Acute Stroke Care

- Annually, about 795,000 people have a new or recurrent stroke
  - Approximately 610,000 of these strokes are first attacks and about 185,000 are recurrent attacks
- On average, in the United States, every 40 seconds someone has a stroke
- Stroke is the fourth leading cause of death in the United States, ranking behind heart disease, cancer and lower respiratory tract diseases.
- From 1995 to 2005, the stroke death rate fell 29.7%, and the actual number of stroke deaths declined 13.5%
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Percentage of People Who Were Ever Told They Had a Stroke, 2008

Age-adjusted to the 2006 U.S. standard population.
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Age-adjusted Average (Annual) Deaths per 100,000

Reference: CDC
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- Before age 85, men are more likely than women to have a stroke; after age 85, the trend reverses
- Each year, about 55,000 more women than men have a stroke
- 87% of all strokes are ischemic. 10% are intracerebral hemorrhages, and 3% are subarachnoid hemorrhage strokes
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Stroke: the primary cause of long-term disability in the United States

Disabilities in patients* 6 months after acute ischemic stroke

- Hemiparesis: 50%
- Unable to walk without assistance: 30%
- Dependent in activities of daily living: 26%
- Aphasia: 19%
- Depressive symptoms: 35%
- Institutionalized in a nursing home: 26%

Many patients see the disabilities associated with severe stroke as worse than death.

*Among ischemic stroke survivors at least 65 years of age.

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The cost of stroke

The direct and indirect costs of stroke in 2008 in the United States were estimated at $65.5 billion

Direct costs $43.7 billion

Hospital care $18.9 billion
Nursing home care $15.7 billion
Home healthcare $4.2 billion
Physicians, other professionals $3.6 billion
Drugs, medical durables $1.3 billion

Indirect costs $21.8 billion

Lost productivity, mortality $15.1 billion
Lost productivity, morbidity $6.7 billion

*Estimated for 2008.
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- Recombinant Tissue Plasminogen Activator (t-PA) was approved by the FDA in 1996 based on the NINDS trial for use in patients with acute ischemic stroke within 3 hours of onset of symptoms.
- This remains the mainstay in the treatment of ischemic stroke patients.
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- Characteristics of Patients With Ischemic Stroke Who Could Be Treated With r-tPA
  - Diagnosis of ischemic stroke causing measurable neurological deficit
  - The neurological signs should not be clearing spontaneously.
  - The neurological signs should not be minor and isolated.
  - Caution should be exercised in treating a patient with major deficits
Acute Ischemic Stroke

Characteristics of Patients With Ischemic Stroke Who Could Be Treated With rtPA

- The symptoms of stroke should not be suggestive of subarachnoid hemorrhage.
- Onset of symptoms 3 hours before beginning treatment
- No head trauma or prior stroke in previous 3 months
- No myocardial infarction in the previous 3 months
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Characteristics of Patients With Ischemic Stroke Who Could Be Treated With rtPA

- No gastrointestinal or urinary tract hemorrhage in previous 21 days
- No major surgery in the previous 14 days
- No arterial puncture at a noncompressible site in the previous 7 days
- No history of previous intracranial hemorrhage
- Blood pressure not elevated (systolic 185 mm Hg and diastolic 110 mm Hg)
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Characteristics of Patients With Ischemic Stroke Who Could Be Treated With rtPA

- No evidence of active bleeding or acute trauma (fracture) on examination
- Not taking an oral anticoagulant or, if anticoagulant being taken, INR \( \leq 1.7 \)
- If receiving heparin in previous 48 hours, aPTT must be in normal range.
- Platelet count 100,000 mm\(^3\)
- Blood glucose concentration 50 mg/dL (2.7 mmol/L)
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Characteristics of Patients With Ischemic Stroke Who Could Be Treated With rtPA

- No seizure with postictal residual neurological impairments
- CT does not show a multilobar infarction (hypodensity 1/3 cerebral hemisphere).
- The patient or family members understand the potential risks and benefits from treatment
Numerous studies establish the efficacy and safety profile\(^1\text{-}^4\)

<table>
<thead>
<tr>
<th>Clinical study</th>
<th>N</th>
<th>Follow-up period</th>
<th>Clinical outcomes (% of patients)</th>
<th>SICH</th>
</tr>
</thead>
</table>
| NINDS\(^1\)   | Part 1: 291*  
Part 2: 333*  
(144 patients) | 90 days  
(Part 2 data) | Favorable outcome\(^1\):  
Death:  
- t-PA: 39%  
- Placebo: 26%  
(6.4% within 36 hours, Parts 1+2) |                                    |
| STARS\(^2\)   | 389  | 30 days\(^3\)   | Favorable outcome\(^2\):  
Death:  
- t-PA: 35%  
- Placebo: 32%  
(3.3% within 3 days) |                                    |
| CASES\(^3\)   | 1135 | 90 days         | Favorable outcome\(^3\):  
Death:  
- t-PA: 32%  
- Placebo: 22%  
(4.6%) |                                    |
| SITS-MOST\(^4\) | 6483 | 90 days\(^4\)   | Favorable outcome\(^4\):  
Death:  
- t-PA: 39%  
- Placebo: 11%  
(1.7% within 24 hours\(^5\)) |                                    |

\(^*\text{t-PA}=144; \text{placebo}=147.\)
\(^1\text{t-PA}=168; \text{placebo}=165.\)
\(^2\text{Based on a Modified Rankin Scale score of 0 or 1 (minimal or no disability).}\)
\(^3\text{Data at 30 days available for 382 patients.}\)
\(^4\text{Data at 90 days available for 6136 patients.}\)
\(^5\text{SICH in SITS-MOST is defined as local or remote parenchymal hemorrhage type 2 on imaging scan combined with a neurologic deterioration of 4 points or more on the NIHSS.}\)


\(\text{In the NINDS pivotal study, approximately half of the patients who experienced SICH had nonfatal outcomes at 36 hours}\(^1\)\)

\(- 55\% (11 of 20) \text{ of patients treated with Activase (t-PA) and 50\% (1 of 2) of patients given a placebo}\)
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- Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke – ECASS III Trial
  - Done in 2008 in Europe
  - AHA/ASA Guidelines changed to extend window for Acute Stroke
- Additional Contraindications:
  - Age greater than 80 years
  - Oral Anticoagulants
  - History of prior stroke and Diabetes

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○ Case 1:
○ 83 yr. old man with h/o HTN, DM, CAD, MI who had lunch at 1:00 pm with his wife. At 1:15 she went to ask him a question about the recipe that she was preparing for dinner and found him to be unresponsive.
○ Patient taken to OSH where ED physician noted left sided weakness and dysarthria
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- CT head was negative.
- Risks and benefits discussed with family and they wished to proceed with t-PA.
- IV t-PA was initiated at 3:37 pm.
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24 hours post t-PA, patient had minimal residual left hemiparesis.
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- 80 yr. old woman with history of hypertension who was last seen normal at 5:00 am by son. Daughter noticed difficulty with speech at 7:30 am and taken to local ER where she arrived at 8:30 am.
- Initial CT head was negative
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What should be the next step in the management of this patient?

- A. Give ASA
- B. Give IV t-PA
- C. Consider IA t-PA
- D. Discharge home
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- Patient was administered IV t-PA at 9:15 am.
- Patient at 12:00 pm was able to talk in sentences though still was still non fluent.
- Patient was found to have new onset Atrial fibrillation with rapid ventricular response.
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Acute Stroke Care
Acute Stroke Care

- Case 3:
  - 67 yr. old woman with history of hypertension was in the car with her daughter when at approximately at 2:15 pm, the daughter noticed that patient had slurred speech and left sided weakness.
  - She kept on driving and came to EMMC ER at 3:00 pm where code stroke was initiated.
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- Blood pressure was 186/104.
- Initial CT head showed no evidence of abnormalities.
- What should be the next step in the management of this patient?
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Acute Stroke Care

○ Patient was given Labetolol 10 mg intravenously and repeat blood pressure measurement was 160/90.
○ What should be the next step?
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- IV t-PA was initiated and 2 hours post infusion, patient had complete resolution of her symptoms

- Her imaging is as follows:
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- Secondary Stroke Prevention:
- Risk factor modification:
  - Hypertension: Remains the most common modifiable risk factor. Multiple trials including HOPE, PROGRESS etc.
  - An absolute target BP level and reduction are uncertain and should be individualized, but benefit has been associated with an average reduction of approximately 10/5 mmHg, and normal BP levels of < 120/80.
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- A trial called the Secondary Prevention of Small Subcortical Strokes (SPS3) is underway to try and establish an ideal target for reducing BP to prevent secondary strokes.

- Patients are divided into 2 arms
  - BP reduction goal of less than 130 mmHg or
  - Between 130-149 mmHg
  - Study to end in April 2012.
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- This study was also done to see if combination of Aspirin (ASA) and Plavix was efficacious in preventing subcortical strokes.

- This arm was terminated early due to 6.5% of patients taking both drugs experienced bleeding events by mid-June. 5.5% suffered non CNS hemorrhage compared to 3.3% taking ASA alone.
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- The mortality was also higher in the combination arm at 5.8% versus the aspirin-placebo arm at 4.1%
- Prior 2 trials for combination therapy including MATCH (2004) and CHARISMA (2006) trial showed no benefit to dual therapy in preventing atherosclerotic events.

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- On the flip side, a study where combination of ASA and Plavix was superior is the “Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis (SAMMPRIS)”. 

- In this study, patients with recent TIA or stroke attributed to stenosis of 70-99% of the diameter of a major intracranial artery were randomized to either stenting using the Wingspan system or to aggressive medical management.
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- Medical Management consisted of
  - ASA 325 mg daily
  - Plavix 75 mg for 90 days after enrollment
  - Management of primary risk factors including HTN, Hyperlipidemia; and management of secondary risk factors including diabetes, elevated HDL, smoking, excess weight, and insufficient exercise
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- SBP target was < 140 mmHg or < 130 for patients with Diabetes.
- LDL was targeted for < 70
- Enrollment was stopped after 451 patients were randomized because of the 30 day rate of stroke or death was 14.7% in the stenting group with non fatal stroke accounting for 12.5% and fatal stroke of 2.2%
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- 30 day stroke or death rate was 5.8% in medical management arm (Nonfatal stroke 5.3% and non stroke related death 0.4%).
- Follow up is still ongoing in the study
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- Atrial Fibrillation and Stroke
  - Exciting time due to multiple new agents showing good results
  - Dabigatran (Pradaxa) a direct thrombin inhibitor, has been approved and is used for patients with non-valvular Atrial fibrillation for primary and secondary stroke prevention based on the results of the RELY study.
  - Word of caution- start 14 days after stroke to prevent hemorrhagic conversion.
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○ Newer agents like Apixaban which is a direct factor Xa inhibitor showed promising results based on the ARISTOTLE study for preventing stroke or systemic embolism. (await FDA approval)

Thank you