STROKE

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Background

- One of the leading causes of death worldwide
- Leading cause for long-term adult disability
  - 15-30% of survivors have permanent disability
  - 20% require institutional care at 3 mo post-stroke
- Rising rates expected due to aging population
- Ischemic (87%) vs. hemorrhagic (13%)

Risk Factors

- Ischemic
  - Non-modifiable: age > 55, gender M>F, race, genetics, low birth wt
  - HTN- most important factor
  - AF- 20% of strokes are cardiogenic
  - DM, HLD, cigarette smoking, alcohol, sickle cell, carotid stenosis, postmenopausal hormone therapy, obesity, physical inactivity, diet, other cardiac disease (CAD, CHF, LVH..)
- Hemorrhagic
  - Uncontrolled HTN (ICH)
  - Cerebral aneurysm (SAH)
  - Trauma, anticoagulants, thrombolytics..

Classification

- Cerebral ischemic events
  - TIA
    - Transient (< 1h), no infarction, no sequalae
    - Precedes stroke in 15% of cases
  - Stroke
    - Non-transient
    - Usually has sequalae and residual deficits
- Hemorrhagic stroke
  - Subarachanoid (SAH), Intraparenchymal (ICH), Subdural (SDH)

Pathophysiology
Ischemic Stroke

- Brain tissue ischemia and necrosis 2/2 cerebral occlusion
  - Primary cerebral atherosclerotic rupture
  - Cardiogenic and non-cardiogenic embolisms
- Cell death occurs in two phases
  - Primary: infarct formation and vessel damage
  - Secondary: cell death 2/2 resultant inflammation, edema, and free radical accumulation. Occurs within 2-3h post infarct, can lead to widespread cell death and deficits

Pathophysiology
Hemorrhagic Stroke

- Also primary and secondary mechanism for cell death
  - Primary: 1) blood build-up increases intracranial pressure (ICP) where clot volume is the most important predictor of outcome 2) chemical toxicity of blood to surrounding tissue
  - Secondary: resultant inflammation and cerebral edema leads to increased ICP, causing more tissue damage and swelling, with possible herniation and brain death

Signs/Sypmtoms/Diagnosis

- Signs: AMS, neuromotor deficits, hemi- or monoparesis, vertigo or double vision (posterior), aphasia (anterior)
- Symptoms
  - Ischemic: Weakness. Imbalance. Memory, language and speech difficulties
  - Hemorrhagic: "Worst headache of their lives" or "thunderclap headache" in the case of SAH
- Diagnosis:
  - Head CT vs. MRI, ECG, TTE Vs. TEE, carotid doppler
  - NIH Stroke Scale (NIHSS)

Treatment

- Goals:
  1. Cardio-respiratory support, control of increased ICP
  2. Reduction of secondary brain damage and salvaging surrounding tissue (neuroprotection)
  3. Prevention of recurrent strokes through surgery and/or risk modification

Treatment
Ischemic Stroke

- IV alteplase is recommended for select pts within 3h of stroke onset
- IA fibrinolysis is beneficial for select pts (MCA stroke within 6h)
- BP is allowed to remain high (<220 for non-lytic, < 185 for lytic) for up to 24-48h post stroke (Permissive HTN)
- DVT Px should not be started until 24h after lytic therapy

Pharmacotherapy
Ischemic Stroke Treatment

- Alteplase
  - rtPA
  - Reduced disability 3 months post-stroke by 30%
  - No proven mortality benefit
  - ICH complication up to 6.4% vs. 0.6% with placebo
  - Indicated within 3h of stroke onset
  - May be beneficial in select pts 3-4.5h post-stroke
  - 0.9 mg/kg, max 90 mg
    - 10% as IV bolus, remainder over 1h
  - Use of antiplatelets, anticoagulants, and invasive procedures C/I for 24h post rtPA

Pharmacotherapy
Ischemic Stroke Treatment

- Anticoagulants: not recommended in stroke pts except for DVT px to start > 24h post rtPA
- ASA
  - Give initial dose of 325 mg in all stroke pts within 48h after stroke onset, and no sooner than 24h after rtPA, then continue with 50-100 mg/d
  - Reduces stroke recurrence, death, and disability

Pharmacotherapy:
Ischemic Stroke Prevention

- Primary Prevention
  - ASA: generally not rec'd unless high risk for CV events
  - HTN: Most significant risk factor for stroke- good control is recommended regardless of agent used
  - DM: independent risk factor for stroke. Intensive glycemic control has been shown to reduce stroke risk in DM1 or DM2
  - Statins: shown to reduce risk for first stroke in pts with CAD or DM even with normal cholesterol
  - Smoking cessation: clear relationship with ischemic and hemorrhagic strokes

Pharmacotherapy:
Ischemic Stroke Prevention

- Secondary Prevention (TIA and stroke)
  - Antiplatelets
    - ASA: decreases stroke recurrence by 25%. Usual choice for initial therapy. Dose: 50-100 mg/d
    - Clopidogrel: slightly more effective than ASA. Valid option for initial therapy. More side effects and drug interactions/genetic polymorphisms. Dose: 75 mg QD
    - Dipyridamole/ASA: more efficacious than ASA alone. Valid option for initial therapy. Dose: ASA 25 mg BID, ER dipyridamole 200 mg BID
    - Ticlopidine: slightly more beneficial than ASA but severe side effects, expensive, and requires monitoring

Pharmacotherapy:
Ischemic Stroke Prevention

- HTN: diuretics and ACEI have been shown to reduce stroke risk in pts with stroke or TIA
- Statins: those with intensive lipid-lowering effects are rec'd in pts with pervious stroke or TIA regardless of history of CAD or cholesterol levels. SPARCL study showed atorvastatin 80 mg/d post-stroke reduced recurrence by 16%
- Carotid endarterectomy: recommended in select pts to reduce stroke risk

Treatment
Hemorrhagic Stroke

- Often requires surgical intervention to evacuate clot, decrease ICP, or clip/coil aneurysm
- Hypertonic therapy (hypertonic saline, mannitol) may be used to manage cerebral edema and lower ICPs
- Pts with ICH 2/2 HTN need control of their BP preferably with nicardipine
- In SAH, PO nimodipine is used to treat vasospasms
- Pts on AC require reversal with appropriate antidote and possibly clotting factors