



**TIA and minor stroke
Acute and preventative management
CMAJ 2008: Best practice guidelines**

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Outline

1. TIA: epidemiology and subtypes
2. Diagnosis and differential diagnosis TIA
 1. Stroke mimics
 2. Predicting stroke after TIA
3. CMAJ: TIA Management guidelines

***A,B,C**...indicates level of evidence (note labeling through the talk)

CMAJ Dec 2008 Canadian Best Practice Recommendations for Stroke Care

Canadian best practice recommendations for stroke care
 CMAJ • December 2, 2008; 179

joint initiative of the Canadian Stroke Network and the Heart and Stroke Foundation of Canada

- "Best Practices and Standards represent 1 of 5 Canadian Stroke Strategy national priority platforms. The goal of the Best Practices and Standards platform is to **transform stroke prevention and care, ensuring that evidence-based best practices are integrated into the Canadian health system.** The Best Practices and Standards Working Group was established in response to the observation that **stroke research findings do not always reach health care professionals, hospital administrators, health ministries and, most importantly, persons with stroke.** Thus, best practices are not consistently applied, leaving a significant gap in the quality of stroke care between what should be done and what is being done. The primary goal of the Canadian Stroke Strategy is to help close this gap. ... the result of an extensive review of international stroke research and published evidence-based best practice recommendations or guidelines related to stroke... They are for use by health professionals throughout the health care system..."

TIA and minor stroke

DEFINITION

DIAGNOSIS

PATHOPHYSIOLOGY

ETIOLOGY

RISK OF STROKE FOLLOWING TIA

TIA: definition, mortality, diagnosis

- ~ 40% of TIA's last more than 1 hour, and 90% last less than 6 hours.
- ~15% of all strokes are preceded by a TIA. Schwartz JAMA 285 (2001), pp. 1711–1718.
- TIA is defined as an acute focal neurologic deficit that is localized to one vascular territory, lasting less than 24 hours, with abrupt onset and abrupt or gradual resolution.
- A TIA is as a stroke-like event which resolves in less than 24 hours (< 1 hour; normal MRI!) N Eng J Med: Volume 347:1713-1716 200: 21
Transient Ischemic Attack — Proposal for a New Definition

TIA: definition, mortality, diagnosis

- The mortality rate during a follow-up of 389 days in a small cohort of 83 patients with TIA was 2% Purroy et al 2004
- Cardiac event rate in 1,327 patients with TIA's due to all causes who had any abnormal ECG findings was found to be 7 times higher than in age-matched controls within the first 3 months after the index event Elkins et al 2002

TIA: symptoms territory dependent

Diagnosis of transient ischemic attack is **clinical**.

Symptoms depend on vascular territory affected:

- **Left carotid:** include transient dysarthria, or aphasia, right limb weakness, right face weakness, left eye or right field visual impairment and right body or face numbness or paresthesia.
- **Right carotid:** similar symptoms on the left side of the body, but dysphasia is rare.
- **Vertebrobasilar:** dizziness/vertigo, diplopia, dysathria, dysphagia, X'ed motor or bilateral, X'ed or bilateral sensory
- **Retinal TIA's:** (amaurosis fugax) or transient monocular blindness (TMB) described as a unilateral fog, blur, clou mist, shade, or curtain in one eye, "curtain effect" common.

TIA: Pathogenesis and Etiology

- The underlying pathology for the ischemia of TIA's may be **atherothrombotic, embolic, inflammatory**.
- Ischemia of the internal carotid artery territory or vertebro-basilar territory and its branches via **cardiac or arterial embolism or hemodynamic insufficiency** form the underlying basis.
- Rarely, **vasospasm** may be responsible for the symptoms of transient monocular blindness.
- **Limb shaking TIA:** clonic movements, positional, hypoperfusion-related, typically In association with high-grade carotid stenosis.

Etiology Hankey et al 1991

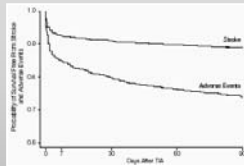
In a cohort of patients with TIA's (carotid and vertebrobasilar):

- 68% were male
- 47% smoked
- 42% had hypertension
- 21% had coronary disease
- 15% had valvular disease
- 4% had atrial fibrillation
- 5% had congestive heart failure,
- 16% had cardiomegaly
- 17% had peripheral vascular disease
- 5% had diabetes,
- 42% had elevated cholesterol, and
- 18% had a history of migraine

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TIA: risk of stroke

- Individuals who experience a TIA are at high risk of subsequent stroke:
 - 90 days after a TIA: 10-25% of patients experience a stroke or other adverse event, 50% of these occurring within 2 days of the TIA
 - 21% of these strokes are fatal and 64% result in disability. Johnson et al JAMA 2000 284 2901-2906



- Age > 60 years, diabetes, symptom duration of greater than 10 minutes, weakness, and speech impairment were associated with a higher risk.

Non-recent TIA and stroke risk

- Even in patients with a non-recent TIA, there is an increased risk of stroke and cardiac events.
- In an analysis of patients from the Oxford community stroke project who had a TIA at a median of 3.8 years previously, there was a 18.8% risk of stroke over 10 years and a 27.8% risk of myocardial infarction or cardiac death over 10 years Clark et al 2003

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Amaurosis fugax and stroke risk

- In the North American Symptomatic Carotid endarterectomy Trial, in which patients with carotid stenosis and TIA or minor stroke were studied, the stroke risk in patients with TMB was ~ half that of patients with hemispheric TIA (hazard ratio 0.53) Benavente et al 2001

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TIA: risk of stroke following TMB, TIA, stroke

- In a large group of TIA patients: patients with TMB had a 2.2% annual stroke risk compared with 1.3% for asymptomatic internal carotid artery stenosis, 3.7% for patients with any territory TIA, and 9% for patients with major stroke. Wilterdink and Easton 1992
- In another prospective study, the 90-day risk of stroke after TIA ranged from 10-15%, whereas the stroke risk at 6 months was 17%, and the combined risk (stroke, TIA and death) was 30% Kleindorfer et al 2005

C-reactive protein and stroke risk following initial ischemic stroke and TIA

- Biological markers such as C-reactive protein are predictive of vascular recurrence.
- In a cohort of 135 TIA patients, high levels of high-sensitivity C-reactive protein (greater than 4.1 mg/l) determined in the first 24 hours after the index event were found to be independently associated with a high risk (hazard ratio 2.81) of further vascular events during a 1-year follow-up Purroy et al 2007

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MISDIAGNOSIS, DIFFERENTIAL DIAGNOSIS AND STROKE MIMICS

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Stroke mimics

- Knowing a stroke is a stroke is difficult in ~ 5-10% of patients. Many conditions, including systemic abnormalities and other nervous system diseases, present with focal neurologic deficits that "mimic" acute ischemic stroke.
- Must also consider the possibility of dual diagnoses.
- A recent prospective study of 336 patients who presented to an urban teaching hospital with suspected stroke found **mimics in 31% at the time of final diagnosis.**¹

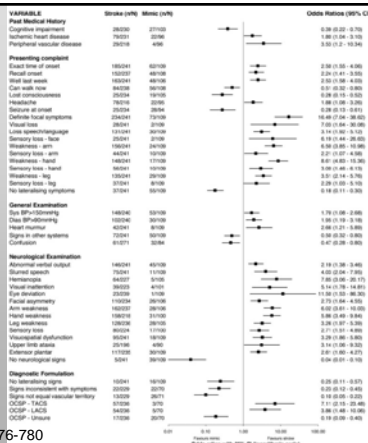
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1. Hand et al: Stroke 2006 37: 776-780

Stroke mimics¹

predicted stroke

- Exact time of onset
 - focal symptoms/signs
 - abnormal vascular exam
 - normal cognition
 - NIHSSS(>10)
- ### Predicted mimic
- Seizure at onset
 - Cognitive impairment
 - No focal findings
 - Lost consciousness



1. Hand et al: Stroke 2006 37: 776-780

Case 1

79 year old male seen SPC 2 3 2009: recurrent episodes of language difficulty ("can't get his words out") accompanied by "numbness" of the right upper extremity.

First episode Feb 7 2009 one day after VVIR pacemaker insertion for syncope x 2 attacks.. Admitted to local hospital 2 days. No change in medications (on coumadin following DVT 7 years previously, INR 2.1).

Second episode 5 days later with further episodes near daily x 7 days prior to assessment in SPC. Reports low grade headaches left parietal x 3 days. Wife states seems vaguely confused.

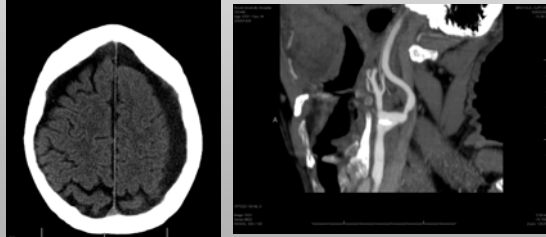
Neurological examination: nil focal. Slow to respond. Gait unsteady.....Pulse 60 min, regular. BP 150/95. Vascular examination is normal.

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79 year old male seen SPC 2 3 2009: recurrent episodes of language difficulty ("can't get his words out") accompanied by "numbness" of the right upper extremity.

First episode Feb 7 2009 one day after VVIR pacemaker insertion for syncope x 2 attacks.. Admitted to local hospital 2 days. No change in medications (on warfarin, INR 2.1). Second episode 5 days later with further episodes near daily x 7 days prior to assessment in SPC. Reports low grade headaches left parietal x 3 days. Wife states seems vaguely confused.

Neurological examination: nil focal. Slow to respond. Gait unsteady.....



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Stroke mimics

TABLE 2. Causes of Stroke Mimics (n=109)*, Subdivided by Time to Presentation

Condition	Total Number (%)†	Mimics Presenting	
		Within 6 Hours	After 6 Hours
Seizure	23 (21.1%)	18 (29.0%)	5 (10.6%)
Sepsis	14 (12.8%)	6 (9.7%)	8 (17.0%)
Toxic/metabolic	12 (11.0%)	6 (9.7%)	6 (12.8%)
Space occupying lesion	10 (9.2%)	3 (4.8%)	7 (14.9%)
Syncope/presyncope	10 (9.2%)	9 (14.5%)	1 (2.1%)
Acute confusional state	7 (6.4%)	3 (4.8%)	4 (8.5%)
Vestibular dysfunction	7 (6.4%)	3 (4.8%)	4 (8.5%)
Acute mononeuropathy	6 (5.5%)	4 (6.5%)	2 (4.3%)
Functional/medically unexplained symptoms	6 (5.5%)	4 (6.5%)	2 (4.3%)
Dementia	4 (3.7%)	2 (3.2%)	2 (4.3%)
Migraine	3 (2.8%)	2 (3.2%)	2 (4.3%)
Spinal cord lesion	3 (2.8%)	0 (0%)	3 (6.4%)
Other	3 (3.7%)	2 (3.2%)	1 (2.1%)
Total	109 (100%)	62 (100%)	47 (100%)

Hand et al: Stroke 2006 37: 776-780

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TIA diagnosis and misdiagnosis

- The diagnosis of TIA is subjective and based on history. The kappa value for inter-observer agreement on the diagnosis of transient ischemic attack is only 0.65 ^{Hankey et al 1991}
- One **third to one half** of patients labelled with a diagnosis of TIA evaluated in primary care or ER are likely to be misdiagnosed and thus inappropriately investigated and treated. ^{Joseph Harbison et al Stroke. 2003;34:71; J.M. Ferro Stroke.}

1996;27:2225-2229

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Differential diagnosis

- One study in which TIA's were reported by patients through questionnaire, subsequent evaluation confirmed following diagnoses:
 - mononeuropathy, radiculopathy, psychoneuroses, Bell's palsy, migraine, cerebral infarction.
 - Migraine and seizures are important alternatives
 - tumors, subdural hematomas, aneurysms, amyloid angiopathy, MS, hypertensive encephalopathy, hypoglycemia and hyperventilation.

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Hand et al: Stroke 2006 37: 776-780

**Canadian Best Practice Guideline
recommendations
TIA diagnosis**

*'All patients should have immediate evaluation and additional investigation for dx, r/o mimics, est plan rx.. **B**'*

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**STRATIFYING STROKE RISK
FOLLOWING TIA**

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CASE 2

- A 55-y-o right-handed, 5th grade English teacher presents ER with complaints of left facial and left upper extremity numbness accompanied by visual blurring that lasted 30 minutes shortly after awakening on the day of presentation. He smokes 2 packs of cigarettes per day for approximately 20 years. Vascular risk profile: ½ pack cigarettes per day; previous MI; diabetes mellitus. Current medications: ASA 81 mg po od; lipitor 10 mg po od. Nitrolingual 0.3 prn; atenolol 50 mg daily. BP 135/85
- What is his risk of stroke ? What is the appropriate management ?

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CASE 3

- A 65-year old right-handed housewife presents to the ED after experiencing a 20 minute episode of weakness of the left upper extremity accompanied by slurring of speech shortly before going to bed yesterday evening. Vascular risk factors: Obesity (BMI 38); hypertension, diabetes mellitus. Medications: glyburide 5 mg bid; HCTZ 25 mg po od; Amlodipine 5 mg daily. She does not smoke. BP 160/100
- What is her risk of stroke ? What is the appropriate management?

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Stratification tools for TIA Predicting stroke risk

Physicians evaluating TIA patients need reliable method to stratify an individual's stroke-risk profile in order to make appropriate clinical decisions.

- 6-point ABCD^{Rothwell et al 2005}
and
- 7 point ABCD2 scores^{Johnston et al 2007}

validated to identify patients with an early high risk of stroke after a TIA.

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ABCD and ABCD2

- The ABCD acronym signifies A (age of greater than 60 years), B (blood pressure greater than 140/90), C (clinical features: unilateral weakness, speech disturbance), and D (duration of symptoms in minutes).
- The ABCD2 has been suggested as a refinement of the original score, with diabetes as a factor

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Clinical scoring ABCD and ABCD2

- The score is based only on clinical parameters: age, blood pressure, clinical features (weakness and speech impairment), and spell duration.
- Patients with a score of 6 have a 30% risk of stroke within 7 days after the index TIA Rothwell et al 2005
- Recently, this score has been refined by the addition of a point for diabetes--ABCD2 Johnston et al 2007

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ABCD and ABCD2

- The usefulness limited in patients with symptoms affecting the [posterior circulation](#).
- Radiological findings from [diffusion-weighted MRI improve the ability of the ABCD2 clinical score to discriminate](#) the low or high risk of subsequent stroke Coutts et al 2008

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ABCD² score

The ABCD² score was generated in the 2 original derivation cohorts by multivariate logistic regression analysis of individual risk factors from the ABCD and California scores.

Age	≥ 60 years	1
Blood pressure	≥ 140/90	1
Clinical deficit	Unilateral weakness	2
	or Speech disturbance	1
	or Other symptom	0
Duration symptoms	< 10 mins	0
	10-59 mins	1
	≥ 60 mins	2
Diabetes	present	1
TOTAL SCORE		7

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Lancet 2007;369:283-92

CASE 2

- A 55-y-o right-handed, 5th grade English teacher presents ER with complaints of left facial and left upper extremity numbness accompanied by visual blurring that lasted 30 minutes shortly after awakening on the day of presentation. He smokes 2 packs of cigarettes per day for approximately 20 years. Vascular risk profile: ½ pack cigarettes per day; previous MI; diabetes mellitus. BP 135/85
- What is his risk of stroke? What is the appropriate management?

age	< 60 years	0
	≥ 60 years	1
SBP/DBP	< 140/90	0
	≥ 140/90	1
deficit	Unilateral weakness	2
	Speech disturbance	1
	Other symptom	0
Duration symptoms	< 10 mins	0
	10-59 mins	1
	≥ 60 mins	2
Diabetes		1
TOTAL SCORE		1

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CASE 3

- A 65-year old right-handed housewife presents to the ED after experiencing a 60 minute episode of weakness of the left upper extremity accompanied by slurring of speech shortly before going to bed yesterday evening. Vascular risk factors: Non smoker; Obestiy (BMI 38); hypertension, diabetes mellitus. BP 160/100. What is her risk of stroke? What is the appropriate management?

age	< 60 years	0
	≥ 60 years	1
SBP/DBP	< 140/90	0
	≥ 140/90	1
deficit	Unilateral weakness	2
	Speech disturbance	1
	Other symptom	0
Duration symptoms	< 10 mins	0
	10-59 mins	1
	≥ 60 mins	2
Diabetes		1
TOTAL SCORE		6

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Acute management of TIA and minor stroke

“Use a **stratification tool** at point of initial contact whether 1^o, 2^o or 3^o care..**B**”
(NIHSS, ABCD/D2)

- **Emergent investigation** for patients with highest classification risk (~ABCD2..7) within 24 hours and **urgent assessment** (~ABCD2..5-6) within 7 days...**B**

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STROKE PREVENTION CLINICS

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SOS TIA

A TIA clinic with round-the-clock access
(SOS-TIA)
feasibility and effects

Philippa C Lavallée Lancet Neurology 2007 6(44)
953-960

SOS-TIA

- SOS-TIA examined the effect of providing **24-hour rapid referral and assessment** of patients with TIA Hospital-based clinic.
- Outcomes: 90-day stroke rate, 1-year mortality, and other outcomes

Philippa C Lavallée Lancet Neurology 2007 6(41)
953-960

SOS Results

- Median follow up 16 months. 3% lost to follow-up
- The **90-day stroke rate was 1.24%** compared with the **predicted stroke rate of 5.96%**. (based on ABCD2)
- Represents a **risk reduction of 80%** (HR, 0.2).

Philippa C Lavallée Lancet Neurology 2007 6(41)
953-960

Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke

EXPRESS study

a prospective population-based sequential comparison

[The Lancet: 2007; 370; 432-1442](#)

P. Rothwell, M. Giles, A. Chandratheva, L. Marquardt, O. Geraghty, J. Redgrave, C. Lovelock, L. Binney, L. Bull, F. Cuthbertson

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EXPRESS

- Study *within* the Oxford Vascular Study (OXVASC).
- OXVASC: **population-based incidence study** of all TIA and stroke in Oxfordshire UK.
- OXVASC study population consists of **91,000 individuals**, registered with **63 primary-care physicians** in nine primary-care practices in Oxfordshire,



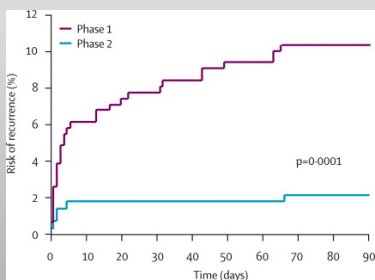
³² PM Rothwell et al (Oxford Vascular Study), Lancet 366 (2005), pp. 1773–1783.
³³ PM Rothwell et al. for the Oxford Vascular Study, (Oxford Vascular Study), Lancet 363 (2004), pp. 1925–1933.

Express Methods

- The **primary outcome was the risk of stroke within 90 days** of first seeking medical attention, with independent blinded (to study period) audit of all events.

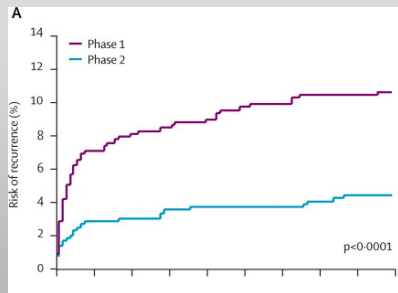
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Express Results



the **90-day risk of stroke in all patients** in the study population presenting with TIA was significantly higher in phase 1 than in phase 2 ($p=0.0015$)

Express Results



- The risk of recurrent stroke within 90 days of first presentation with TIA or stroke in the whole population was significantly higher in phase 1 than it was in phase 2 ($p < 0.0001$) 52

Acute management of TIA and minor stroke Stroke Prevention Clinic CBPG

"Patients with minor stroke or TIA should be referred to a designated Stroke Prevention Clinic....B"

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Testing for cause assessment following stroke or high risk TIA

Canadian Best Practice Recommendations for stroke ca 55
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INVESTIGATION FOLLOWING TIA/MINOR STROKE

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Diagnostic workup

- Testing proceeds in an orderly fashion to exclude carotid bifurcation disease, cardiac disease, hematological disease, and structural diseases of the brain that mimic transient ischemic attack.

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Hospital admission for high risk patients

- Hospitalization is advised for patients with transient ischemic attack in the previous 48 hours, for those with crescendo transient ischemic attacks, or patients at high risk of early stroke recurrence Johnston et al 2006

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Cranial neuroimaging for TIA

Cranial CT:

- Initial imaging mode of choice, particularly in the ER because of its ease of use, widespread availability, and ability to image blood.
- ~1% of patients will have a non-ischemic lesion (tumor, subdural hematoma, AVM or aneurysm) identified on CT scan with a TIA-LIKE presentation Douglas et al 2003

Cranial MRI/DWI:

- The posterior circulation vessels and blood flow can be visualized more readily using conventional MRI rather than standard CT.
- patients meeting clinical criteria of TIA's, 1/3 and 2/3 demonstrate appropriate infarcts for the symptoms on brain CT and MRI, respectively Saver and Kidwell 2004

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MRI and DWI in TIA

- Meta-analysis including 1242 patients with transient ischemic attacks, 16% to 67% showed acute lesions on diffusion.
- Positive diffusion-weighted imaging was associated with TIA's lasting longer than 60 minutes or those occurring with motor weakness or language impairment. Redgrave et al 2007

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DWI imaging

TIA and minor stroke – identifying high risk patient

- 90 day stroke risk after presenting TIA:
 - Absence of DWI lesion: 2.4%
 - DWI lesion present: 11%
 - DWI lesion and large artery stenosis: 32% Coutts Ann Neurology 2005 57
- Multiple ischemic lesions on DWI are the strongest predictor of early ischemic lesion recurrence Kang Ann Neurol 2003 54



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Vascular imaging

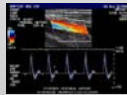
- Duplex US
- Transcranial doppler ultrasound
- MR angiography (MRA)
- CT angiography

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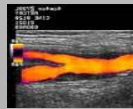
Ultrasound doppler/Duplex scanning



- Duplex - pulsed wave doppler with B mode

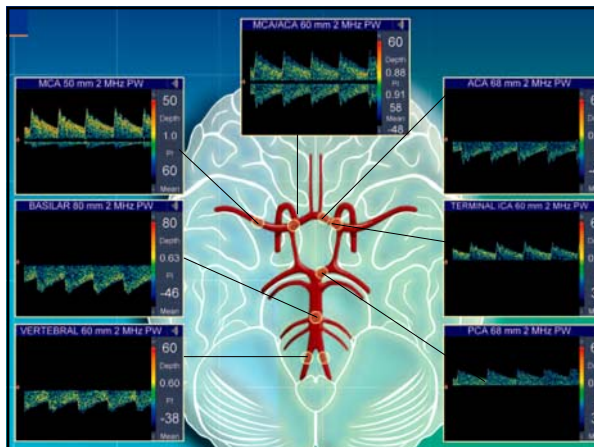


B mode scanning: images the arterial wall rather than blood flow velocity producing an US map of the lumen



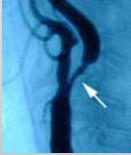

- Colour coded Doppler uses colour to superimpose flow velocities on 2 D US image
- The positive and negative predictive values for surgical disease (70% to 99% angiographic stenosis) for color duplex are 0.84 and 0.98

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Catheter Angiography


- Catheter inserted femoral or brachial artery – fed through to carotid or vertebral using “guide wire”. Contrast injected with high pressure pump.
- Current role predominantly interventional management. Reduced use as a diagnostic test due to availability of other imaging modalities (CTA, MRA). **Invasive** – 1% stroke risk. Intra-arterial digital subtraction angiography should be reserved for those in whom intra-arterial therapeutic interventions are planned or for whom noninvasive tests are not diagnostic.


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MR angiography

- Non invasive
- **Intracranial disease:** aneurysm, AVM, arterial or venous occlusive disease, vasculitis
- **Carotid stenosis**



MRA Spontaneous Carotid Artery Dissection

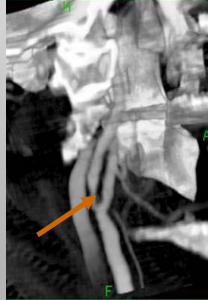


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CT angiography ICA stenosis

~90% correlation between CTA findings and conventional angiography

During CTA, a spiral CT scanner is used to perform a rapid singular rotation of the gantry around the patient while the table is continuously advanced through the scanner during the acquisition. As a result, whole-brain views with thin sections can be completed in 30 seconds



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Investigating for a cardioembolic source

- The extent of the diagnostic evaluation is substantially influenced by how the results will influence patient management.
- In patients with normal or mildly diseased carotid arteries or those at high risk of embolicogenic heart disease, cardiac testing is initiated.
- Holter monitoring is performed when an emboligenic arrhythmia is suspected, such as intermittent atrial fibrillation.

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Echocardiography

- Transthoracic echocardiography is now part of the routine evaluation for TIA or stroke of unclear cause or associated with clinical cardiac disease.
- Transesophageal echocardiography (TEE) is more sensitive than transthoracic echo (TTE) for identifying potential sources of embolism cardiac patients with recent ischemic stroke or TIA, regardless of age^{Debruin et al 2006}

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Echocardiography (TTE and TEE)

- To identify cardiac sources of emboli:
 - Atrial fibrillation
 - LV or LA thrombus
 - Endocarditis
 - Atrial myxoma
 - PFO/ASA
 - Aortic arch evaluation



LV thrombus

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Systemic and coagulation abnormalities

- In patients where carotid and cardiac tests are unrevealing.
- antiphospholipid antibodies and other hypercoagulable states, perform toxic drug screening, and perform serological tests for vasculitis.

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In patient evaluation TIA and Stroke cause

"TIA patients should undergo rapid work-up, if necessary in hospital. Much of the evaluation is a "plumbing assessment"

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CBPG TIA investigation recommendations

Neurovascular imaging:

- *“All patients with suspected stroke or TIA should undergo **brain imaging** immediately...**A**”*
- *“If indicated MRI should include DWI and GE and FLAIR...**B**”*
- *“Vascular imaging ASAP (US, CTA, MRA or DSA)...**B**”*
- *“Carotid imaging if carotid TIA or non-disabling stroke within 24 hours...**B**”*

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Evaluation TIA and Stroke cause

- Standard evaluation includes:
- CT and/or MRI: (confirm stroke and acuity; pattern may suggest cause)
- Vessel assessment: US, CTA, MRA, TCD. Evaluation intracranial vessels (atherosclerosis, dissection, vasculitis). Extracranial (stenosis, dissection)..sensitivities (85-98% per modality). Catheter angiography rarely employed.
- TTE/TEE: (thrombus, LA enlargement, PFO)
- Blood: CBC, ESR, PT, aPTT, VDRL, FBC, HbA1c; C-RP; thrombophilia; blood culture”

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MEDICAL INTERVENTIONS FOLLOWING TIA/MINOR STROKE

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Management

- The short-term risk of stroke can be reduced with rapid evaluation and institution of treatment with antiplatelet agents, statins, and antihypertensives Rothwell et al 2007
- the Oxford Vascular Study, patients referred to a rapid evaluation stroke and TIA clinic had a 2.1% risk of stroke at 90 days, compared to a 10.3% risk with the "standard" evaluation system (p=0.0001).

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Antiplatelet therapy

- Patients with noncardioembolic transient ischemic attack should be immediately started on long-term daily antiplatelet therapy.
- Aspirin in doses ranging from 50 to 325 mg/day, clopidogrel (75 mg per day), or a combination of extended-release dipyridamole (200 mg twice daily) plus aspirin (50 mg/day) are all acceptable options for initial therapy Adams et al 2008; Hankey and Eikelboom 2005; Johnston et al 2006

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ASA and clopidogrel

- Due to increased risk of hemorrhagic complications, adding aspirin to clopidogrel is not justified in the treatment of transient ischemic attacks or ischemic stroke unless specific conditions such as acute coronary syndrome or coronary stent exist. Adams et al 2008

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ASA and Plavix Match Trial

- In the MATCH trial, patients were enrolled with transient ischemic attack or stroke and additional risk factors, such as a prior ischemic event or diabetes.
- The addition of 75 mg of aspirin to the clopidogrel did not achieve the hypothesized 14% reduction in vascular events; instead a nonsignificant 6% risk reduction was documented.
- In addition, aspirin plus clopidogrel was associated with a 1.3% increase in life-threatening bleeding. Diener et al 2004

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2008 American Stroke Association Stroke prevention update

- aspirin alone (50 to 325 mg), clopidogrel, or aspirin plus extended-release dipyridamole are all acceptable for initial therapy .
- aspirin and extended-release dipyridamole are recommended over aspirin alone (Class I).
- administration of a statin with intensive lipid-lowering effects is recommended in patients with an atherosclerotic stroke or TIA, even in the absence of overt ischemic heart disease Adams et al 2008

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CBPG recommendations Antiplatelet therapy

- *Standard of care unless CI or needs anticoagulation.*
- *No benefit for combination therapy*.*
- MATCH Sacco Stroke 2006 37 577 compared CPD+ASA vs. CPD in high risk patients with stroke/TIA with risk factors: PEP: stroke, MI, Va death. *Insignificant trend favouring combination but highly significantly increased life threatening bleeds.. B* (CHARISMA, MATCH)
- *“Combination is indicated for patients with stents.”*
- *“ASA 80-325 mg... A, CPL, *DIPYR/ASA... A all acceptable”*

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Anticoagulation

- Indications:
 - Atrial fibrillation (INR 2-3)...**A**...ASA etc.
 - Prosthetic heart valves (INR 2.5-3.5 or 2-3 low risk valves)
 - CVT
 - Dissection ??
 - coagulopathy
- Warfarin (W) for non-cardioembolic stroke (NCS):
 - WARSS: ischemic NCS: ASA 325 vs. W: NS
 - WASID: stopped early because of safety issues in W group.

5

SURGICAL INTERVENTIONS FOLLOWING TIA/MINOR STROKE

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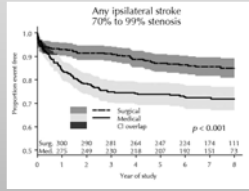
Case 4

- A 66-year-old man presented to the emergency room with the acute onset of expressive speech difficulty, which lasted for 20 minutes and then resolved.
- The past medical history was notable for diabetes mellitus and hypertension for 10 years each.
- On examination, the patient was in sinus rhythm with a blood pressure of 150/80 mm Hg.
- His exam revealed intact speech, no facial weakness, no limb weakness, and flexor plantar responses.
- Subsequent testing revealed 70-99% stenosis of the left internal carotid artery on duplex. This was confirmed as severe stenosis on CTA of 85%
- Successful left carotid endarterectomy was performed 2 days after presentation.

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Management –surgical Carotid stenosis > 70% stenosis

- Patients with > 70% carotid stenosis and a recent ipsilateral carotid TIA should be treated surgically, if the perioperative stroke and death rate is less than 6% North American Symptomatic Carotid Endarterectomy Trial Collaborators 1991
- CEA reduces the ipsilateral stroke rate in patients with TIA or stroke and 70-99% stenosis from 26% to 9% after 2 years follow-up North American Symptomatic Carotid Endarterectomy Trial Collaborators 1991



NNT 6

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NASCET 50-69% carotid stenosis

- Symptomatic Carotid Endarterectomy Trial demonstrated a modest benefit from surgery (absolute risk reduction 1.3% per year) but the benefit was heterogeneous.
- Women and patients with retinal ischemia did not derive benefit. Below 50%, there was no benefit seen in the North American Symptomatic Carotid Endarterectomy Trial. Barnett et al 1998

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Does early intervention make a difference ? Carotid endarterectomy

- Benefit from surgery is time-dependent and
- Carotid endarterectomy was most effective when performed within 2 weeks from the qualifying ischemic event (stroke/TIA). Rothwell PM et al... 2004 Mar 20;363(9413):915-24.

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CEA and perioperative complication rate

The perioperative complication rate for carotid endarterectomy may be increased by certain clinical and angiographic variables. In one analysis, 2 or more of the following factors doubled the risk: age greater than 75 years, diastolic blood pressure greater than 110 mm/Hg, history of angina, performance of endarterectomy in preparation for CABG thrombus in the internal carotid artery lumen, or a downstream siphon stenosis

[\(McCrory et al 1993\).](#)

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American Academy of Neurology recently published an updated statement on carotid endarterectomy

- Information from the pooled analysis for symptomatic patients:
- *' The absolute benefit at 5 years is 16% for patients with 70% to 99% stenosis and 4.6% for patients with 50% to 69% stenosis'* Rothwell et al 2004

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Carotid stenting

- CAVITAS trial that compared carotid angioplasty with carotid endarterectomy did not find a significant difference in the periprocedure rate of stroke or death between the 2 modalities.
- With surgery, the 1 month rate was 9.9% and it was 10.0% in the angioplasty group.
- There was a lower rate of cranial nerve palsy with angioplasty, although the restenosis rate was higher. CAVATAS Investigators 2001

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Asymptomatic carotid stenosis

- Compared with symptomatic stenosis, the risk of stroke with asymptomatic carotid artery disease over 2 years is:
 - 2.6% with stenosis < 70% and
 - 3.3% with stenosis over 75% (1.6% per year)
- In the ACAS trial, risk of stroke in surgically treated patients was 1% per year vs. 2% per year in medically treated patients if the perioperative stroke risk was 2.3% and less JAMA 1995

94

Carotid surgery for symptomatic disease Canadian best practice guideline recommendations

If candidate for CEA or stenting CTA or US within 24 hours for highest risk (7) and within 7 days for high risk (5-6)..C"

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RISK FACTOR MANAGEMENT FOLLOWING TIA/MINOR STROKE

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Case 5: A 60 year old female presents with sudden onset right hemiparesis and expressive aphasia due to a L MCA territory TIA. Risk factors include hypertension, DMII, dyslipidemia and smoking; BMI is 32, BP is 180/90, HR 85 min and regular; mild expressive language difficulty and 4/5 weakness right arm and leg, deficits improving over 30 mins. CT normal, US carotids 50% ICA stenosis bilaterally. TEE shows a small PFO. Fasting glucose 7.2; LDL 4.3.

Which of the following is the most important modifiable risk factor for future stroke risk?

1. Hyperlipidemia
2. Hypertension
3. Patent foramen ovale
4. Diabetes mellitus
5. Smoking
6. Obesity

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Stroke – modifiable risk factors

- Hypertension
- Diabetes
- Smoking
- Hyperlipidemia
- Carotid disease
- Obesity
- TIA
- Sedentary life style
- Atrial fibrillation
- Substance abuse
- Iatrogenic (angiography, CEA, CABG)

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Hypertension

- Hypertension: major stroke risk factor. BP reduction of 12/5 results in 43% reduction of recurrent stroke risk in both hypertensive and non-hypertensive individuals Lancet 2001 358 1033
- CMAJ-2008 Recommendations:
 - For prevention of first stroke: BP rx goal < 140/90
 - For stroke and TIA patients: rx goal < 140/90.. **C**
 - For stroke/TIA patients: ACE-I or diuretic...**B**
 - First or recurrent stroke prevention in diabetics and patients with chronic renal disease: rx goal < 130/80.. **A**
 - Treatment initiation prior to discharge from hospital following stroke or TIA (**B**..EXPRESS, PROGRESS)

hypertension

- Acute: blood pressure should be reduced as follows:
 - Within 24 hours of tPA:
 - SBP < 185 and DBP < 110 mm Hg
 - No tPA or after 24 hours after tPA:
 - SBP < 220 and DBP < 120 mm Hg
 - Use labetalol IV to control; lower by 15% per 24 hours
- Hypertension after hyperacute phase:
- Lowering BP reduces stroke risk by 30-40% ¹
- Starting anti-hypertensive treatment in hospital reasonable and leads to improved long-term compliance.

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1. Lawes et al. Stroke 2004 35: 776-785

Lipid management

- Less definite link between dyslipidemia and stroke vs. CVD.
- Meta-analysis confirmed statins reduce risk of stroke in patients with CAD 26% [Corvol Arch Int Med 2003 163 669](#)

- *Fasting lipids should be assessed each 1-3 yrs in men > 40 years and women > 50 yrs. C*
- *More aggressive tx of diabetics (target LDL ≤ 1.7 mmol/l)*

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Statins: SPARCL and JUPITER

SPARCL: Atorvastatin 80 mg resulted in a 16% reduction in PEP (non-fatal or fatal recurrent stroke) over 5 years in patients with and without dyslipidemia [N Eng J Med 2006 163 355](#)

JUPITER [Ridker Engl J Med. 2008;359:2195-2207](#)

- multinational, DBPC trial randomized 17,802 men and women to 20 mg/day rosuvastatin or placebo.
- Hypothesis was that statin therapy, given to apparently healthy individuals with normal LDL-cholesterol levels (< 3.2 mmol/L) but elevated CRP levels (≥ 2.0 mg/L), would reduce a composite primary end point, including nonfatal myocardial infarction (MI), nonfatal stroke.

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Statins Jupiter

Ridker *Engl J Med.* 2008;359:2195-2207

- After 1.9 years of follow-up, treatment with rosuvastatin
- significantly reduced the primary composite end point 44% compared with placebo. This reduction was observed among nearly all of the individual end points, including a 55% reduction MI, 51% reduction in stroke, and a 47% reduction MI, stroke, and death

- Absolute benefits: absolute risk reduction of 1.2%

- CMAJ 2008 BPG: "Statins should be used for most patients with ischemic stroke or TIA... **A**"
- Target LDL ≤ 2.0 mmol/L."

Diabetes mellitus and metabolic syndrome

- Diabetics have 1.5 to 2 x greater risk of ischemic stroke.
- 1/3 stroke patients are diabetic. Woo Stroke 1999 30 2517
- Metabolic syndrome (IR, waist circ > 89 or 100 cm, hyperTG, low HDL, HTN) increased stroke risk (OR 2.16) Lancet 2001 358
- Tight glycemic control reduces microvascular disease.

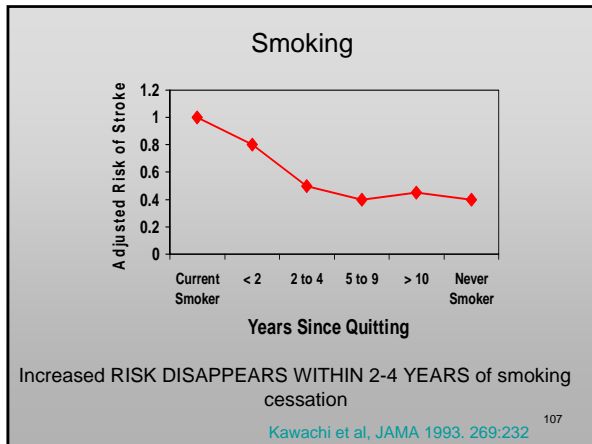
- Recommended HBA_{1c} $\leq 7\%$... **B**
- Vigorous BP management in diabetics with ACEI's or ARB's
- Additional benefit to statin use in diabetics...28% reduction in strokes vs. placebo (HPS). Target LDL ≤ 2.0 ... **A**
- ASA 81 mg for all diabetics with CV risk factors... **A**

Smoking cessation

- Smoking promotes endothelial dysfunction and atherosclerosis
- Smoking increases stroke risk 50% and SAH risk 100%
- Dose-response relationship. Risk of stroke in users > 40 cigs/day 2x < 10 cigarettes per day
- Stroke risk decreases significantly 2 years after cessation and is at level of non-smokers by 5 years Wolf Arch Int Med 2002

- CMAJ BPG: 2008: Smoking cessation, smoke free environment, nicotine replacement, nicotine partial agonist rx and behavioural therapy **B,A**... ASA, CHEP

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Canadian best practice guideline recommendations Risk factor management

- All risk factors for CVD must be **AGGRESSIVELY** *rxed* by pharmacological and non-pharmacological mx....**A**
- Smoking cessation counseling with pharmacological and non-pharmacological mx...**B**

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Lifestyle

- **Sodium intake:** ≤ 2300 mg per day any age... **B**
- **Exercise:** accumulation 30-60 mins walking/jogging/dynamic exercise per day 4-7 days per week in addition to routine activities... **A**. Medically supervised programs for high risk.
- **Weight:** BMI 18.5-24.9 kg/m² and waist circumference < 88 (female) or 102 cm (male)...**B**
- **Alcohol:** < 2 per day; < 14 per week for males; < 9 per week for females ...**C**..ASA, CHEP

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