband by phone previous evening

**Telestroke exam**
- Near plegia on right, mute
- NIHSS=21

Outside CT 11:22 AM unremarkable
54 y/o Woman Found at 10 AM

- Not a tPA candidate, treated with embolectomy

Pre treatment

Recanalized after one pass with Trevo device at 14:36
54 y/o Woman Found at 10 AM

• MRI at 10:51 PM showed lesion has not grown appreciably; NIHSS=5 (dysarthria, drift, neglect)
• By the following AM, NIHSS=1 for right naso-labial fold flattening

Any New Recommendations for Supportive Treatments in Acute Stroke?
Supportive Measures for Acute Stroke: ASA Guidelines 2013

- Optimal blood pressure still unknown
  - Consensus to withhold treatment unless >220/120, if the patient is not receiving therapies to recanalize vessels
  - Can restart medications at 24 hours if the patient is stable

- Treat fever and underlying causes
  - Hypothermia has not yet been assessed in Phase 3 trials

- Supplemental oxygen not routinely recommended
  - Maintain saturations at > 94%

*Stroke* 2013; 44:870-947