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Acute Stroke: The Down and Dirty

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Disclosures

- Current PI for the MaRISS study that is funded by the American Heart Association

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Why does this matter?

Other than there will be a 17% shortage of neurologist by 2020

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Transient Ischemic Attack

- Temporary and "nonmarching" neurological deficit of sudden onset attributed to focal ischemia
- Last less then 24 hours with resolution of deficits
  - Most last 5 to 20 minutes
  - No imaging correlate
- ⅓ of patients will have a stroke in the next 5 years
- 1/10 will have a stroke within the next 3 months
- 50% of stroke associated with TIA occurred within 48 hours of TIA

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Transient Ischemic Attack

- TIA Mimics
  - Seizures
  - Complicate Migraines / Reversible Cerebral Vasoconstriction Syndrome
  - Encephalopathy
  - REM Sleep behavior disorders
  - Transient Global Amnesia
  - Early Onset Neurodegenerative Disorders
- 60% of referrals to neurology for TIA will not have a TIA as a final diagnosis
- ABCD2 Score

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Stroke

- 750,000 new or recurrent strokes annually in the US
- 80% are ischemic
  - 8-12% of ischemic stroke result in death within 30 days
  - Intracerebral hemorrhage (15%) and Subarachnoid hemorrhage (5%)
- 5th leading cause of morbidity and mortality
  - 30% require assistance with activities of daily living
  - 20% require assistance with ambulation
  - 16% need/require institutional care

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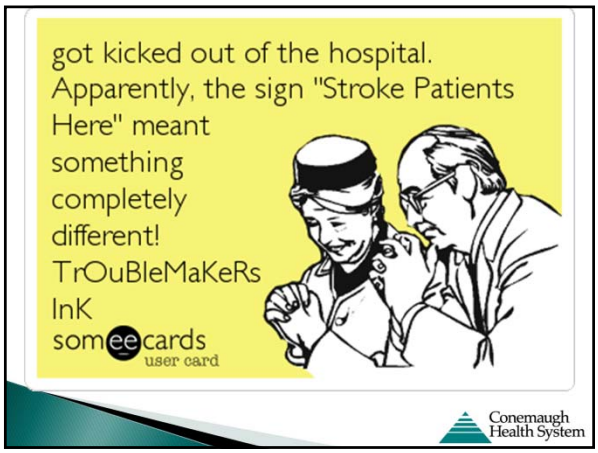

Presentation

75 y.o. F with right side weakness
- Started 1 hour prior to presentation
- Right arm, face, and difficulty speaking
- History of HTN, HLD, and DM
- Never smoker, no atrial fibrillation
- Not on any blood thinners
- Brother with history of stroke

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Initial Work Up

- Head CT
- Point of care glucose
- BP and Tele
- 12 lead EKG
- CBC, BMP, and Coags

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IV Thrombolytic Therapy

- Recombinant tissue plasminogen activator
- Alteplase
- FDA Approved for treatment of acute ischemic stroke for patients within 3 hours of onset of symptoms
- 0.9 mg/kg
  - 10% given as a bolus over 1 minute
  - 90% infused over 1 hour
  - Not to exceed 90 mg

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Contraindications

American Heart Association Guideline 2013[1]	American Heart Association Scientific Statement 2015[2]	US Food and Drug Administration (FDA) Package Insert 2015[3]
Indications		
Diagnosis of ischemic stroke with measurable neurologic deficit	Same	Same
Symptom onset[a] within 4.5 hours	Same	Within 3 hours
Age ≥18 years	Same	Warning for age ≥17 years with risk factors for intracranial hemorrhage
Contraindications		
Severe head trauma within 3 months	Same	Contraindicated
Ischemic stroke within 3 months	Risk increased, but degree is unclear	Removed[b]
Arterial puncture at noncompressible site within 7 days	Risk uncertain	Not listed
Previous intracranial hemorrhage	Same	Warning for recent intracranial hemorrhage (contraindicated if active intracranial hemorrhage)
Suspected subarachnoid hemorrhage	Same	Contraindicated
Intracranial neoplasm, arteriovenous malformation (AVM), or aneurysm	Probably recommended if extraaxial neoplasm is present; not recommended if intraaxial neoplasm is present; risk unclear for AVM; probably recommended for unruptured unaneurysm <10 mm is present, but risk unclear if greater size	Contraindicated
Recent intracranial or intraspinal surgery (within 3 months)	Same	Contraindicated
Active internal bleeding	Same	Contraindicated
Systolic blood pressure (BP) >185 mm Hg or diastolic BP >110 mm Hg	Same, but treatment recommended if BP can be lowered safely	Contraindicated for severe uncontrolled hypertension (BP values removed[b]); warning for BP >175/110 mm Hg
Bleeding diathesis	Consider case by case in patients with history of bleeding diathesis; platelets <100,000/mm[3] or low-molecular-weight heparin/oral within 24 hours, direct thrombin inhibitor or factor Xa inhibitor within 48 hours (unless coagulation tests[c] are normal)	Contraindicated for bleeding diathesis (laboratory values removed[b])
International normalized ratio (INR) >1.7		
Heparin within 48 hours with elevated activated partial thromboplastin time		
Platelets <100,000/mm[3]		
Current use of direct thrombin inhibitor or factor Xa inhibitor with abnormal coagulation tests[c]		

American Heart Association Guideline 2013[1]	American Heart Association Scientific Statement 2015[2]	US Food and Drug Administration (FDA) Package Insert 2015[3]
Contraindications (continued)		
Blood glucose <50 mg/dL	Consider recombinant tissue plasminogen activator (rtPA) if deficits still present after glucose normalization	Removed[b]
CT showing hypodensity >⅓ of the cerebral hemisphere	Same	Removed[b]
Relative contraindications		
Minor stroke (typically National Institutes of Health Stroke Scale [NIHSS] score <3)	rtPA should be administered to patients with mild but disabling symptoms within 3 hours of onset; possible risk and benefit should be weighed in patients with nondisabling symptoms	Removed[b]
Rapidly improving symptoms	rtPA should be administered if symptoms are still disabling	Not listed
Pregnancy	rtPA may be considered in moderate to severe stroke when anticipated benefit outweighs the anticipated risk of uterine bleeding	Warning (Category C)
Seizure at onset with postictal residual deficits	rtPA may be considered if residual deficits are thought to be caused by a stroke	Removed[b]
Major extracranial trauma within 14 days	rtPA can be considered	Warning for recent trauma
Major surgery within 14 days	rtPA can be considered in carefully selected cases	Warning for recent surgery
Gastrointestinal or genitourinary surgery within 21 days	Consider rtPA if no structural bleeding lesions	Warning
Acute myocardial infarction within 3 months	Administer rtPA (stroke dose) if concurrent stroke and acute myocardial infarction (MI); it is also reasonable to give rtPA after recent MI unless it was a STEMI involving the left anterior myocardium	Not listed
Additional contraindications for 3- to 4.5-hour window		
Age >80 years	rtPA recommended	
Warfarin use (regardless of INR)	rtPA probably recommended if INR <1.7	FDA has not approved rtPA for use after 3 hours
NIHSS >25	Risk and benefit uncertain	
Previous stroke or diabetes mellitus	rtPA probably recommended	

Rabinstein, Alejandro A. Treatment of Acute Ischemic Stroke. CONTINUUM: Lifelong Learning in Neurology. 23(1, Cerebrovascular Disease):62-81, February 2017.

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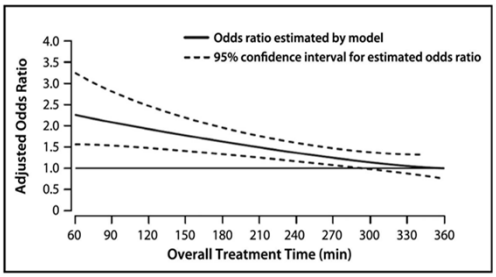
IV Thrombolytic Therapy



Lees KR, Bluhmki E., von Kummer R, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. Lancet 2010; 375 (9727): 1695–1703.

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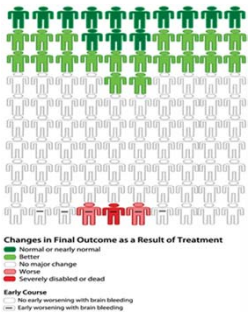
IV Thrombolytic Therapy

Risk versus benefit



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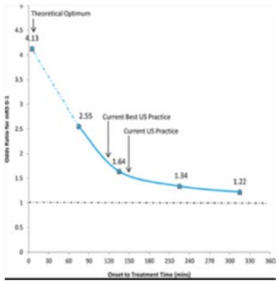
IV Thrombolytic Therapy

- NINDS 1 and 2
- ATLANTIS A and B
- ECASS 1, 2, 3
- EPITHET



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Interventional Therapy

Study	MR CLEAN[25]	ESCAPE[26]	EXTEND-IA[27]	SWIFT PRIME[28]	REVASCAT[29]	THRACE[30]
Size (intervention versus control)	500 (233 versus 267)	315 (165 versus 150)	70 (35 versus 35)	196 (98 versus 98)	206 (103 versus 103)	414 (204 versus 208)
Age, median (years)	65.8 versus 65.7	71 versus 70	68.6 versus 70.2	65 versus 66.3	65.7 versus 67.2	66 versus 68
Time to randomization	6 hours	12 hours[a] Image to puncture ~60 minutes	6 hours	6 hours Image to puncture ~90 minutes	3.7 hours	4.5 hours Onset to groin puncture 5 hours
Clinical selection	Any age NIHSS ≥2	Any age Any NIHSS (disabling symptoms) Barthel Index<90	Any age Any NIHSS Premorbid mRS <2	Age 18-80 years NIHSS ≥8 Premorbid mRS <2	Age 18-80 years NIHSS ≥6 Premorbid mRS <2	Age 18-80 years NIHSS 10-25
Imaging selection	CTA (+/- CTP)[b] Any ASPECTS	CT ASPECTS 6-10 with good collaterals <50% of MCA	CTA/CTP (core <70 mL)	CTA (+/- CTP)[c] ASPECTS 6-10 No cervical ICA occlusion	CTA ASPECTS 7-10	CTA or MRA Any ASPECTS
NIHSS, median	17 versus 18	16 versus 17	17 versus 13	17 versus 17	17 versus 17	18 versus 17
ASPECTS, median	9	9 versus 9	Not reported	9 versus 9	7 versus 8	Median not reported
IV rtPA, %	87.1 versus 90.6	72.7 versus 78.7	100 versus 100	100 versus 100	68.0 versus 77.7	100 versus 100
Onset to groin puncture, median (minutes)	260	185	210	224	269	250
Onset to reperfusion, median (minutes)	Not reported	241	248	250	355	303
M1 occlusion, %	66.1 versus 62	68.1 versus 71.4	57 versus 51	67 versus 77	64.7 versus 64.4	86 versus 79
TICI 2b-3, %	58.7	72.4	86	88	65.7	69
mRS 0-2 at 90 days, %	32.6 versus 19.1 OR 1.7 (95% CI 1.2-2.3)	53 versus 29.3 OR 1.8 (95% CI 1.4-2.4)	71 versus 40 OR 4.2 (95% CI 1.4-12)	60.2 versus 35.5 OR 1.7 (95% CI 1.2-2.3)	43.7 versus 28.2 OR 2.1 (95% CI 1.1-4.0)	53 versus 42 OR 1.55 (95% CI 1.05-2.30)
mRS 0-2 at 90 days, NNT	7.1	4.2	3.2	4.0	6.3	9.1
sICH, %	6 versus 5.2	3.6 versus 2.7	0 versus 6	1 versus 3	1.9 versus 1.9	2 versus 2

Rabinstein, Alejandro A. Treatment of Acute Ischemic Stroke. CONTINUUM: Lifelong Learning in Neurology. 23(1, Cerebrovascular Disease):62-81, February 2017.

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"Stroke! Stroke! Stroke! ..."

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Inpatient admission

- Admit to a stroke unit
- Physical Therapy / Occupational Therapy / Speech Therapy
- Swallow Evaluation
- DVT Prophylaxis
- Antiplatelet Therapy within 24 hours

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Work Up

- Hemoglobin A1c
- Lipid panel with LDL
- Vasculature Studies (Carotid Doppler, CTA, MRA)
- Telemetry
- Echocardiogram
- Hypercoagulable workup

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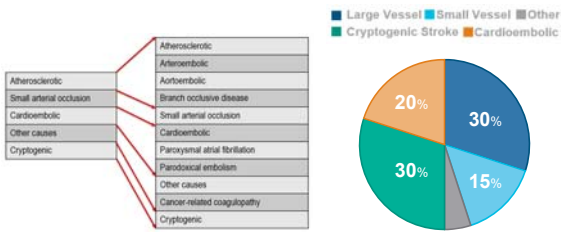
Etiologies



Bang OY et al. Stroke. 2014;45:1186-1194

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Large Vessel Atherosclerosis

- NASCET Results
- CREST
- SAMMPRIS

- Aspirin 325 mg daily
- Clopidogrel 75 mg daily for the first 90 days after enrollment
- Management of primary risk factors
  - Systolic blood pressure: target <140 mm Hg (<130 mm Hg if diabetic)
  - Low-density lipoprotein cholesterol: target <70 mg/dL
- Management of secondary risk factors
  - Diabetes mellitus: target hemoglobin A_{1c} <7%
  - Non-high-density lipoprotein cholesterol: target <100 mg/dL
  - Smoking cessation
  - Excess weight: body mass index (BMI) <25 kg/m^2 if the enrollment BMI is 25 kg/m^2-27 kg/m^2 or 10% weight loss if the enrollment BMI is >27 kg/m^2
  - Insufficient exercise: moderate intensity exercise at least 3 times/wk for 30 min/session

Chaturvedi, S and Bhattacharya, P. Large Artery Atherosclerosis: Carotid Stenosis, Vertebral Artery Disease, and Intracranial Atherosclerosis. Continuum: Lifelong learning in Neurology. April 2014. (20.2) 323-334.

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Risk Factor	Treatment Goals
Hypertension	Patients with hypertension: <140/90 mm Hg; 10-mm Hg reduction in systolic BP and 5-mm Hg reduction in diastolic BP from baseline
	Patients with diabetes mellitus or renal disease: <130/80 mm Hg; 10-mm Hg reduction in systolic BP and 5-mm Hg reduction in diastolic BP from baseline
	Patients without hypertension: <120/80 mm Hg; 10-mm Hg reduction in systolic BP and 5-mm Hg reduction in diastolic BP from baseline
Dyslipidemia	Atherosclerotic stroke or TIA: low-density lipoprotein (LDL) cholesterol level <70 mg/dL or 50% reduction in LDL-cholesterol level from baseline
	Nonatherosclerotic stroke or TIA: per National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP-III) goals
Diabetes mellitus	HgA_{1c} level <7%
Cigarette smoking	Complete cessation
Alcohol consumption	Men: two or fewer drinks per day
	Nonpregnant women: one or fewer drinks per day
Physical activity	At least 30 minutes of moderate intensity physical exercise 1–3 times per week
Diet	Low-fat, low-sodium, and Mediterranean or Dietary Approaches to Stop Hypertension diets (diabetic diet when applicable)
Obesity	Goal body mass index of 18.5–25 kg/m^2

Prabhakaran S and Chong JY. Risk Factor Management for Stroke Prevention. Continuum: Lifelong learning in Neurology. April 2014. (20,2) 296-308.

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