

## Transient Ischemic Attack – an opportunity for stroke prevention

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8/20/10

## Disclosures

- I have no disclosures or conflicts of interest related to this topic

## Overview

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

## PROBLEMS IN DIAGNOSIS



## 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

**RUSH UNIVERSITY MEDICAL CENTER 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

Johnston SC Neurology 2003; Giles MF Stroke 2006  
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**RUSH UNIVERSITY MEDICAL CENTER 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 upto 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

Nguyen-Huynh MN, Neurology 2003  
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**RUSH UNIVERSITY MEDICAL CENTER Making the diagnosis**

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

Symptom	GPs (n=20)			Neurologists (n=22)		
	Liberty or Two	Three	Validity or No	Liberty or Two	Three	Validity or No
Syncope	1	7	12	0	1	23
Aphasia	11	8	1	20	0	2
Dysarthria	14	5	1	13	7	2
Unilateral facial palsy*	4	6	10	17	5	0
Homonymous hemianopia	14	2	4	18	2	0
Motor weakness	10	2	2	14	7	1
Motor weakness of face	2	10	8	14	2	6
Motor weakness, arm & leg	2	3	12	2	2	18
Motor weakness, half body	4	8	6	12	6	4
Motor weakness, hand/foot/face	4	8	7	2	6	11
Cerebellar	4	13	3	0	2	20
Cerebellar	0	7	13	0	2	20
"Tics", face or hand	0	3	17	0	0	22
Vertigo	2	4	12	1	7	14
Urinary incontinence	5	6	9	1	0	21
Scalloping of scapula	3	4	13	0	2	20
Stroke-like	4	6	10	2	10	10
Diagnosis	2	7	11	4	13	5
Diagnosis	2	8	10	0	1	21
Diagnosis of IBS	4	11	5	1	4	17

Ferro JM, Stroke 1996  
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**RUSH UNIVERSITY MEDICAL CENTER 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. vertebral 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)

Kraaijeveld, Stroke 1984; Koudstaal PJ, Stroke 1986  
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**RUSH UNIVERSITY MEDICAL CENTER 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)

Martin PJ QJM 1997; Koudstaal PJ Lancet 1992  
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**RUSH UNIVERSITY MEDICAL CENTER Differential diagnosis**

**Excluded mimics:** migraine with aura, witnessed seizure, peripheral vertigo, transient global amnesia, syncope or presyncope, and delirium

Prabhakaran S, Cerebrovasc Dis 2009  
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**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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**Overview**

- Problems in diagnosis
- **Definitions**
  - Classical definition
  - New definition
- Stroke risk stratification
  - Clinical
  - Radiographic
- Management
  - To admit or not to admit

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**DEFINITIONS**



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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 upto 24 hours?
  - Can acute neuroimaging help us?

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**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

Bots ML Stroke 1997  
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**Characteristics of TIA**

- 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

Bots ML Stroke 1997  
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**RUSH UNIVERSITY MEDICAL CENTER** **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  
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**RUSH UNIVERSITY MEDICAL CENTER** **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

TIA Duration (Hours)	Percent with DWI Lesions
0-1	33%
1-3	33%
3-6	55%
6-12	50%
12-24	71%

Kidwell CS, Stroke 1999  
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**RUSH UNIVERSITY MEDICAL CENTER** **MRI of TIA**

**RUSH UNIVERSITY MEDICAL CENTER** **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 neuro-imaging (approximately 30% have MRI acutely following TIA)

Easton DL, Stroke 2009  
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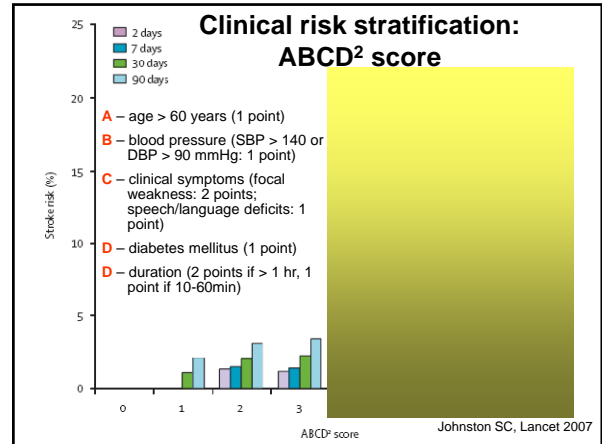
**RUSH UNIVERSITY MEDICAL CENTER** **STROKE RISK STRATIFICATION**

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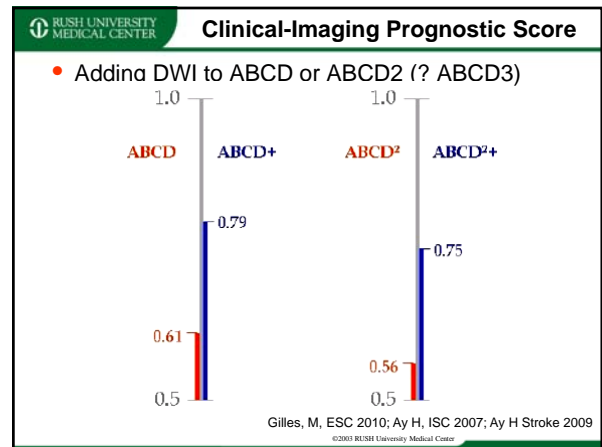
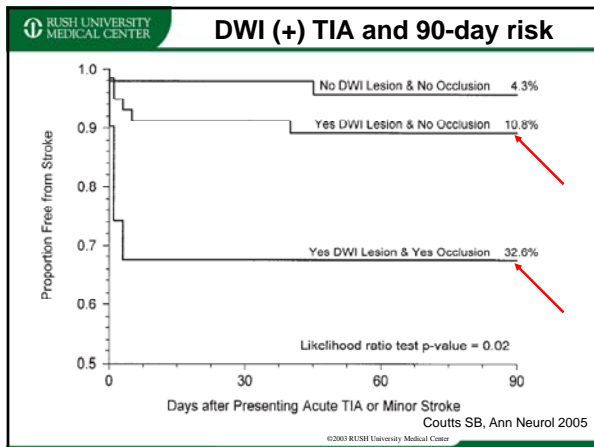
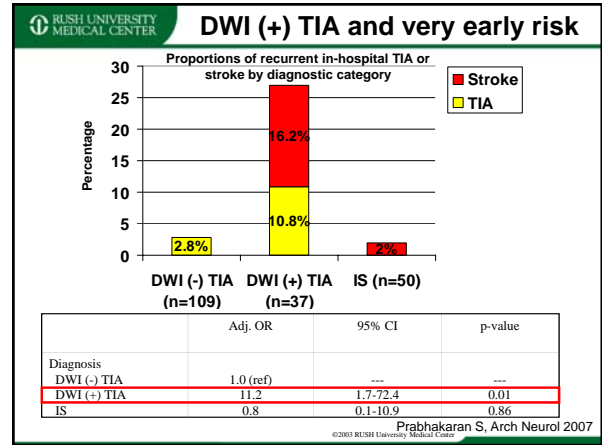
### Prognosis after classical TIA

Study Setting	Publication Year	N	Delay (d)	Stroke Risk	Projected 90-Day Stroke Risk (%)*
<b>Transient Ischemic Attack</b>					
Rochester, Minnesota <sup>33</sup>	1973	198	0	10%/3 m	10
London, UK <sup>37</sup>	1981	117	0	29%/6 m	27
Iowa City, Iowa <sup>38</sup>	1985	74	1	6.8%/6 m	13
Iowa City, Iowa <sup>38</sup>	1989	55	2	9.1%/6 m	16
Essex, UK <sup>34,41</sup>	1990	209	0	12%/1 m	15
Northern California <sup>39</sup>	2000	1707	0	10.6%/3 m	11
Essex, UK <sup>34</sup>	2004	87	0	17.3%/3 m	17
NASCET <sup>25</sup>	2004	803	0	20.1%/6 m	20
Nueces County, Texas <sup>42</sup>	2004	612	0	4.03%/3 m	4
Alberta, Canada <sup>31</sup>	2004	2295	1	9.5%/3 m	10
Ontario, Canada <sup>32</sup>	2004	265	0	6%/3 m	6
Southwest Germany <sup>34</sup>	2004	1150	0	13%/6 m	11
Brester Cincinnati/Northern Kentucky <sup>43</sup>	2005	927	0	11.2%/1 m	15
Average					11

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



**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

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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)?

The graph plots Odds Ratio (y-axis, 0 to 5) against Percent Recovery in NIHSS at 24 Hours (x-axis, 0% to 100%). Two lines are shown: a solid line for TIA and a dashed line for IS. The TIA line starts at an Odds Ratio of approximately 1.5 at 0% recovery and rises to about 4.5 at 100% recovery. The IS line starts at an Odds Ratio of approximately 1.0 at 0% recovery and rises to about 2.0 at 100% recovery.

Johnston SC, Ann Neurol 2003

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**Spectrum of acute ischemic cerebrovascular disease**

TIA		ISCHEMIC STROKE	
<b>TIA without infarction</b> Example: 5-10 minutes of left sided numbness	<b>TIA with infarction</b> Example: 120 minutes of hemiparesis and aphasia	<b>IS with incomplete recovery</b> Example: left hemiplegia at onset that recovers to mild weakness within 6 hours	<b>IS with no recovery</b> Example: right hemiplegia without improvement

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

The graph shows the 90-day rate of clinical recurrence (%) on the y-axis (0 to 25) against the degree of recovery on the x-axis. A red curve peaks at approximately 20% recurrence for 'DWI (+) TIA' and 'Typical TIA'. Other points on the curve include 'Atypical TIA', 'Not TIA', 'Partial recovery', and 'No recovery'.

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**Overview**

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  - New definition
- Stroke risk stratification
  - Clinical
  - Radiographic
  - Degree of rapid recovery (complete vs. incomplete)
- Management
  - To admit or not to admit

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**MANAGEMENT**

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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

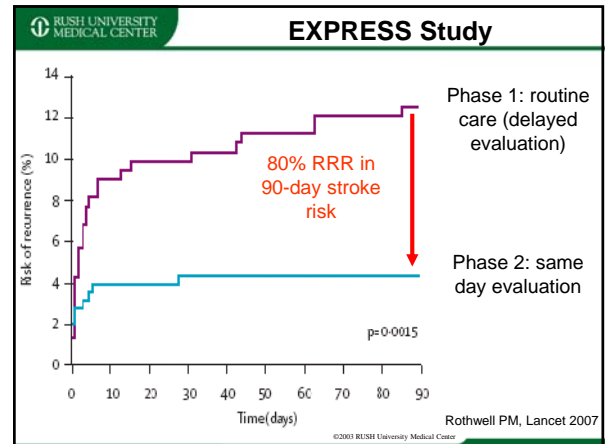
Nguyen-Huynh MN, Neurology 2005; Ovbiagele B, Stroke 2004

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**TRIAGING TIA PATIENTS**

- 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

Nguyen-Huynh MN, Neurology 2005; Rothwell PM, Stroke 2006

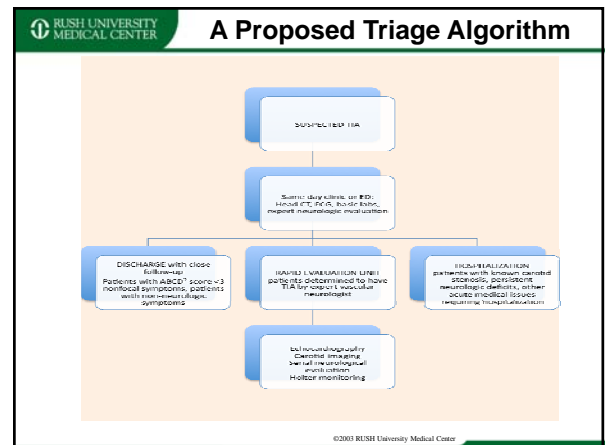


**TIA evaluation models**

Table 1. Strengths and weaknesses of each proposed model.

	Strengths	Weaknesses
Hospitalization model	<ul style="list-style-type: none"> <li>Increased opportunity for time sensitive therapies (ie, tPA)</li> <li>Increased access to carotid revascularization</li> <li>Ease of implementation</li> </ul>	<ul style="list-style-type: none"> <li>Increased risk of nosocomial infection and iatrogenic complications</li> <li>Increased health resource allocation and costs</li> </ul>
Same-day specialty clinic model	<ul style="list-style-type: none"> <li>Decreased long-term costs and health resource use</li> <li>Patient and physician convenience</li> </ul>	<ul style="list-style-type: none"> <li>Difficult to implement as a result of staffing requirements</li> <li>Increased startup costs</li> </ul>
Rapid evaluation unit model	<ul style="list-style-type: none"> <li>Decreased hospital bed days</li> <li>Decreased long-term costs</li> <li>Increased access to carotid revascularization and time sensitive therapies (ie, tPA)</li> </ul>	<ul style="list-style-type: none"> <li>Intermediate costs and logistics of implementation</li> </ul>

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**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

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

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**Guidelines**

- 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

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**RUSH UNIVERSITY MEDICAL CENTER** **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  
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**RUSH UNIVERSITY MEDICAL CENTER** **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
      - Models include admission, clinic, rapid evaluation units
      - 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%

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**RUSH UNIVERSITY MEDICAL CENTER** **The future: AICS like ACS?**

**Classification of Acute Ischemic Cerebrovascular Syndrome (AICS)**

Category	Definition	Examples
definite AICS		
Probable AICS	Acute onset of neurologic dysfunction of any severity suggestive of focal brain ischemic syndrome but WITHOUT imaging/laboratory	1. Sudden onset of painless homonymous hemianopia with normal CT at 12 hours after onset. MRI was not performed.
Possible AICS	Acute neurologic dysfunction of any duration or severity possibly consistent with focal brain ischemia WITHOUT imaging/laboratory	1. Two-hour episode of isolated vertigo and headache in a 65-year-old man with a history of hypertension, arrhythmia, not suggest nonischemic etiology; possible alternative etiologies ARE ruled out.
Not AICS	Acute onset of neurologic dysfunction with imaging/laboratory	1. Sudden onset of left hemiparesis and homonymous hemianopia with normal CT at 12 hours after onset. MRI was not performed.

**Any confirmed stroke → STEMI**  
**DWI/CT (+) TIA → NSTEMI**  
**DWI (-) typical TIA → unstable angina**  
**DWI (-) atypical TIA → stable angina**  
**Stroke/TIA mimics → non-cardiac chest pain**

Kidwell CS, 2003  
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**THANK YOU FOR YOUR ATTENTION!**

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