Stroke for the Internist

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Objectives

• Ischemic Stroke: Initial evaluation
  – Imaging
  – Hypertension management

• Acute treatment and interventions
  – Beyond t-PA

• Medical management: Evidenced based?
  – Acute treatment
  – Secondary prevention

• TIA management
Projected US Stroke Deaths

Elkins and Johnston, Stroke, 34:2109-13, 2003
Stroke Classification

STROKE
- Hemorrhage
  - Subdural Hematoma
  - Epidural Hematoma
  - Intraparenchymal Hematoma
- Ischemic
  - Embolic
  - Thrombotic
    - Large Vessel
    - Small Vessel

Stroke Classification

Hemorrhage
- Subdural Hematoma
- Epidural Hematoma
- Intraparenchymal Hematoma

Ischemic
- Embolic
- Thrombotic
  - Large Vessel
  - Small Vessel
## Frequency of Stroke by Type

<table>
<thead>
<tr>
<th>Stroke Subtype</th>
<th>Estimated Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage</td>
<td>15%</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Lacunar (small vessel) stroke</td>
<td>25%</td>
</tr>
<tr>
<td>Cardiogenic embolism</td>
<td>20%</td>
</tr>
<tr>
<td>Artery-artery embolism</td>
<td>15%</td>
</tr>
<tr>
<td>Cryptogenic stroke</td>
<td>30%</td>
</tr>
<tr>
<td>Other Causes</td>
<td>10%</td>
</tr>
</tbody>
</table>
Case 1: Acute stroke

52 year old man having dinner with his wife

- He suddenly stopped talking and dropped his fork, at 6:30 p.m.
- His wife called 911, paramedics found him awake, but unable to speak with weakness of his face and arm.
- He arrives in the Emergency Room at 7:00 p.m.
What study would you order next?

A. Non-contrast Head CT scan
B. MRI Brain
C. Head CT with CTA
D. Cerebral angiogram
Initial Evaluation

Advances in Imaging
Patient Arrives in CT

Positioned

Non-contrast CT Head

CT Perfusion (40 cc contrast)

CTA brain to chest (110 cc contrast)

Patient transported to ED, angiography suite or ICU
External Carotid a
Internal Carotid a
CT angiography
Risk of Contrast Nephropathy

N = 2109
Had stroke CT protocol

N = 1075
Included in study

N = 52
Creatinine rise of \(\geq 0.5\) mg/dl

N = 4
Possible contrast nephropathy

N = 2
Required temporary hemodialysis

0.37%

0.19%

Josephson et al, Neurology (2005) 64:1805
CT Advantages Over MRI

- Excludes hemorrhage
- Image all relevant vessels in 15 minutes
  - May replace
    - Doppler of Neck
    - Intracranial MRA
    - Conventional angiography
- Better tolerance to patient motion
- Provides cerebral perfusion
- More widely available
Case 1: Acute stroke contd.

tPA Exclusion Criteria

- CT: hemorrhage or major early infarct signs
- BP > 185/110 mmHg
- prior stroke < 3 month
- recent surgery, trauma, PUD
- plts < 100K, gluc <50 or >400 mg/dl, HCT < 25%

- The patient had a Stroke CT which revealed no hemorrhage or evidence of large infarct
- He was treated with IV t-PA at 90 minutes after symptom onset.
- He was able to recover full motor function, but had residual aphasia
Ischemic Stroke: Thrombolysis

Safe and Effective:
- IV t-PA 0.9 mg/kg, < 3 hr
- IA pro-UK MCA < 6hr

NINDS
ATLANTIS
ECASS-I
ECASS-II
PROACT

Hours from onset
NINDS t-PA Ischemic Stroke

- Intravenous t-PA vs. placebo (N=312 each group)
  - 0.9 mg/kg t-PA IV (10% bolus, 1 hr infusion)
  - within 90 mins and 180 mins of symptom onset
- CT exclude hemorrhage

\[
\begin{array}{c|c|c|c}
\text{NIHSS} & \text{Barthel} & \text{mRS} & \text{GOS} \\
\leq 1 & 95-100 & \leq 1 & = 1 \\
\end{array}
\]

\[
\begin{align*}
p &= 0.033 & p &= 0.026 & p &= 0.019 & p &= 0.033 \\
\end{align*}
\]

- Symptomatic intracranial hemorrhage
  - 6% vs. 0.6% (t-PA vs. placebo)
- 3% hemorrhage related death

Case 2: Acute Stroke
Treatment beyond IV t-PA

- 72 y/o man with HTN, DM, elevated cholesterol
- Presented to ED at 5 hours with R-sided weakness, gaze deviation, language impairment
- Stroke CT performed: non-con CT, CTA, CT perfusion
Cerebral angiogram before and after thrombectomy
MERCI Clot Retrieval Device
## Merci Trial Primary Results

<table>
<thead>
<tr>
<th>measure</th>
<th>result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retriever Revascularization (%)</td>
<td>48.2%</td>
</tr>
<tr>
<td>Compared to 18% PROACT-II control</td>
<td>P &lt;0.0001*</td>
</tr>
<tr>
<td>Procedural complications (%; 95% CI)</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>12% (7.3-18)</td>
</tr>
<tr>
<td>Clinically significant</td>
<td>7% (2.9-11)</td>
</tr>
<tr>
<td>Symptom onset to groin puncture (hr ± SD)</td>
<td>4.3 ± 1.7</td>
</tr>
<tr>
<td>Procedure duration (hr ± SD)</td>
<td>2.1 ± 1.0</td>
</tr>
<tr>
<td>Attempts to remove clot (n ± SD)</td>
<td>2.9 ± 1.5</td>
</tr>
<tr>
<td>Enrolled &lt;3 hours of symptom onset, n (%)</td>
<td>37 (26%)</td>
</tr>
</tbody>
</table>

* - exact binomial test
The patient’s BP on admission was 210/110 mmHg. How would you manage blood pressure?

A. Lower blood pressure to 180/100 mmHg
B. Lower blood pressure to 160/90 mmHg
C. Lower blood pressure to 140/90 mmHg
D. No treatment
Acute Medical Management

Blood pressure control
Ischemic Stroke
HTN after Acute Stroke

• Acute HTN is common after acute stroke (>60%)

• Risk of acute deterioration with aggressive reduction of BP

• Mean BP reduction 24h after stroke is associated with better prognosis at 3 months
  *Blood Press Monit 2006; 11(4):199-205*

• Blood pressure reduction within 24 hours is associated with poor outcome
  – OR 1.89 per 10% decrease in BP of poor outcome at 3 months (p= 0.047)
  *Neurology 2003; 61:1047-51*
Blood Pressure Management

- Treatment for SBP > 220mmHg or DBP > 120 mmHg or if evidence of end-organ damage
- With thrombolytic therapy, goal BP < 180/105mmHg
- Relative hypotension can cause regional hypoperfusion after ischemic stroke
- Need for careful titration and monitoring to minimize BP fluctuations
- Ongoing clinical trials will help refine goals of BP management

*Current Treat Options Neurol 2006; 8(6): 477-85
CHHIPS, J Hypert 2005;23(3): 649-55*
Induced Hypertension

**For**
- May increase pial-pial blood flow
- Increase perfusion to the ischemic penumbra
- Is probably safe

**Against**
- Requires ICU care and central line access
- May cause coronary or gut ischemia
- Could cause cerebral vasoconstriction
Hypertension

Secondary Prevention
High Risk / Secondary Stroke Prevention

- **HOPE Trial: (n = 9297)**
  - Ramipril vs. Placebo
  - % Subjects without hypertension: 53%
  - Mean BP (all subjects) at trial entry: 139/79
  - RR in Treated hypertensives: 0.75
  - in Treated non-hypertensives: 0.79

- **PROGRESS Trial: (n = 6105)**
  - Perindopril ± Indapamide vs. Placebo
  - % Subjects without hypertension: 52%
  - Mean BP in non-hypertensives: 136/79
  - RR in Treated hypertensives: 0.66
  - in Treated non-hypertensives: 0.68
Choice of Agents

• Is there a special status for Angiotensin receptor blockers or ACE-Inhibitors? Class effects:
  – LIFE Trial: (High Risk Hypertensives)
    • Identical reductions in BP
    • relative risk of stroke reduced by 25% in losartan group vs. atenolol group (p < 0.001).
  – MOSES Trial: (Secondary Stroke Prevention):
    • Identical reductions in BP
    • relative risk of stroke reduced by 25% in eprosartan group vs. nitrendipine group (p < 0.001).
Choice of Agents (Cont.)

• ACE vs. ARB?
  – OPTIMAAL study (2002): Captopril vs. Losartan
    • 5477 patients with acute MI or heart failure
    • RR for mortality 1.13 (95%CI, 0.99 – 1.28; P = 0.07) favored captopril

• Thiazides as alternatives:
  – ALLHAT Study: Chlorthalidone equivalent to lisinopril for primary stroke prevention in whites and superior among blacks
    • Risk of ACE-associated angioedema 2-4 times higher in African Americans compared to whites
Case 3: Stuttering stroke

72-year old woman with new right sided weakness

**History**
- stuttering in onset
- right arm and leg weakness without sensory symptoms
- no visual, language or speech symptoms

**PMH**
- Hypertension, DM

**Meds:** ASA 81 mg

**Examination**
- BP 188/102 Pulse Regular
- no bruits
- cranial nerves normal
- right pronator drift, right foot drop
- sensory exam normal
- no ataxia
- reflexes elevated on right, right toe upgoing
Initial evaluation: Advances in MRI

- Able to detect hyperacute infarct
- Best for posterior circulation
- Ability to perform perfusion
- Use of diffusion/perfusion mismatch for assessment of tissue at risk, prediction of infarct volume
Hyperacute Infarct
Hyperacute Infarct - 2 days later
Hyperacute Infarct

EP T2

DI

DWI

ADC map
How would you manage stuttering stroke symptoms?

A. IV heparin  
B. Plavix load 300 mg  
C. Pressors to raise blood pressure  
D. Aspirin
Case 3: Thrombotic Stroke

- **MRI Brain**
  - Increased signal intensity in the posterior limb of the internal capsule

- **Carotid Doppler**
  - no significant stenosis

- **Laboratory work-up unremarkable**

MRI: T2-first echo
Thrombotic Strokes

Risk factors:
- Hypertension
- Hyperlipidemia
- Diabetes
- Advanced age
- Gender

Small vessels
- Lenticulostriate
- Thalamoperforators
- Brainstem penetrators
- Cerebellar hemisphere
- Deep cerebral white matter
The patient had a stroke while on aspirin. What antiplatelet treatment would you choose?

A. Continue ASA 81 mg  
B. Increase ASA to 325 mg  
C. Switch to clopidogrel 75 mg  
D. Switch to ASA/dypiridamole 25/250 mg bid  
E. Add Plavix to baby ASA
Secondary Stroke Prevention

Antiplatelets and Lipid lowering
Aspirin vs. Clopidogrel

• **CAPRIE Trial: (n ~ 19000)  (Lancet 1996)**
  – Relative risk reduction of 8.7% for (Stroke/Death/CV event) in Clopidogrel arm vs. aspirin
  – Number needed to treat ~ 200
  – Smaller benefit when restricted to those with prior stroke
  – Safety similar to ASA

• **MATCH Trial: (Lancet 2004)**
  – Combination ASA/Clopidogrel did not reduce stroke risk vs. Clopidogrel alone (p = 0.35)
  – Risk of major bleeding significantly greater in combination arm (2.6% vs. 1.3%; p< 0.001)
Aspirin vs. Aggrenox

• ESPS-2 Trial: (n = 6602)  (J Neurol Sci 1996)
  – Combination ASA/extended release dipyridamole (Aggrenox) reduced stroke risk by 23% vs. aspirin alone
  – No effect on death risk
  – Caution in patients with unstable angina
  – Safety profile similar but higher incidence of headache

• Profess Trial
  – Head to head trial of Clopidogrel vs. Aggrenox underway
  – Stroke recurrence endpoint: HR 1.01 (95% CI 0.92 – 1.11), p=0.783
Fast assessment of stroke and transient ischaemic attack to prevent early recurrence (FASTER): a randomised controlled pilot trial

James Kennedy, Michael D Hill, Karla J Ryckborst, Michael Eliasziw, Andrew M Demchuk, Alastair M Buchan, for the FASTER Investigators*

Summary
Background Patients with transient ischaemic attack (TIA) or minor stroke are at high immediate risk of stroke. The optimum early treatment options for these patients are not known.

Methods Within 24 h of symptom onset, we randomly assigned in a factorial design 392 patients with TIA or minor stroke to clopidogrel (300 mg loading dose then 75 mg (40 mg daily; 199 patients) or placebo (193 patients). All Descriptive analyses were done by intention to treat haemorrhagic) within 90 days. Safety outcomes include simvastatin. This study is registered as an International and with ClinicalTrials.gov (NCT00109382).

Findings The median time to stroke outcome was 16h 45 min to recruit patients at the prespecified minimum 14 (7.1%) patients on clopidogrel had a stroke within 90 days compared with placebo (2/7; p=0.5). TIA (absolute risk reduction 3.3% [2.3 to 8.9]; p=0.14). Two patients on clopidogrel had a stroke outcome 1.0% [0.4 to 2.4]; p=0.5). TIA safety outcomes.

Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial

The ESPRIT Study Group*

Summary
Background Results of trials of aspirin and dipyridamole combined versus aspirin alone for the secondary prevention of vascular events after ischaemic stroke of presumed arterial origin are inconsistent. Our aim was to resolve this uncertainty.

Methods We did a randomised controlled trial in which we assigned patients to aspirin (30–325 mg daily) with or without dipyridamole (200 mg twice daily) within 6 months of a transient ischaemic attack or minor stroke of presumed arterial origin. Our primary outcome event was the composite of death from all vascular causes, non-fatal stroke, non-fatal myocardial infarction, or major bleeding complication, whichever happened first. Treatment was open, but auditing of outcome events was blinded. Primary analysis was by intention to treat. This study is registered as an International Standard Randomised Controlled Trial (number ISRCTN73824458) and with ClinicalTrials.gov (NCT00161070).

Findings Mean follow-up was 3.5 years (SD 2.0). Median aspirin dose was 75 mg in both treatment groups (range 30–325); extended-release dipyridamole was used by 83% (n=1131) of patients on the combination regimen. Primary outcome events arose in 173 (13%) patients on aspirin and dipyridamole and in 216 (16%) on aspirin alone (hazard ratio 0.80, 95% CI 0.66–0.98; absolute risk reduction 1.0% per year, 95% CI 0.1–1.8). Addition of the ESPRIT data to the meta-analysis of previous trials resulted in an overall risk ratio for the composite of vascular death, stroke, or myocardial infarction of 0.82 (95% CI 0.74–0.91). Patients on aspirin and dipyridamole discontinued trial medication more often than those on aspirin alone (470 vs 184), mainly because of headache.

Interpretation The ESPRIT results, combined with the results of previous trials, provide sufficient evidence to prefer the combination regimen of aspirin plus dipyridamole over aspirin alone as antithrombotic therapy after cerebral ischaemia of arterial origin.
WARSSS Trial

- **Setting:** Ischemic stroke (n=2206) (NEJM 2001)
  - no carotid stenosis
  - no identified cardioembolic source
  - Mean age 63 years
- **Intervention:**
  - Warfarin (INR 1.4 to 2.8) vs.
  - Aspirin (325 mg)
- **Outcome:** (2-year follow-up)
  - Recurrent stroke/death 17.8% in warfarin group vs.
  - Recurrent stroke/death 16.0% in ASA group (p=.25)
  - No difference by stroke subtype
Current AHA/ASA Guidelines

• Aspirin, Clopidogrel, or Aggrenox all acceptable first-line agents after noncardioembolic stroke
• Don’t routinely add ASA to Clopidogrel for stroke prevention
• For patients with stroke while on ASA, do not increase ASA dose.
• Consider warfarin for atrial fibrillation
Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL 2006)

- First study exclusively in recent stroke/TIA patients (6 months)
- N = 4,731
- Randomly assigned to atorvastatin 80mg/day
- Average baseline LDL = 133 mg/dL
## SPARCL: Main results

<table>
<thead>
<tr>
<th>Type of stroke</th>
<th>Hazard ratio with atorvastatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>0.84</td>
</tr>
<tr>
<td>Fatal</td>
<td>0.57</td>
</tr>
<tr>
<td>Nonfatal</td>
<td>0.87</td>
</tr>
<tr>
<td>Ischemic</td>
<td>0.78</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>1.66</td>
</tr>
</tbody>
</table>
Case 4: Carotid disease
65-year old man with aphasia and weakness

- **History**
  - Transient aphasia and right hemiparesis 3 weeks ago
  - Lasted 10 minutes

- **PMH**
  - HTN, diabetes
  - Other ROS negative

- **Examination**
  - Left carotid bruit
  - Neurological examination normal
Any ipsilateral stroke per year
Medical    Surgical
Symptomatic  18%    4.5%
Asymptomatic 2.2%    1.0%

Risk Factor Modification:
- Antithrombotic
- Statin
- ACE Inhibitor

NASCET, 1991
ACAS, 1995
Stenosis Measurement: NASCET

Proven benefit:
NASCET method > 50%
ECST method > 80%

Benefit in NASCET 50-79% modest but increases with time.

Surgical complication rate <7%
What about carotid stenting?

- **SAPPHIRE trial** *(NEJM 2004)*
  - Stenting non-inferior to endarterectomy and trended to being better in high-risk patients.
  - High risk defined by:
    - Asymptomatic 80% stenosis (or 50% symptomatic) **AND** (at least one)
    - Severe Cardiac or Pulmonary disease
    - Contralateral occlusion
    - Previous neck surgery or restenosis
    - Age >80 years
Table 3. Cumulative Incidence of Adverse Events within One Year.※

<table>
<thead>
<tr>
<th>Event</th>
<th>Intention-to-Treat Analysis</th>
<th>Actual-Treatment Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stenting (N=167)</td>
<td>Endarterectomy (N=167)</td>
</tr>
<tr>
<td></td>
<td>no. (%)</td>
<td>no. (%)</td>
</tr>
<tr>
<td>Death</td>
<td>12 (7.4)</td>
<td>21 (13.5)</td>
</tr>
<tr>
<td>Stroke</td>
<td>10 (6.2)</td>
<td>12 (7.9)</td>
</tr>
<tr>
<td>Major ipsilateral</td>
<td>1 (0.6)</td>
<td>5 (3.3)</td>
</tr>
<tr>
<td>Major nonipsilateral</td>
<td>1 (0.6)</td>
<td>2 (1.4)</td>
</tr>
<tr>
<td>Minor ipsilateral</td>
<td>6 (3.7)</td>
<td>3 (2.0)</td>
</tr>
<tr>
<td>Minor nonipsilateral</td>
<td>3 (1.9)</td>
<td>4 (2.7)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>5 (3.0)</td>
<td>12 (7.5)</td>
</tr>
<tr>
<td>Q-wave</td>
<td>0</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Non-Q-wave</td>
<td>5 (3.0)</td>
<td>10 (6.2)</td>
</tr>
<tr>
<td>Cranial-nerve palsy</td>
<td>0</td>
<td>8 (4.9)</td>
</tr>
<tr>
<td>Target-vessel revascularization</td>
<td>1 (0.6)</td>
<td>6 (4.3)</td>
</tr>
<tr>
<td>Conventional end point (stroke or</td>
<td>9 (5.5)</td>
<td>13 (8.4)</td>
</tr>
<tr>
<td>death at 30 days plus ipsilateral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>stroke or death from neurologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>causes within 31 days to 1 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary end point (death, stroke, or</td>
<td>20 (12.2)</td>
<td>32 (20.1)</td>
</tr>
<tr>
<td>myocardial infarction at 30 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>plus ipsilateral stroke or death</td>
<td></td>
<td></td>
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<tr>
<td>from neurologic causes within</td>
<td></td>
<td></td>
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<tr>
<td>31 days to 1 yr</td>
<td></td>
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</tbody>
</table>
TIA Management
Case 6: TIA

- 65 y.o. right-handed man h/o DM, HTN, presents with 10 minutes of left-sided weakness.
- Meds: ASA, HCTZ, glucophagae.
- Neuro exam is now normal.
What would you do for this patient?

A. Admit for evaluation
B. Expedited outpatient evaluation
C. Treat with IV heparin
D. Treat with antiplatelets
Transient Ischemic Attacks

- True incidence of transient ischemic attack (TIA) is not known
- Many TIAs are misdiagnosed or never diagnosed
- ~ 15-20% of patients with stroke have a prior TIA
- 200,000-500,000 TIAs in the US each year
## Risk of Stroke after TIA

<table>
<thead>
<tr>
<th>Type of Study</th>
<th>N</th>
<th>Stroke Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester, Minnesota [1] Population-based cohort</td>
<td>198</td>
<td>10% within 90 days</td>
</tr>
<tr>
<td>London, UK [2] Cohort study</td>
<td>83</td>
<td>29% within 6 months</td>
</tr>
<tr>
<td>Iowa City, Iowa [3] Cohort study</td>
<td>74</td>
<td>6.8% within 6 days</td>
</tr>
<tr>
<td>Iowa City, Iowa [4] Pilot Trial (placebo group)</td>
<td>55</td>
<td>9.1% within 6 days</td>
</tr>
<tr>
<td>NASCET [5] Randomized trial (medical therapy)</td>
<td>603</td>
<td>20.1% within 90 days</td>
</tr>
<tr>
<td>Northern California [6] ED Cohort study</td>
<td>1707</td>
<td>5% within 2 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10.5% within 90 days</td>
</tr>
<tr>
<td>Oxfordshire, UK [7] Population-based cohort</td>
<td>209</td>
<td>12% with 30 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.6% within 7 days</td>
</tr>
<tr>
<td>Cincinnati, Ohio [8] ED Cohort study</td>
<td>790</td>
<td>9.2% within 30 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13.3% within 90 days</td>
</tr>
<tr>
<td>Ontario, Canada [9] ED Cohort study</td>
<td>271</td>
<td>6% within 30 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8% if first-ever TIA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9% if speech impaired</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12% if hemiparetic</td>
</tr>
<tr>
<td>Oxfordshire, UK [10] Population-based cohort</td>
<td>87</td>
<td>11.5% within 30 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17.5% within 90 days</td>
</tr>
<tr>
<td>Alberta, Canada [11] ED Cohort study</td>
<td>2285</td>
<td>9.5% within 90 days</td>
</tr>
<tr>
<td>Corpus Christi, Texas [12] Population-based cohort</td>
<td>612</td>
<td>3.15% within 30 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.03% within 90 days</td>
</tr>
<tr>
<td>Cincinnati, Ohio [13] Population-based cohort</td>
<td>927</td>
<td>3.9% within 2 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.0% within 7 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11.2% within 30 days</td>
</tr>
<tr>
<td>Northern Portugal [14] Cohort study</td>
<td>141</td>
<td>9.9% within 2 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12.8% within 7 days</td>
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<tr>
<td></td>
<td></td>
<td>17.7% within 30 days</td>
</tr>
</tbody>
</table>

ED = emergency department
Risk of Stroke after TIA

- Risk within 7 days: ~ 8%
- Risk within 30 days: ~ 10%
- Risk within 90 days: 10-20% (average 11%)
- Risk of stroke after a stroke ranges 2-7% (average 4%) at 90 days.
Timing of TIA and Stroke

- Of 2,416 patients with acute ischemic stroke, 23% had preceding TIA
  - 17% occurred the same day
  - 9% the day prior
  - 43% during the 7 days prior
High Risk TIAs: ABCD Score

- Age > 60 y/o (1)
- Blood pressure > 140/90mmHg (1)
- Clinical features:
  - Unilateral weakness (2)
  - Isolated speech disturbance (1)
- Duration:
  - >60 min (2)
  - 10-59 min (1)
- Score of 5-6 is independently associated with risk of stroke within 30 days.
Guidelines for Prevention of Stroke in Patients With Ischemic Stroke or Transient Ischemic Attack

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association Council on Stroke

Co-Sponsored by the Council on Cardiovascular Radiology and Intervention

The American Academy of Neurology affirms the value of this guideline.

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Stroke Guidelines: Highlights

- Early brain imaging
- 12-lead ECG and cardiac workup
- IV t-PA within 3 hours
- Early treatment with aspirin/antiplatelets
- High dose statins?
- Secondary prevention: HTN, hyperlipidemia, DM
- CEA/stent for carotid disease, warfarin for afib
Ischemic?

Consider Thrombolysis Thrombectomy

Atrial Fibrillation, Mechanical Valve, Mural Thrombus?

Carotid Atherosclerosis?

Small Vessel?

Intracranial Atherosclerosis?

Sinus Thrombosis?

Dissection?

Other

Warfarin, or aspirin if contraindicated

CEA or Stent

Risk Factor Modification:
- Antithrombotic
- Statin
- ACE Inhibitor

Anticoagulation

Treat specific cause, consultation

Risk Factor Modification
Conclusions

• Acute stroke requires rapid recognition and assessment
  – Stroke Centers can improve patient care
  – Treatment with IV tPA within 3 hours
  – New advances with CT simplify evaluation

• Avoid treatment of moderate HTN in the acute stroke period

• Consider new interventions beyond t-PA
Conclusions

• Secondary stroke prevention
  – Get with the Guidelines
  – Antiplatelet therapy, aggressive lipid lowering and blood pressure control
  – Early treatment of symptomatic carotid disease
  – Anticoagulation for afib

• TIAs warrant rapid evaluation to prevent subsequent stroke
Case 5: Intracranial stenosis

66-year old woman with recurrent dizziness, weakness

• History
  – Symptoms worse with standing
  – Progressive symptoms despite ASA, clopidogrel and warfarin therapy

• Neurologic exam
  – Normal

• Cerebral angiogram
  – Severe stenosis of intracranial carotid artery
The WASID study was a randomized clinical trial involving 569 patients with symptomatic intracranial atherosclerosis.

- Warfarin sodium INR 2-3
- ASA 1300 mg

Primary endpoint: ischemic stroke, MI, death from vascular causes other than stroke.

**Figure 2. Cumulative Incidence of Major End Points According to Treatment Assignment**

The primary endpoint was ischemic stroke, MI, or death from vascular causes other than stroke.

**Figure 3. The Product-Limit Estimate of the Cumulative Probability of Death (Panel A) and the Cumulative Incidence of Major Hemorrhage (Panel B) after Randomization, According to Treatment Assignment.**
<table>
<thead>
<tr>
<th>Event</th>
<th>Aspirin (N=280, 504.4 Patient-yr)</th>
<th>Warfarin (N=289, 541.7 Patient-yr)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with an Event no. (%)</td>
<td>Events per 100 Patient-yr %</td>
<td>Patients with an Event no. (%)</td>
<td>Events per 100 Patient-yr %</td>
</tr>
<tr>
<td>Death</td>
<td>12 (4.3)</td>
<td>2.4</td>
<td>28 (9.7)</td>
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<tr>
<td>Death from vascular causes</td>
<td>9 (3.2)</td>
<td>1.8</td>
<td>17 (5.9)</td>
<td>3.1</td>
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<tr>
<td>Ischemic stroke</td>
<td>5</td>
<td></td>
<td>3</td>
<td></td>
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<tr>
<td>Brain hemorrhage</td>
<td>0</td>
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<tr>
<td>Other hemorrhage</td>
<td>1</td>
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<td>0</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Sudden death</td>
<td>2</td>
<td></td>
<td>9</td>
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<tr>
<td>Aortic aneurysm</td>
<td>1</td>
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<td></td>
</tr>
<tr>
<td>Death from nonvascular causes</td>
<td>3 (1.1)</td>
<td>0.6</td>
<td>11 (3.8)</td>
<td>2.0</td>
</tr>
<tr>
<td>Cancer‡</td>
<td>3</td>
<td></td>
<td>6</td>
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<tr>
<td>Congestive heart failure‡</td>
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<tr>
<td>Diabetes</td>
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<td>1</td>
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<tr>
<td>Respiratory failure</td>
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<td>Sepsis</td>
<td>0</td>
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<tr>
<td>Major hemorrhage</td>
<td>9 (3.2)</td>
<td>1.8</td>
<td>24 (8.3)</td>
<td>5.0</td>
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<tr>
<td>Brain hemorrhage</td>
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<td>Subdural hematoma</td>
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<td>Genitourinary hemorrhage</td>
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<tr>
<td>Other</td>
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<td>4</td>
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<tr>
<td>Myocardial infarction</td>
<td>7 (2.5)</td>
<td>1.6</td>
<td>12 (4.2)</td>
<td>2.2</td>
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<tr>
<td>Fatal</td>
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<tr>
<td>Nonfatal</td>
<td>7</td>
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<td>9</td>
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</tbody>
</table>
WASID Trial (2005)

• **Setting:** (NEJM 2005)
  – Ischemic stroke with intracranial atherosclerosis >50% (n=569)
  – Mean age 63 years

• **Intervention:**
  – Warfarin (INR 2.0-3.0)
  – Aspirin (1300 mg/day)

• **Outcome:** (1.8 year follow-up)
  – Recurrent stroke/death = 21.8% in warfarin group vs
  – Recurrent stroke/death = 22.1% in ASA group
  – Death and major hemorrhage more common in warfarin group