Transient Ischemic Attack – an opportunity for stroke prevention

Shyam Prabhakaran, MD, MS
8/20/10

Overview

• Problems in diagnosis
• Definitions
  – Classical definition
  – Other definitions
• Stroke risk stratification
  – Clinical
  – Radiographic
• Management
  – To admit or not to admit

Common episodic conditions

• General medical
  – Paroxysmal atrial fibrillation
  – Angina
  – Asthmatic attack
  – Panic attack
• Neurological
  – Seizure
  – Migraine
  – Positional vertigo
  – Transient ischemic attack

Problems in diagnosis

• Event occurred in past, often unwitnessed
• Relies almost entirely on patient history
• Patients may be unable to recall or describe symptoms
  – Inaccurate history confounds diagnosis
  – Descriptions often vague
    • “heaviness”
    • “dizziness”
    • “confused”
• No objective markers on clinical examination
• Depends on patient and physician knowledge

Disclosures

• I have no disclosures or conflicts of interest related to this topic
Patient knowledge of TIA

- Based on a telephone survey of over 10,000 US adults:
  - Less than 10% can identify even 1 TIA symptom or define it even vaguely
  - Of those with a diagnosis of TIA, only 64% of patients sought medical attention within 24 hours
- Recent study also found 45% delayed >1 day to seek medical attention
  - Motor symptoms or duration greater than 1 hour predicted less delay
  - Occurrence on weekend predicted more delay

Physician knowledge of TIA

- Among 200 primary care physicians:
  - Only 22% correctly identified all 5 typical TIA symptoms (focal weakness, focal sensory loss, aphasia, dysarthria, and visual loss) and knew that TIA was defined as < 24 hours
  - 44% thought TIA could last up to 48 hours and 9% thought even > 1 week
  - 47% consider isolated vertigo a TIA symptom
  - Only 37% routinely consulted a neurologist for evaluation of suspected TIA patients

Making the diagnosis

- Does it matter if a neurologist or an non-neurologist makes the diagnosis?

Making the diagnosis

- How many neurologists does it take to make the diagnosis of TIA?
  - Even among neurologists, agreement is far from perfect (kappa 0.65)
  - Even worse for localization of TIA: carotid vs. vertebrobasilar territory (kappa 0.31)
  - Using a check-list of high-probability TIA symptoms increased kappa to 0.77
  - Further increase to 1.0 if 2 raters conferred afterwards (i.e. they always came to an agreement)

Differential diagnosis

- 508 patients in a neurovascular clinic
  - 73% had diagnosis confirmed
  - 27% had another diagnosis
    - Migraine
    - Multiple sclerosis
    - Seizure
    - Hyperventilation
    - Unclassifiable spell
- Atypical TIA symptoms may also be harbinger of cardiac events (arrhythmia)
TIA: terribly inaccurate acronym

- Should we just call these episodes transient neurologic disorders (TND) or abnormalities (TNA)?
- Balance between costs of misdiagnosis (unnecessary tests and treatments) and benefits among true positive TIA patients (stroke risk reduction)
- Are there ways to increase our diagnostic certainty?

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Classical definition of TIA

- A focal neurologic deficit of presumed vascular etiology involving the brain or retina and lasting less than 24 hours
- Does this definition make sense?
  - Can we be more specific about the characteristic symptoms?
  - Do most TIAs last up to 24 hours?
  - Can acute neuroimaging help us?

DEFINITIONS

Classical definition of TIA

Characteristics of TIA

- Typical TIA (likelihood of TIA high)
  - Weakness, clumsiness, or sensory alteration in one or both limbs on the same side, speech or language disturbance, loss of vision in one eye or part of the eye, or homonymous hemianopsia
  - Weakness or clumsiness (sometimes changing from one side to another), sensory alteration, complete blindness or homonymous hemianopsia, ataxia, imbalance, or unsteadiness
  - Two or more of the following: diplopia, dysphagia, dysarthria, or vertigo

- Atypical TIA (likelihood of TIA is low)
  - Disturbances of vision consisting of flashes, objects, distorted-view tunnel vision, or image moving on change of posture
  - Alteration of strength consisting of tiredness or heavy sensation in one or more limbs, either unilateral or bilateral
  - Positive sensory symptoms alone (unilateral or bilateral) or a gradual spread of sensory symptoms
  - Brain stem symptoms and coordination difficulties consisting of isolated dysphagia or dysarthria, double vision, dizziness, or uncoordinated movements
  - Accompanying symptoms including unconsciousness, limb jerking, tingling of the limbs or lips, disorientation, and amnesia
Duration of TIA

- Most TIAs last minutes to few hours
  - Among classical TIAs
    - 50% recovered in < 30 minutes
    - 9.7% within 30-60 minutes
    - 15.2% within 60-180 minutes
    - 90% recovered within 240 minutes (4 hours)
  - Only 13.8% of all patients with deficits at 60 minutes completely recovered by 24 hours (i.e. majority were actually strokes)

Levy DE Neurology 1988; Wedelin L Neurology 1988

Imaging of TIA

- Tissue-based diagnosis of TIA
  - Diffusion-weighted imaging (DWI) can identify cytotoxic injury (i.e. infarction)
  - "Troponin" for the brain
    - DWI studies suggest many TIA patients permanent cytotoxic tissue injury

MRI of TIA

New Definition – circa 2009

- A brief episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia and without evidence of acute infarction on brain imaging
  - Tissue-based definition, not time-based
  - Persistent deficits or acute infarction on imaging define ischemic stroke
  - Limited by availability and timing of neuroimaging (approximately 30% have MRI acutely following TIA)

Easton DL, Stroke 2009

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STROKE RISK STRATIFICATION
Prognosis after classical TIA

<table>
<thead>
<tr>
<th>Study Setting</th>
<th>Cerebral Attack</th>
<th>Population</th>
<th>Year</th>
<th>N</th>
<th>Delay</th>
<th>Stroke</th>
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Half of risk (5.5%) is within 48 hours

Radiographic risk stratification

- Can acute neuro-imaging help assess stroke risk following classical TIA (old definition)?
  - Presence of acute infarction (DWI)
- Does DWI-positive TIA carry a greater risk of subsequent stroke than either completed ischemic stroke or DWI-negative TIA?
- Large vessel stenosis or occlusion (MRA, TCD, or CTA)
  - Based on NASCET, 90-day risk of stroke following hemispheric TIA ipsilateral to >70% stenosis was 20% in the medical arm

DWI (+) TIA and very early risk

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<th>Diagnosis</th>
<th>Adjust. OR</th>
<th>95% CI</th>
<th>P-value</th>
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Clinical-Imaging Prognostic Score

- Add DWI to ABCD or ABCD2 (?) ABCD3

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<th>Score</th>
<th>Probability</th>
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<td>0.5</td>
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<td>0.56</td>
<td>95%</td>
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<tr>
<td>0.61</td>
<td>95%</td>
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Johnston SC, Lancet 2007
Prabhakaran S, Arch Neurol 2007
Coutts SB, Ann Neurol 2005
Gilles, M, ESC 2010; Ay H, ISC 2007, Ay H Stroke 2009
**Criticisms of ABCD score**

- Is it really a prognostic score or just a way to increase diagnostic certainty?
  - High scores may indicate true TIA and low scores suggest mimics
- Application without thought could be dangerous
  - 55 year-old man without medical history presents with hemianopia, vertigo, and ataxia for 5 minutes has ABCD score of 0
  - Is this patient really low-risk?
- Individualized neurologic assessment and judgment should still matter

**Degree of reversibility**

- Rather than static clinical and imaging parameters, is risk of stroke linked more closely with degree of acute recovery (100% in TIA)?

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  - Degree of rapid recovery (complete vs. incomplete)
- Management
  - To admit or not to admit

**Triaging TIA patients**

- Balance between costs of misdiagnosis (unnecessary tests and treatments) and benefits among true positive TIA patients (stroke risk reduction)
- Arguments for admission
  - Rapid evaluation for high-risk conditions
  - Risk factor modification and initiation of treatments
  - Time-sensitive and highly efficacious treatments
    - IV tPA or intra-arterial therapy if stroke occurs in-hospital (< 8 hours window)
    - Anticoagulation for atrial fibrillation
    - Early CEA for >70% stenosis (< 2 week window)
  - Opportunity for stroke education

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**Spectrum of acute ischemic cerebrovascular disease**

- Mechanisms of recurrence: inadequate collaterals / perfusion failure, re-oclusion of large artery, re-oclusion of perforator vessel, de-novo embolism or thrombosis

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**Critical points**

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**Diagnosis of TIA**

- High scores may indicate true TIA and low scores suggest mimics
- Application without thought could be dangerous
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**Degree of reversibility**

- Rather than static clinical and imaging parameters, is risk of stroke linked more closely with degree of acute recovery (100% in TIA)?

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**Triaging TIA patients**

- Balance between costs of misdiagnosis (unnecessary tests and treatments) and benefits among true positive TIA patients (stroke risk reduction)
- Arguments for admission
  - Rapid evaluation for high-risk conditions
  - Risk factor modification and initiation of treatments
  - Time-sensitive and highly efficacious treatments
    - IV tPA or intra-arterial therapy if stroke occurs in-hospital (< 8 hours window)
    - Anticoagulation for atrial fibrillation
    - Early CEA for >70% stenosis (< 2 week window)
  - Opportunity for stroke education

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**TIA**

- Ischemic Stroke

- TIA without infarction
  - Example: 5-10 minutes of left sided numbness
- TIA with infarction
  - Example: 120 minutes of hemiparesis and aphasia
- TIA with incomplete recovery
  - Example: left hemiplegia at onset that recovers to mild weakness within 4 hours
- TIA with no recovery
  - Example: right hemiplegia without improvement

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**Degree of reversibility**

- Rather than static clinical and imaging parameters, is risk of stroke linked more closely with degree of acute recovery (100% in TIA)?
To admit or not admit
- Arguments against admission
  - 95% do not have stroke in 48 hours
  - Costs outweigh benefits?
    - Hospitalization and diagnostic tests
    - Use of limited resources
    - Erroneous diagnosis – psychological impact
- Rapid access (same-day) outpatient clinics
  - Early evaluation and management (blood thinners, carotid and cardiac testing, statins, and risk factor modification) lead to risk lowering

EXPRESS Study
Phase 1: routine care (delayed evaluation)
Phase 2: same day evaluation

TIA evaluation models

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Weaknesses</th>
</tr>
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</table>
| Isolation model | Increased access for time sensitive treatments (e.g., I.V.)
| | Increased risk of nosocomial infection and nosocomial complications
| | Limited access to on-site imaging laboratory
| Same-day specialty clinic model | Decreased long term costs and health care utilization
| | Patient and clinician convenience
| | Increased startup costs
| Rapid evaluation unit model | On-site hospital staff
| | Limited access to on-site imaging laboratory
| | Increased long term costs
| | Increased access to patient's prior imaging and medical history

Guidelines
- Diagnostic tests
  - Blood: CBC, BMP, fasting glucose and lipids
  - Neurovascular: CTA, MRI/A, or Doppler
  - Cardiac: ECG and Holter/telemetry (r/o AF; TTE +/- TEE (<45 y/o with negative head and neck vessel imaging and hematologic screening)
  - Consider other tests when indicated
    - Hypercoagulable panel
    - Lumbar puncture
    - Cerebral angiogram

- Treatment
  - Non-cardioembolic TIA
    - Antiplatelet therapy
      - Aspirin, clopidogrel, or aspirin/extended release dipyridamole
    - Carotid endarterectomy if symptomatic carotid stenosis >70%
  - Cardioembolic TIA
    - Anticoagulant therapy with warfarin
      - Atrial fibrillation, mechanical valves, post myocardial infarction, and possibly low EF
    - Warfarin is indicated unless strong contraindication such as falls risk or major bleeding risk

Johnston SC, Ann Neurol 2006; Easton D, Stroke 2009
Guidelines

- Treatment
  - Behavior and lifestyle modification
    - Stroke education
    - Smoking cessation
    - Weight loss and exercise
  - Treatment of hypertension
    - 30-40% RRR in stroke with 9/4 mmHg lowering
  - Treatment of dyslipidemia
    - 15-20% RRR in stroke with statin therapy
  - Treatment of diabetes

Johnston SC, Ann Neurol 2006; Easton D, Stroke 2009

Conclusions

- TIA often heralds ischemic stroke and provides a golden opportunity for prevention
- New definitions are being developed for TIA but critical question remains:
  - Do you think the patient had reversible brain ischemia?
    - If yes, same-day management should be the rule
  - Choice determined by costs, convenience, health care systems
- Clinical and imaging stratification tools maybe useful to triage patients based on risk
- Early management can reduce stroke risk 80%

The future: AICS like ACS?

<table>
<thead>
<tr>
<th>Classification of Acute Ischemic Cardiogenic Stroke (AICS)</th>
<th>Outcome</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>DWI (-) atypical TIA</td>
<td>Non-cardiac chest pain</td>
<td></td>
</tr>
<tr>
<td>DWI (+) typical TIA</td>
<td>Unstable angina</td>
<td></td>
</tr>
<tr>
<td>DWI/CT (+) TIA</td>
<td>NSTEMI</td>
<td></td>
</tr>
<tr>
<td>DWI/CT (-) TIA</td>
<td>STEMI</td>
<td></td>
</tr>
</tbody>
</table>

Any confirmed stroke $\rightarrow$ STEMI

DWI/CT (+) TIA $\rightarrow$ NSTEMI

DWI (-) atypical TIA $\rightarrow$ stable angina

Stroke/TIA mimics $\rightarrow$ non-cardiac chest pain

THANK YOU FOR YOUR ATTENTION!