Minor stroke/TIA risk stratification and management

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Cumulative risk of stroke after a transient ischaemic attack (TIA) or minor stroke
Minor Cerebrovascular Syndrome

One-Year Risk of Stroke after Transient Ischemic Attack or Minor Stroke

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![Figure 1. Cumulative Incidence of the Composite Outcome in the Overall Population.](chart)
The composite outcome included stroke, an acute coronary syndrome, and death from cardiovascular causes.
Transient ischemic attack (TIA): a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction.

Reference to duration of symptoms removed, emphasis on brain imaging.
Most Neuro Spells are TNAs

Transient Neurologic Attacks

Visual: Sees flashes of light, scotomas, unilateral or bilateral blurring

Postcentral gyrus

Precentral gyrus

Central fissure

Les

Left

Right

LEGS

TRUNK

ARM

FACE

Contraversive. Head and eyes turned to opposite side

Focal motor. Tonic-clonic movements of upper (or lower) limb

Auditory. Hears ringing, hissing or noises

Visual. Hears ringing, hissing or noises
Case 1

38 year old
Acute onset of violent vertigo, nausea and vomiting worsening over several hours
# Acute Prolonged Vertigo

**NEJM**

## Table 1. Differential Diagnosis of Common Causes of Acute, Prolonged Vertigo.

<table>
<thead>
<tr>
<th>Cause</th>
<th>History</th>
<th>Physical Examination</th>
<th>Laboratory Testing†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vestibular neuritis</td>
<td>Develops over a period of hours; resolves over a period of days; may follow an influenza-like illness</td>
<td>Spontaneous “peripheral” nystagmus; positive head-thrust test; imbalance</td>
<td>Electronystagmography: unilateral caloric hypoexcitability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Audiography: normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Brain imaging: normal</td>
</tr>
<tr>
<td>Labyrinthitis</td>
<td>Develops over a period of minutes to hours; may be associated with systemic, ear, or meningeval infection</td>
<td>Same as for vestibular neuritis, but also unilateral hearing loss</td>
<td>Electronystagmography: unilateral caloric hypoexcitability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Audiography: moderate-to-severe ipsilateral sensorineural hearing loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Brain imaging: normal</td>
</tr>
<tr>
<td>Perilymph fistula</td>
<td>Abrupt onset associated with head trauma, barotrauma, or sudden strain during heavy lifting, coughing, or sneezing; may be associated with chronic otitis with cholesteatoma</td>
<td>Same as for vestibular neuritis, but usually associated with unilateral hearing loss; possible perforation of the tympanic membrane; positive fistula test (vertigo and nystagmus induced by pressure in external ear canal)</td>
<td>Electronystagmography: unilateral caloric hypoexcitability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Audiography: mild-to-moderate ipsilateral sensorineural hearing loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Brain imaging: CT of temporal bone may show erosion from cholesteatoma</td>
</tr>
</tbody>
</table>
Benign Paroxysmal Positional Vertigo

Often initiated by bump to head
Brief vertigo <60 sec of spinning
Flurry of episodes at peak
Triggered by: turning in bed
sitting up
lying down
bending forward
Vague imbalance afterward that can last hours

Dix Hallpike Maneuver diagnostic!
Case 2

57 year old
Visual disturbance followed by numbness marching
From face to hand to arm to leg over minutes
Complex Migraine / Migraine Equivalents

Visual phenomenon KEY
Squiggly lines, shimmering, sparkles, prisms, “blurry vision”
Google images: “migraine visual auras”

Marching numbness hand-arm-face-leg

Followed by typical pounding unilateral Photophobic migraine

Sometimes no headache

Beware if last more than a couple hours or many episodes in a week
Migraine

Speech, motor, >10 min, age >60, diabetes

ONSET

20 MINUTES

10 MIN

MI

SC

40 MIN
Migraine

motor, >10 min, age >60, diabetes
Non-ischemic events are very low risk for stroke

1 year risk of stroke: no events
1 year risk of stroke, MI, vascular death: 0.48%
Case 3

77 year old Htn smoker

10 minute episode of trouble finding words yesterday

Today episode of right arm and leg weakness lasting 30 minutes
## Minor stroke/TIA Risk Stratification

<table>
<thead>
<tr>
<th></th>
<th>Benign/low risk</th>
<th>Intermediate risk</th>
<th>Malignant/high risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing since event</strong></td>
<td>months</td>
<td>weeks</td>
<td>days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>hours</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>minutes</strong></td>
</tr>
<tr>
<td><strong>age</strong></td>
<td>&lt;45y</td>
<td></td>
<td>&gt;60y</td>
</tr>
<tr>
<td><strong>BP in ED/clinic</strong></td>
<td>normal</td>
<td>high</td>
<td>very high?</td>
</tr>
<tr>
<td><strong>DM/glucose</strong></td>
<td>no/normal</td>
<td>high</td>
<td>very high</td>
</tr>
<tr>
<td><strong>symptoms</strong></td>
<td>dizziness/vertigo</td>
<td>sensory</td>
<td>blurry curtain</td>
</tr>
<tr>
<td><strong>duration</strong></td>
<td>seconds</td>
<td><strong>few-60 min</strong></td>
<td>&gt;60 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>persisting</strong></td>
<td></td>
</tr>
<tr>
<td><strong>frequency</strong></td>
<td>many</td>
<td></td>
<td>one</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>few</td>
</tr>
</tbody>
</table>
CATCH study:
CTA has high yield in high risk TIA
n=510 prospective study;
onset to CTA 5.5 hours;
yield 1 in 3 for major plumbing problem

Aortic dissection
Carotid ILT
Aortic thrombus
Growing Carotid ILT
iNOT
### Calgary CTA Guidelines

<table>
<thead>
<tr>
<th>EMERGENCY CT/CTA (minutes; without Creatinine)</th>
<th>URGENT CT/CTA (hours; with eGFR &gt;30 ml/min)</th>
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<tr>
<td>1. Acute stroke with major deficits &lt;12h from onset</td>
<td>3. High risk TIA (motor or speech symptoms that occurred in the past 48 hours)</td>
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<tr>
<td>2. Sudden stupor or coma with hemiparesis or quadriplegia</td>
<td>4. Rule out carotid or vertebral artery dissection – focal neurological symptoms in setting of neck pain, recent trauma etc.</td>
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<td>5. Amaurosis Fugax or central retinal artery occlusion</td>
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<td>6. Minor stroke - patients with persistent minor deficits</td>
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</table>
INVESTIGATIONS

- CT scan of head
- Carotid Investigations: carotid ultrasound or CT angiogram
- ECG: if atrial fibrillation strongly consider anticoagulation
- Echocardiogram: only if suspicion of cardiac cause
- Holter Monitor: if suspect atrial fibrillation
- CBC, electrolytes, creatinine, glucose, PTT, INR, fasting glucose and lipid profile

HIGH RISK: Contact TIA HOTLINE: see over
  Complete investigations within 24 hours
  * May require referral to Primary or Comprehensive Stroke Centre to ensure timely completion of investigations
  Stroke Prevention Clinic Referral (seen within 24 hours)

MEDIUM RISK: Complete investigations within 3 days
  Stroke Prevention Clinic Referral (seen within 3 days)

LOW RISK: Complete investigations within 2 weeks
  Stroke Prevention Clinic Referral (seen within 2 weeks)

Risk is Front End Loaded

NIHSS ≤3: 8.3%
NIHSS >3: 9.5%

NIHSS ≤3: 7.3%
NIHSS >3: 9.9%

NIHSS ≤3: 1.9%
NIHSS >3: 16.8%

Onset to ED: 1.9 hrs
Onset to MRI: 7.3 hrs
Case 3

77 year old Htn smoker

10 minute episode of trouble finding words yesterday

Today episode of right arm/leg weakness lasting 30 min
Who is vulnerable?
The depth of a soul is not measured by what appears on the surface, but what lies in the heart.
Case 4

62 year old Diabetic
Felt lightheaded. Vision blurred during episode
Numbness to her right hand
CTA Not For Everyone Though!

Dizzy, Woozy, Blurry Patients do not need CTA

Vertigo in isolation does not need CTA

Resolved numbness/tingling does not need CTA
# Calgary CTA Guidelines

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<tr>
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<td>6. Minor stroke - patients with persistent minor deficits</td>
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Minor cerebrovascular syndrome triaging

“TIA event”

Clinician determines risk/TIA Hotline called

Low/intermediate risk

Referred to SPC

Seen within days

High risk/persisting minor deficit

Sent to ED

ED assessment

CT/CTA based testing

More ultrasound based testing
Minor cerebrovascular syndrome triaging
CTA negative no admission, send to TIARA!

High risk TIA/
persisting minor deficit

Sent to ED

ED assessment

CTA positive

admit

home

CTA negative

TIARA clinic

Fast MRI protocol
DWI, FLAIR, SWI
< 7 days from event
Cardiac investigations
Minor cerebrovascular syndrome triaging

“TIA event”

Clinician determines risk/TIA Hotline called

Low/intermediate risk  High risk TIA/persisting deficit

TIA

Sent to ED

Refereed to SPC

Seen within days/wks

ED assessment

CTA negative

home

CTA positive

admit

TIARA/SPC
Minor cerebrovascular syndrome triaging

- Sent to ED
  - ED assessment
    - CTA positive
      - admit
      - CTA negative
    - CTA negative
    - Other vascular pathology (eICAd, dissection, aorta, arteriopathies, venous)
      - tailored tx
  - admit
    - no ILT → urgent CEA/CAS
    - ILT → dual antithrombotics → CEA/CAS in few days
    - intracranialAS → dual antithrombotics/POINT
- home
Alteplase for the Treatment of Acute Ischemic Stroke in Patients with Low NIHSS and Not Clearly-Disabling Deficits: Primary Results of the PRISMS Trial

Pooja Khatri, Dawn Kleindorfer, Thomas Devlin, Robert Sawyer, Matthew Starr, Jennifer Mejilla, Joseph Broderick, Anjan Chatterjee, Edward C Jauch, Steven Levine, Jose Romano, Jeffrey Saver, Achala Vagal, Barbara Purdon, Jenny Devenport, Andrey Pavlov, Sharon Yeatts

On Behalf of the PRISMS Collaborators

Sponsor: Genentech, Inc
NCT02072226
IV TPA May Be Harmful In Minor Stroke

- **mRS 0-1 78.2%**
  - Alteplase Arm: 44.9%
  - Control Arm: 50.3%

- **mRS 0-1 81.5%**
  - Alteplase Arm: 33.3%
  - Control Arm: 31.2%

Percentage of Subjects

- 0
- 1
- 2
- 3
- 4
- 5-6

*
### Primary Safety Outcome (As Treated)

<table>
<thead>
<tr>
<th></th>
<th>Alteplase (n=154)</th>
<th>Control (n=153)</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sICH within 36 hours</td>
<td>5 (3.2)</td>
<td>0 (0.0)</td>
<td>3.3% (0.8%, 7.4%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Alteplase (n=154)</th>
<th>Control (n=153)</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ICH within 36 hours (central reader)</td>
<td>11 (7.1)</td>
<td>5 (3.3)</td>
<td>3.9% (-1.2%, 9.5%)</td>
</tr>
</tbody>
</table>

#### Radiological Subtype of ICH*

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Alteplase</th>
<th>Control</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HI-1</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>HI-2</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>PH-1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>PH-2</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Remote PH-1</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>IVH</td>
<td>2*</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>SAH</td>
<td>3*</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Mortality**

<table>
<thead>
<tr>
<th></th>
<th>Alteplase</th>
<th>Control</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 (0.6)**</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*These patients have more than one subtype
**Patient death unrelated to study drug (volvulus)
Onset to ED: 1.9 hrs
Onset to imaging: 7.3 hrs

### Table 2: Final Multivariable Cox Proportional Hazards Regression Models for Progression, Recurrence, and Death

<table>
<thead>
<tr>
<th>NIHSS 0 to 5 (N=229)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-value (FDR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Progression (19 and 10 events)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DWI lesion (one or more vs none)</td>
<td>12.4 (1.6, 93.3)</td>
<td>0.014 (0.028)</td>
</tr>
<tr>
<td>Intracranial occlusion</td>
<td>11.3 (4.4, 29.2)</td>
<td>&lt; 0.001 (&lt; 0.001)</td>
</tr>
<tr>
<td><strong>Recurrence (15 and 8 events)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic ICA stenosis</td>
<td>5.6 (2.0, 15.6)</td>
<td>&lt; 0.001 (0.004)</td>
</tr>
</tbody>
</table>
Refinement of Imaging Predictors of Recurrent Events following Transient Ischemic Attack and Minor Stroke

<table>
<thead>
<tr>
<th>Variable</th>
<th>Progression % (no./No.)</th>
<th>No Progression % (no./No.)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging Findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute ischemia on CT</td>
<td>21 (4/19)</td>
<td>12 (57/480)</td>
<td>1.9 (0.6–5.8)</td>
</tr>
<tr>
<td>Intracranial occlusion or stenosis ≥50%</td>
<td>74 (14/19)</td>
<td>19 (90/480)</td>
<td>13.9 (5–39)</td>
</tr>
<tr>
<td>Intracranial occlusion</td>
<td>53 (10/19)</td>
<td>9 (42/480)</td>
<td>9.9 (4.0–24.4)</td>
</tr>
<tr>
<td>Intracranial stenosis ≥50%</td>
<td>26 (5/19)</td>
<td>6 (31/480)</td>
<td>4.7 (1.7–13)</td>
</tr>
</tbody>
</table>
Minor cerebrovascular syndrome triaging

- High risk TIA/persisting minor deficit
  - Sent to ED
  - ED assessment
  - CTA positive

- ED assessment
  - CTA positive
    - no ILT → urgent CEA/CAS
    - ILT → dual antithrombotics → CEA/CAS in few days
      - If fails then CEA
    - web → dual antithrombotics
    - eICAS

- Other vascular pathology
  - (eICAd, dissection, aorta, arteriopathies, venous)
    - tailored tx

- Intracranial occlusion/near-occlusion
  - IV tPA if disabling deficits → TEMPO-2 trial
  - Neurologic deterioration → ENDO-LOW trial
  - Mechanical thrombectomy
TNK tPA 0.25 mg/kg versus antiplatelet(s) in minor stroke with CTA intracranial occlusion

ClinicalTrials.gov Identifier: NCT02398656

Calgary led/coordinated: SB Coutts (PI) and MD Hill (co-PI)

Canada, Spain, Belgium, Austria, Australia,
Study progress: 42 enrolled
ENDO-LOW Study Question

To test efficacy and safety of:

Immediate mechanical thrombectomy versus Initial medical treatment

in ischemic stroke patients with large vessel occlusions (LVO) and low baseline NIHSS (NIHSS 0-5)

Prospective, randomized, open-label, blinded-endpoint (PROBE) design
Key Messages

• Most neurologic spells are not brain ischemia: vertigo, syncope, visual auras and recurrent sensory spells
• TIAs have high early risk of progression or recurrence

• The “unstable angina” equivalent/ high risk TIA is one with unilateral motor weakness or speech deficit lasting more than 5 minutes that occurred in the past 48 hours!
• Consider ASA + Clopidogrel loading dose in such patients
• Call the TIA hotline or send to nearest ED with such cases

• The remainder should be referred to a stroke clinic or investigated to rule out carotid stenosis or serious cardiac source of embolus
Thank-you for your attention!
Email me if you need anything:
ademchuk@ucalgary.ca