Transient Ischemic Attacks
Myths, Controversies and Pitfalls

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Disclosure:
Dr. Birnbaumer has no relationships with entities producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

TIAs: The Issues

- What IS a TIA?
- How do we work up these patients?
- How should we dispo these patients?
  - Admit?
  - Neurology consultation urgently?
  - Neurology or PCP follow-up?
  - How soon should they follow up?
  - What, if any, medications are indicated?

TIA

The Scope of the Problem

- "Incidence"
  - Around 300,000 cases per year
  - Up to 1 in 15 elderly patients will have a TIA
  - 12-30% of stroke patients have antecedent history of TIA

What IS a TIA, anyway?

- Both over- and underdiagnosed
- Particularly by non-neurologists
- Agreement on diagnosis even problematic between neurologists
- Progression to stroke is major concern... cerebrovascular disease is 3rd to 4th leading cause death in US
What IS a TIA?

1975 NIH definition

"A transient ischemic attack is a sudden focal neurologic deficit lasting for less than 24 hours, of presumed vascular origin, and confined to an area of the brain or eye perfused by a specific artery"

1975 NIH definition... the issues

- Based on arbitrary 24 hour time limit
- Diagnosis made on temporal course rather than on pathophysiology
- Assumes no permanent brain injury
- Implies TIA is a benign entity

Recent views

- TIA is like "unstable angina of the brain"
- TIA is a neurologic emergency
- Requires urgent / emergent workup
- MAY cause permanent brain injury
- More advanced imaging shows damage in up to 50% of TIA patients (old definition)

Recent views... continued

- Terms began cropping up...
  - "Mini-stroke"
  - "Transient stroke"
  - "Transient brain attack"
  - "Warning stroke"
- Led to redefinition of TIA...

2002 TIA Working Group definition

"A TIA is a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction."

TIA: Presentation

- Abrupt onset of symptoms
- Specific symptoms determined by vascular distribution
- Usually lasts < 30 minutes
  - Majority < 10 minutes

**TIA: Presentation**

- Abrupt onset of symptoms
- Specific symptoms determined by vascular distribution
- Usually lasts < 30 minutes
  - Majority < 10 minutes
  - What is the implication of this for you?
  - Much of evaluation will be based on history – patient / family / bystanders

**TIA: Presentation**

- Current definition of TIA (2009) eliminated a time frame
  - "A transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction"
- Now is a tissue-based definition, not a time-based definition
- Emphasis is now on neuroimaging

**TIA: Presentation**

- New definition led to a new clinical entity - radiographic infarction without lingering symptoms
- What does that mean?
  - By old definition – fit TIA diagnosis
  - Creates a new entity: TSI - Transient Symptoms with Infarction
  - Likely that CVA, TSI and TIA are a spectrum like the cardiac ACS spectrum

**TIA: Evaluation**

- Time sensitive diagnosis if still symptomatic (TIA vs CVA?)
- Need to consider broad differential diagnosis

**TIA**

- Differential Diagnosis
  - Hypoglycemia / hyperglycemia
  - Structural brain lesion
  - CNS infection
  - Todd's paralysis
  - Epilepsy
  - Complicated migraine
  - MS flare
  - Syncope
  - Labyrinthine disorders
  - Hyperventilation syndrome / panic attack
  - SAH… etc, etc
TIA: Evaluation

- Thorough history and physical exam
- Detailed neurologic exam warranted
  - Include exam for subtle findings
- Cardiac exam: Rate, rhythm, murmurs
- Carotids for bruits
- Goal is to determine if episode was a true TIA or not
  - If so, helpful to determine anterior or posterior circulation involved

TIA: Testing in the Urgent Setting

- Rapid glucose
- CBC
- Chem panel
- ECG
- Coagulation studies
- Head CT
- MRI
- Vascular imaging

TIA: Testing in the Urgent Setting

- There are a gazillion new tests coming down the pike
  - We’ll see if they pan out… don’t hold your breath

TIA: Neuroimaging

- Now that TIA is a tissue-based diagnosis, neuroimaging becoming more critical
- Recommended by AHA/ASA that it be done within 24 hours of symptom onset
- Diffusion weighted imaging MRI is the preferred first imaging modality
  - However, CT is most common study first performed

TIA: Neuroimaging

- Why DWI MRI?
  - Shows areas of restricted diffusion associated with cytotoxic edema
  - Much more sensitive than traditional MRI
  - False negatives seen in 3-17%
    - Very early ischemia
    - Small infarcts – especially internal capsule and brainstem
TIA: Neuroimaging

- Diffusion-weighted MRI
  - Show lesions in 16-67% of patients with TIA
  - Positive studies = high-risk group
  - Doubles the risk of subsequent vascular event
  - 4-fold increase if positive MRI plus TIA symptoms lasting > 1 hour
  - Positive studies associated with...
    - High-grade large vessel stenosis
    - Cardioembolic source

- Issue: Does diffusion-weighted MRI add supplemental predictive value to risk stratification in TIA?
  - Some studies suggest positive study independent risk factor for subsequent stroke
  - More studies addressing it as independent risk factor required
  - Begs issue of routine availability of 24/7 MRI scanning

TIA: Neuroimaging

- CT
  - Still most common test performed
  - Not as sensitive as DWI MRI or MRI
- CTA
  - An adjunctive test
  - Evaluates both intracranial and extracranial vasculature

TIA: Further Studies

- After initial H&P, ECG and neuroimaging for a TIA or TSI, what is a “complete etiologic workup”?
  - Echocardiography
  - Vessel imaging (CTA, doppler)
  - The issue is... WHEN do we need to do this workup?

TIA: Neuroimaging

- "Results of neuroimaging combined with risk stratification may help determine actual 7-day risk of stroke”
- Risk ranges from 0.4% to 15%
  - 0.4% - No mimic, negative ECG, DWI MRI without evidence of lesion, ABCD2 < 4
  - 15% - No mimic, negative ECG, DWI MRI with evidence of lesion, ABCD2 > 4

TIA: Neuroimaging

- So... can we wait a week to do a workup in some patients?
- Au contraire...
TIA

- Risk of stroke is highest in the first 48 hours after TIA (and TSI?)
- Still difficult to differentiate which patients fall into this group despite multiple risk stratification schemes

Risk Stratification Tools

- ABCD2-MRI, CIP, ABCD2-I, ABCD3-I, ABCDE+, RRE... seriously?
- Simplest and most studied is ABCD2 score

“ABCD2” Score

<table>
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<tr>
<th>Criteria</th>
<th>Points</th>
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<tbody>
<tr>
<td>Age ≥ 60 years</td>
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<tr>
<td>SBP &gt; 140 and/or DBP &gt; 90 (presentation)</td>
<td>1</td>
</tr>
<tr>
<td>Clinical features</td>
<td>1-2</td>
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<tr>
<td>Unilateral weakness = 2 points</td>
<td></td>
</tr>
<tr>
<td>Speech impairment only = 1 point</td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>1-2</td>
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<tr>
<td>≥ 60 minutes = 2 points</td>
<td></td>
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<tr>
<td>10-59 minutes = 1 point</td>
<td></td>
</tr>
<tr>
<td>History of diabetes</td>
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“ABCD2” Score

- Risk of stroke
- Validated in 4809 patients (previous data)

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<th>90-day</th>
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<tr>
<td>6-7</td>
<td>11%</td>
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<td>4-5</td>
<td>6%</td>
<td>10%</td>
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<tr>
<td>0-3</td>
<td>1.2%</td>
<td>3%</td>
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“ABCD2” Score

- 2 day risk of stroke
- Validated in 4809 patients (previous data)

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<th>2-day risk</th>
<th>% of pts</th>
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<tbody>
<tr>
<td>6-7</td>
<td>8%</td>
<td>21%</td>
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<tr>
<td>4-5</td>
<td>4%</td>
<td>45%</td>
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<tr>
<td>0-3</td>
<td>1%</td>
<td>34%</td>
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TIA Disposition and Workup

- Hence the recommendation (Class II)
- “Complete etiologic workup within 48 hours”
TIA

- So... because
  - Risk of stroke is highest in the first 48 hours after TIA (and TSI?)
  - Difficult to differentiate which patients fall into this group despite multiple risk stratification schemes
  - Recommendation is to get studies to determine possible etiology within 48 hours

TIA: Treatment basics

- Head of bed flat
- Blood pressure control
  - Do not lower BP acutely if under 220/120
  - Unless hypertensive emergency... e.g. aortic dissection
- Adequate hydration and oxygenation
- Antiplatelet therapy
- Heparin – no (unless cardiogenic source suspected)
- Endarterectomy
  - Only consider with high grade lesions

TIA: Treatment

- Antiplatelet therapy
  - Start after CT negative for bleed if no stroke mimic
  - ASA best first choice in ED (CAST trial)
    - Recommended dose: 50-325 mg/day
    - Reduces stroke risk
      - 2.1% to 1.6%
    - Reduces mortality
      - 3.9% to 3.3%
    - Net benefit: 9 per 1000 treated

TIA: Treatment

- Other agents / regimens
  - Clopidogrel
  - Aspirin/dipyridamole combination
  - Both are effective
  - Increased risk of bleeding but small
  - Consider using in patients on aspirin and still having symptoms (consultation?)

TIA: Treatment

- Other agents / regimens
  - Aspirin PLUS clopidogrel?
    - (FASTER study)
    - Not superior to aspirin alone
    - Increased risk of bleeding
    - Do NOT combine
TIA: Treatment

- **Heparin**
  - No good studies evaluating heparin in TIA
  - Data on ischemic strokes does not support its use
  - Should not be used for TIA at this point
  - (If considering heparin... start in consultation with neurologist)

TIA: Treatment

- **Treatment**
  - Suspected cardioembolic source?
    - Anticoagulation with vitamin K antagonist recommended
    - Risk of stroke reduced by 40% over aspirin and 60% over placebo
    - In atrial fibrillation, warfarin better than aspirin alone or aspirin plus clopidogrel
    - INR goal: 2.5

TIA: Treatment

- **Treatment**
  - Suspected cardioembolic source and A Fib?
    - New agent: Dabigatran (Pradaxa)
      - Direct thrombin inhibitor
      - Does not need monitoring

TIA: Treatment

- **Treatment**
  - Suspected cardioembolic source and A Fib?
    - Dabigatran (Pradaxa)
      - 150 mg orally twice a day
      - Superior to warfarin in preventing stroke
      - Similar risk of bleeding complications
      - Lower incidence of intracranial hemorrhage
      - Lower dose (110mg bid) noninferior to warfarin, lower overall bleeding risk

TIA: Treatment

- **Treatment**
  - Suspected cardioembolic source?
    - Rivaroxaban (Xarelto), apixaban (Eliquis)
    - Factor Xa inhibitors
      - Reduce stroke risk in patients with atrial fibrillation
      - Noninferior to warfarin, lower bleeding risk
      - Apixaban superior to warfarin

TIA: Treatment

- **So, what’s an EP to do?**
  - Start aspirin if
    - No stroke mimic
    - Not on aspirin, and
    - No bleed on neuromaging
TIA: Treatment
- So, what’s an EP to do?
  - Already on aspirin, and
  - No stroke mimic, and
  - No bleed on neuroimaging
- Consider changing to clopidigrel or aspirin/dipyridamole
  - Consider consulting with neurology

TIA: Treatment
- So, what’s an EP to do?
  - Suspected cardioembolic source?
    - If considering warfarin or other agents
    - Consult neurology first

TIA: Medicolegal Pitfalls
- Incomplete neurological exam
- Not considering diagnosis in young patient
- Delayed follow up
- Relying on single normal ECG
- Not changing antiplatelet agent if already on aspirin
- Not assuring workup in 48 hour timeframe

TIA: Medicolegal Pitfalls
- Know your regional standard of care
  - Know the controversies re: admission
  - Know the preferences for testing done acutely versus that which can be done as outpatient
  - STRONGLY consider 48 hour workup
  - Document all conversations with consultants

TIA: Medicolegal Pitfalls
- Know your hospital’s capabilities
  - Expedited workups probably best
  - If cannot perform outpatient tests quickly, consider admission
  - If patient may not be able to get to testing, consider admission

TIA: Medicolegal Pitfalls
- Treatment
  - Start antiplatelet therapy for non-cardioembolic source
    - ASA best first choice – 50-325 mg daily
TIA: Medicolegal Pitfalls

- Discuss options / risks with patient and family members
- Explain risk for stroke is significant
- Especially high risk patients
- Explain reasons they need to return to the hospital (if discharging)
- Document your conversation

Document, document, document!!!

TIA: Bottom Line

- New definition based on tissue diagnosis
- Neuroimaging critical to evaluation
- Workup for etiology needs to be done within 48 hours of symptom onset
- Should start medications from the ED
  - Aspirin in most
  - Other agents may be indicated

Thank You for your Attention!

Any Questions?