Management of Patients with TIA

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Disclosures

• none
A patient presents with transient neurological deficit....

– Is it a TIA?
  • What tools can help to make the diagnosis?
  • What are the current tools for risk stratification?
If a TIA is suspected....

• What are the potential aetiologies?
• What urgent investigations should be done?
• What are the current approaches to management?
  – What antiplatelet agents to use?
  – Management of patients with common causes of TIA
    - extracranial atherosclerosis
    - intracranial atherosclerosis
    - atrial fibrillation
    - small vessel disease
TIA

• “transient episode of neurological dysfunction caused by a focal brain, spinal cord or retinal ischemia without acute infarction...”

• majority last for less than an hour (usually less than 30 minutes)

• risk of stroke after TIA in the first 3 months is 10-15% with the highest risk in the first 48 hours
Diagnosis of TIA

• Short duration event
• Based on history
• Collateral history is important
• Clinical features can help with localizing
• Imaging can also assist with reaching the correct diagnosis
  
  (up to 50% of TIAs are associated with infarction on DWI)
Terminology

• TIA and minor stroke are part of the same spectrum
  – TIA short duration, reversible, no evidence of infarction
  – Minor stroke – residual deficits or evidence of infarction on imaging

PATIENT RECOVERS BUT NEED INVESTIGATIONS TO IDENTIFY CAUSE, START APPROPRIATE TREATMENT TO PREVENT RECURRENT STROKE!
Current tools to assist with diagnosis

• Clinical presentation

• Neuro-imaging
  – CT
  – Arterial imaging
  – MRI diffusion study
Clinical Features Supporting TIA

• Fit a vascular territory or stroke syndrome
  – Left MCA
  – Right MCA
  – Brainstem features

• Acuity

• Presence of predisposing factors

• Negative symptoms or loss of function
  (positive symptoms usually associated with seizures, migraine)
TIA mimics

Not all presentations with focal neurological deficits are due to TIA

10-40% are mimics

- Seizure
- Migraine
- Tumor
- Benign positional vertigo
- Subdural hematoma
- Syncope
- Transient global amnesia
<table>
<thead>
<tr>
<th>Diagnosis of TIA mimics (n = 55)</th>
<th>n</th>
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<tbody>
<tr>
<td>Epileptic seizures</td>
<td>26 (43.7)</td>
</tr>
<tr>
<td>Migraine</td>
<td>13 (23.6)</td>
</tr>
<tr>
<td>Psychogenic hyperventilation</td>
<td>4 (7.3)</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>2 (3.6)</td>
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<tr>
<td>Transient global amnesia</td>
<td>2 (3.6)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2 (3.6)</td>
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<tr>
<td>Hypoglycaemia</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>Benign paroxysmal vertigo</td>
<td>1 (1.8)</td>
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<tr>
<td>Cerebral venous thrombosis</td>
<td>1 (1.8)</td>
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<tr>
<td>Neoplasm of the brain</td>
<td>1 (1.8)</td>
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<tr>
<td>Subarachnoid bleeding</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>Peripheral nerve lesion</td>
<td>1 (1.8)</td>
</tr>
</tbody>
</table>

Values in parentheses represent percentages. Diagnostic criteria for epileptic seizures according to the definitions proposed by the International League Against Epilepsy and the International Bureau for Epilepsy [39]. Diagnostic criteria for migraine with aura were those defined by the International Headache Society [40].
TIAs may present in an atypical fashion

Chameleons

• Capsular warning sign
  – Multiple recurrent fluctuations due to disease in a single penetrating artery

• Limb shaking TIAs
  – Involuntary movements that may be mistaken for motor seizures due to hemispheric dysfunction due to hypoperfusion from severe arterial disease
Current tools for risk stratification

• ABCD
• $ABCD^2$
• ABCD$^3$
• ABCD-I, ABCD$^2$-I and ABCD$^3$-I
ABCD² score

- Age
  - ≥ 60 years = 1
- Blood pressure at presentation
  - systolic >140 or diastolic ≥ 90 = 1
- Clinical features
  - Unilateral weakness = 2
  - Speech disturbance without weakness = 1
  - Other = 0
- Duration of symptoms in minutes
  - ≥ 60 = 2
  - 10-59 = 1
  - <10 = 0
- Diabetes = 1
ABCD$_2$ score

48 hour stroke risk

- Score 1-3 (low): 1%
- Score 4-5 (moderate): 4-6%
- Score 6–7 (high): 8-12%
ABCD² score

• Current stratification dichotomizes patients to score <4 and ≥4

• Patients with a score of ≥4 are at higher risk

• But
  • recurrent stroke has been reported in patients with low scores
  • Patients may have high scores because of age and underlying risk factors without relation to underlying mechanism
ABCD$^2$ score

• 58 year old patient with atrial fibrillation presents with visual loss for 5 minutes. Blood pressure normal, not diabetic.
  – Age = 0
  – Blood pressure = 0
  – Clinical feature = 0
  – Duration = 0
  – Diabetes = 0

Low risk score despite a high risk mechanism
ABCD$^2$ score

- 80 year old with hypertension, diabetes referred for one hour episode of right hand numbness
  - Age = 1
  - Blood pressure = 1
  - Clinical feature = 0
  - Duration = 2
  - Diabetes = 1

Total score = 5

Patient with mild nonspecific deficits can have a high score because of risk factors
ABCD$^2$ score

- Not perfect

- Blind to mechanism

- Does not identify patients with high risk etiologies such as severe atherosclerotic disease or atrial fibrillation

- Goal is to have urgent investigations
Other scores

• ABCD$^3$ ($\geq$ 2 episodes within 7 days)
• ABCD$^2$-I (evidence of infarction on CT or MRI)
• ABCD$^3$-I ($\geq$ 2 episodes within 7 days, abnormal finding on neuroimaging such as carotid stenosis or restricted diffusion on MRI)
  – not widely used
  – may increase the accuracy but limited validation studies
  – imaging confirms the diagnosis but does not provide information about the mechanism
  – MRI imaging not readily available
Current models of care

• Hospital

• Same day specialty clinic

• Rapid-evaluation units
Hospital Admission

• Advantages
  – Availability of investigations
  – Close monitoring
  – Access to t-PA (if recurrent stroke)
  – Access to urgent endarterectomy (if required)

• Disadvantages
  – Cost and availability
Same-day clinics

- Exemplified in the Express study conducted in the UK

- Associated with 80% risk reduction compared to patient seen in an appointment-based clinic

Same-day Clinics

- Another model described by French investigators in the SOS-TIA trial
  - 24 hour TIA clinic with access to a 24 hour vascular neurologist
  - Patients were admitted to hospital from the clinic if a high-risk etiology was suspected
  - Associated with reduced stroke rate at 90 days (1.24% compared with the predicted 5.96%)
Key Messages

• The ABCD\textsuperscript{2} score is a guide for assessment of patients with TIA

• Urgent assessment is recommended

• Outpatient models of care in Ontario

• Patients need urgent investigations for high-risk causes of stroke (severe arterial disease and atrial fibrillation) and early implementation of treatment
TIA assessment starts with history

• What are the deficits
  – Episodes in the same territory suggests arterial disease
  – Episodes involving multiple territories suggests cardiac cause
TIA assessment starts with history

• Associated features
  – Presence of vascular risk factors
  – Palpitations suggest atrial fibrillation
  – Preceding trauma - arterial dissection
  – Illicit drug use - endocarditis or vasculitis
Investigations

• Investigations assist by ruling out “stroke mimics” and also evaluate for high risk causes of stroke
  – Brain imaging
  – Arterial imaging
  – Cardiac investigations
  – Risk factor assessment
Brain Imaging

• 27 year old man referred to our TIA unit from the ED after a 40 minute episode of speech difficulty
• Initially unable to speak, followed by nonsensical speech and impaired writing with sparing of comprehension
• Stroke risk factors included use of cocaine
• Neurological examination normal
Key Stroke Investigations

• Brain imaging may confirm an ischemic lesion
• Include CT or MRI
• Larger established lesions can be seen on CT
• Smaller earlier lesions best seen on MRI

• Caveats
  – The absence of imaging does not rule out TIA
  – The pattern does not necessarily provide information about etiology
Key Stroke Investigations

• Arterial imaging
  – CTA or MRA
  – If strong contraindications to both, carotid dopplers for carotid territory TIA

• Cardiac assessment
  – 48 hour Holter
  – If 48 hour Holter study is normal and no arterial abnormalities, prolonged EKG monitoring (2 weeks or 1 month)
Management

• After CT imaging has been completed, if there is no evidence of hemorrhage, patients should be started on antiplatelet therapy until the mechanism of stroke is identified
  – Aspirin (81 mg)
  – If patient using aspirin, then clopidogrel or Aggrenox can be use
  – Ongoing investigations evaluating dual antiplatelet therapy
CHANCE

- Trial of 5170 patients randomized to treatment with clopidogrel (300 mg loading dose followed by 75 mg daily) + aspirin (75 mg) or placebo + aspirin (75 mg)

- Within 24 hours of onset of minor stroke or TIA

- 90 days of treatment but
  - clopidogrel + aspirin was given for 21 days, then clopidogrel day 22-90 days
  - Aspirin for 90 days

- 114 centers in China

- Primary outcome was stroke (ischemic or hemorrhagic) during 90 days of follow-up

NEJM 2013;369:11-19
CHANCE

• Stroke recurrence 8.2% in ASA + Clopidogrel arm compared to 11.7% in ASA + Placebo arm (p< 0.001)

• Moderate to severe hemorrhage 0.3% in both groups
Probability of Survival Free of Stroke.

Hazard ratio, 0.68 (95% CI, 0.57–0.81)
P<0.001

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<tr>
<th></th>
<th>Aspirin</th>
<th>Clopidogrel–aspirin</th>
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<tr>
<td>No. at Risk</td>
<td>2586</td>
<td>2584</td>
</tr>
<tr>
<td>2307</td>
<td>2376</td>
<td></td>
</tr>
<tr>
<td>2287</td>
<td>2361</td>
<td></td>
</tr>
<tr>
<td>1906</td>
<td>1989</td>
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CHANCE

• Although this was a positive trial,
  – Applies to patients with minor stroke or TIA
  – Excluded patients with large ischemic strokes
  – May apply to patients with small vessel disease and not to patients with extracranial atherosclerosis

• POINT trial
  – North American study similar design but within 12 hours of onset, treatment for 90 days. 4000 out of planned 5840 patients recruited (November 10, 2016)
Arterial imaging
Patient

• 84 year old man presented with a 20 minute episode of left arm heaviness and numbness

• Medical hx of HTN, dyslipidemia, vertigo secondary to a peripheral etiology
Patient

- Started on antiplatelet agent*
- Blood pressure control optimized with Ramipril
- Started on statin
- Referred to Neurosurgery* and had endarterectomy one week later
Patient

• If you are referring for endarterectomy, check with your surgeon about antiplatelets

• Angioplasty and stenting is another option for revascularization (patients > 70 years had better outcome with endarterectomy, patients <70 years had better outcome with angioplasty and stenting)
Patient

• 47 year old woman with three episodes of left facial weakness, left arm and leg sensory and motor deficits and dysarthria

• Each episode lasted for less than 30 minutes
Nb Views: 16

Rotation: 11.2 deg.
Patient

- SAMMPRIS trial
  - Dual antiplatelet for 90 days, then aspirin
  - Statin for elevated lipids
  - Lifestyle modification
What to do if the arteries are normal?
Cardiac causes of stroke
Patient

- 92 year old woman referred for transient left facial weakness and slurred speech

- PMH of HTN, NIDDM and angina

- Independent with ADLs, lives alone
Patient

- Vascular imaging normal
- 48 hour Holter normal
- 14 day Holter study showed runs of atrial fibrillation
- Discussion with her about starting anticoagulation (warfarin, dabigatran, rivaroxaban, apixaban)
When arterial and cardiac investigations are both normal
Patient

- 92 year old man with 15 minute history of slurred speech and left facial weakness
Patient

• Cardiac and arterial investigations normal
  – CTA
  – Echo
  – 48 Hour Holter

Pattern is more consistent with small vessel disease and he has been started on an antiplatelet agent and control of his risk factors
Other causes of TIA

• Cardiac
  – Poor LV function
  – Valvular disease (mechanical valves, infection)

• Arterial
  – Dissection
  – Vasculitis

• Hematological
  – Polycythemia, thrombocytosis
  – Antiphospholipid antibody

• Other
  – Sickle cell disease
  – OC
  – HRT
  – Migraine
  – Drug use
Patient

• 19 year old woman with acute onset vertigo associated with head movement in any direction
• Symptoms persisted for 5 days
• Referred to our TIA clinic
Patient

• Cardiac investigations

• Hematological workup negative
Final messages

• Transient neurological deficits can be caused by a number of processes
  – TIA
  – TIA mimics
Final messages

• For patients with TIA, imaging may be helpful in confirming the diagnosis but the clinical features are as important especially if the CT is normal

• Patients require cardiac and arterial investigations to rule out high-risk causes of stroke (hematological testing done if clinical scenario is suggestive)
Final Messages

• For TIA related to atrial fibrillation, patients should be started on anticoagulation if there are no contraindications

• For patients with carotid disease, endarterectomy or angioplasty and stenting within 2 weeks of presentation is recommended

• For other atherosclerotic disease, antiplatelet therapy (monotherapy or dual therapy for intracranial disease)
Final Messages

• All patients need assessment for vascular risk factors

• Treatment include medical therapy and lifestyle modifications