Current Topics in Stroke Management

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Overview

• Stroke Case Presentation
• Acute Stroke Management at-a-glance
• Secondary Prevention
• Management of Carotid Disease
• Stroke Case Wrap-Up
• Ethnic Disparities/Community Outreach/Preventive Strategies

Example Case

69 RHF with Obesity, HTN, DM, CAD is BIBEMS to the emergency department at 2:15 PM after developing sudden onset of slurred speech, R facial droop, R hemiparesis, R homonymous hemianopsia, and R spatial neglect, all of which started in her PCP’s waiting room at 1:45 PM.

Whats the next best step in imaging?

A. Non-contrast Head CT
B. CT Angiogram
C. MR Angiogram
D. Catheter Angiography
Imaging – CTA/CT Perfusion

Imaging – MRI T2 FLAIR

Imaging – MRI Diffusion Weighted

Vitals/Systemic Exam

- BP 204/99, HR 110, RR 22, SaO2 98% RA
- EKG/TELE – atrial fibrillation
- Diaphoretic
- L carotid bruit
- Absent DP pulses
- Labs sent (CBC, Coags, Chemistries/BG wnl)
**Currently Available Treatments**

Time of onset = last time seen normal
- 0-4.5 Hours    IV-tPA
- 0-6 Hours      IA-tPA
- 0-8 Hours      Mechanical Embolectomy
- > 8 hours/subacute Anticoagulant/Antiplatelet agents

**Intravenous Tissue Plasminogen Activator (IV t-PA)**

Pivotal IV t-PA NINDS trial I/II (0-3 hours) *
- Part I (24 hrs) 291 pts, randomized to IV tPA v. placebo, no significant differences
- Part II (90 days) 333 pts; 30% ↑ in 0/minimal disability at 90 days, absolute difference ~12%
- ↑ Symptomatic hemorrhage risk 0.6 to 6.4% during 1st 36 hrs, half were serious and/or fatal

*NEJM 1995

**Expanding IV t-PA Window**

ECASS III trial (3-4.5 hours) *
- 821 pts randomized to IV t-PA v. placebo
- primary endpoint was disability at 90 days
- favorable outcome in 52% vs 45%, p=0.04
- symptomatic ICH: 2.4% vs 0.2%, p=0.008
- NO mortality difference
- Advisory: avoid in pts >80, Hx Stroke + DM, Anticoagulation Tx (any INR value)

*NEJM 2008
IV t-PA – Earlier Is Better

Inclusion Criteria
- Age 18-85 (<80 if beyond 3 hrs)
- Clearly defined time of onset < 4.5 hrs
- Measurable neurologic deficit/no rapid rate of improvement (on NIH Stroke Scale)
- Neuroimaging excluding hemorrhage

Exclusion Criteria
- Recent stroke or serious head trauma
- Active systemic bleed (GI, hematuria, etc)
- SBP > 185, DBP > 110
- Major surgery < 14 days
- History of Intracerebral Hemorrhage
- History of Subarachnoid Hemorrhage

Exclusion Criteria (continued)
- Arterial stick < 7d non-compressible site
- Glucose < 50 or > 400
- Seizure at stroke onset
- Abnormal coags (e.g. INR > 1.4)
- Platelets < 100k
Treatment Delays/Discrepancies

- Only 1-2% of acute strokes occurring in the community receive IV t-PA
- Tremendous variation in treatment exists depending on hospital and region
- CDC-sponsored registry showed that t-PA tx rate was 3% in GA and 8% in MA, despite 20-25% presenting within 3 hrs (10-20% of treated patients received it within 1 hr)*

*Stroke 2005

Example Stroke Case

- Received IV t-PA within 1 hour
- New onset atrial fibrillation
- TTE showed L atrial enlargement
- LDL 150, HDL 35, TG 108
- Fasting glucose 131, HgbA1c 7.2%
- Carotid ultrasound showed bilateral ICA stenosis at origin - R 40%, L 55%

Secondary Stroke Prevention

- Should begin during acute hospitalization
- Vascular/Atherosclerotic Risk Factor Reduction
  *HTN  *Diabetes  *Atrial Fibrillation
  *Lipids  *Smoking  *Sleep Apnea?
- Antithrombotic Therapy
  - Antiplatelet v. Anticoagulation
- Carotid Disease Management

Hypertension

- Most important modifiable risk factor
- Predisposes to atherosclerotic disease of intra- and extracranial vessels, particularly at bifurcation sites
- Maintaining BP < 120/80, ↓ recurrent stroke risk by 30-40%1
- Optimal BP regimen has not been established and treatment is highly individualized
- ACEI and ARBs may ↓ arterial dz progression2
- Lifestyle modifications (e.g. weight loss, exercise, ↓ salt intake)

1, 2 Stroke 2004
Hyperlipidemia

• ↑LDL and ↓HDL linked to athero and heart dz, but direct relationship to stroke unclear
  - ? Dependence on subtype of stroke (i.e. large vessel)
• Several trials have shown efficacy ↓ CV events in patient with hx of stroke
• SPARCL Trial
  - atorvastatin 80mg ↓ RR recurrent stroke 16% at 5yr
• Do statins ↑ risk of hemorrhagic stroke?
  - minimal, benefits outweigh risks
• Retrospective - statins at discharge lowers the risk of 10-year stroke recurrence and improves survival

1 NEJM 2006, 2 Neurology 2007, 3 Neurology 2009

Diabetes (DM)

• ~25% stroke patients have DM, 2-4x risk over non-DM patients
• ↑ likelihood of recurrent ischemic stroke
• ↑ morbidity and mortality after stroke
• Current AHA/ASA guidelines recommend near normoglycemic levels (HgA1c <7%) for patients with recent ischemic stroke
• Tighter target LDL control goals (<70mg/dL)

*Stroke 1/2011

Obstructive Sleep Apnea & Stroke: A Reciprocal Relationship

• Share common risk factors (e.g. smoking, HTN)
• OSA may be an independent stroke risk factor via promotion of atherosclerosis due to:
  - repeated hypoxemia → endothelial dysfunction and oxidative stress
  - promotion of hypercoagulability through platelet activation and ↑fibrinogen levels
  - chronic elaboration of inflammatory cytokines
• > 50% of stroke patients may exhibit OSA within the first 24 hours after stroke

Seminars in Neurology 2006

Identifying OSA

• Historical Features
  - snoring - fragmented sleep - observed apneas
  - excessive daytime somnolence (EDS)
• Characteristic Phenotypical Features
  - obesity - short neck - low-set soft palate
  - narrow oropharynx - retrognathia
• Orofaciopharyngeal weakness secondary to stroke

TX: Continuous Positive Airway Pressure (CPAP)
Antiplatelet Agents

• Aspirin
• Aspirin/Dipyridimole (Aggrenox)
• Ticlopidine (Ticlid)
• Clopidogrel (Plavix)

Aspirin

• Cyclooxygenase inhibitor through acetylation
• Effects on platelets detectable < 1hr, and may have additional fibrinolytic properties
• 30-1300mg/day conveys significant secondary stroke prevention – optimal dose remains controversial (several positive trials)
• Side effects: gastritis, peptic ulcer disease, and gastrointestinal bleeding (lower doses and enteric coated preps help reduce incidence)

Ticlopidine

• ADP-GIIb/IIIa receptor binding antagonist
• Reduces fibrinogen levels and increases RBC deformity
• 1989 TASS trial → 12% relative risk reduction compared to ASA¹
• Not reproduced in subsequent 2003 trial in AA pts – no difference from ASA²
• 2.4% risk of neutropenia (rare TTP) along with lack of reproducibility – fallen out of favor in U.S.

Clopidogrel (Plavix)

• ADP-GIIb/IIIa receptor binding antagonist
• 1996 CAPRIE trial → 9% relative risk reduction compared to ASA, but no significant difference in patients with prior stroke¹
• 2004 MATCH trial → ASA + Clp v. Clp alone, combo confers ↑ hemorrhage risk w/o ↓ stroke²
• 2006 CHARISMA trial → ASA + Clp v. ASA alone, combo confers ↑ hemorrhage risk w/o ↓ stroke³
• No neutropenia (rare TTP) and generally better tolerated than ASA

¹ NEJM 1989, 2 JAMA 2003
Aspirin/ER Dipyridamole (Aggrenox)

- Dipyridamole is a phosphodiesterase inhibitor in platelets → indirectly blocks activation
- ESPS-2* and ESPIRIT** trials compared aggregate to ASA alone for stroke prevention, convincingly in favor of aggregate
- In both trials, risk of bleeding from dual therapy was not greater than that of ASA alone
- Side effects: headache

2008 PRoFESS TRIAL

- Randomized, double-blind trial of ASA/Dipyridimole versus Clopidogrel in > 20k pts with ischemic stroke
- No significance difference event recurrence rates between the two medications over 2.5 yrs
  - Composite rates of stroke, MI, CV death: both 13.1%
  - Major hemorrhagic events higher in ASA/Dyp group (Clp 3.6%, ASA/Dyp 4.1%; P=.06)
  - More drop-outs in ASA/Dyp group owing to headache (Clp 0.9%, ASA/Dyp 5.9%)

Choosing Antiplatelet Therapy

- Any of the following may be used to help prevent stroke recurrence
  - ASA 50-325mg QD (20x cheaper!)
  - ASA 50mg/ER Dypiridamole 200mg BID
  - Clopidogrel 75mg QD
- Clopidogrel 75mg QD if ASA intolerant
- ASA+Clopidogrel is not more effective and may be dangerous
- No trials supporting antiplatelet switch following stroke

Antiplatelet Failure/“Resistance”

- Is the patient compliant?
- Diagnostic Failure (eg. PAF*, seizures, migraines, meds)?
- Are other risk factor being addressed adequately (eg. BP, Lipids, Hgbaic, Carotid Stenosis)?
- Drug interaction (eg. NSAIDs-ASA, PPI-Clopidogrel)?
- Genetic predisposition to platelet aggregation?
- Is there any data to support switching anyway?


NEJM 2008

*Stroke 2011

*PAF = paroxysmal atrial fibrillation
When should we anticoagulate?

- Atrial Fibrillation
- Mechanical Heart Valve
- Hypercoaguable State (e.g. Factor V Mutation)
- Severe Cardiomyopathy/EF Reduction
- Great Vessel Dissection (limited course)
- Acute Carotid Occlusion
- Aortic Arch Atheroma
- PFO with atrioseptal aneurysm

[* not clearly supported in the literature but employed on a case by case basis]

Carotid Artery Stenosis

- ~60% of strokes stem from carotid bifurcation
- Readily identified and monitored via carotid ultrasound (CUS)
- Confirmatory CT or MR Angiography usually required before surgical intervention
  - CTA 85% sensitivity, 93% specificity
  - MRA 94% sensitivity, 85-96% specificity

Carotid Stenosis - CTA

Carotid Revascularization (for symptomatic stenosis)

Carotid Endarterectomy (CEA)

- NASCET (1990s)*
  - Benefit of CEA in patients with symptoms ipsilateral to 70-99% stenosis
    - Comparison: best medical management at the time
  - 50-69% symptomatic stenosis revascularization has limited benefit, especially in women
- ESCT (1990s)** results comparable to NASCET

*NEJM 1991  **Lancet 1998
Asymptomatic Carotid Stenosis

- Management remains controversial
- Estimated that 5-10% of population has ACAS > 50%, and 1% has >80% ACAS
- 1-3% annual stroke risk if 55-99% ACAS
- ACST* 5 yr stroke risks of 11% and 6% for deferred and immediate surgery respectively
  - no relationship to stenosis severity (60-90+%)  
  - no benefit to age > 75
- Routine screening is not recommended (US Preventive Svcs Task Force)**
  *
  **

Carotid Stenosis Management

- Revascularize all patients with 70-99% symptomatic lesions; consider for clearly symptomatic lesions of 50-69%
- Consider revascularization of asymptomatic lesions > 60% in age <75
- CEA preferred except high surgical risk, etc:
  - active CAD  
  - post-radiation  
  - severe respiratory/cardiac/renal failure  
  - poorly accessible vascular lesions
- Stenting is an effective alternative to CEA for high-risk patients*
  *
  *NEJM 2010

Carotid Stenosis – Example Case

CTA showed Bilateral ICA stenosis;  
R 40%, L 55%

Plan:
- Optimize medical management with Warfarin  
  (? Dabigatran) and aggressive longitudinal vascular risk factor reduction by PCP
- CUS surveillance for progression of carotid stenosis

Ethnic Disparities in Stroke

- Stroke risk, incidence, and mortality are considerably worse for underserved minorities (particularly African Americans)*
- Beyond good guidelines is the need for “Cultural Competence”  
  - staff ethnographic educational programs  
  - diverse healthcare delivery teams  
  - culturally appropriate pt education materials  
  - interpreting services

*Stroke 2005
Community Outreach

- #1 reason for acute stroke patients not receiving timely treatment is delay in presentation to the hospital*
- Ca. Acute Stroke Pilot Registry retrospective analysis determined that rapid presentation would have resulted in 5 fold increase in t-PA treatment rate in < 3hrs**

http://givemeforstroke.org

*Acta Neur (Belgium) 2007  **Neurology 2006

2020 Impact Goal

First ever definition of ideal, intermediate and poor cardiovascular health unveiled in January 2010

My Life Check
Health Assessment Tool
Find it at: heart.org/mylifeccheck

Patient Education Portal

The most credible, easy-to-understand heart health information available online for:
- Patients
- Caregivers
- The public

Features:
- Articles, tips, and guidelines
- Interactive tools
- Videos, podcasts, and animations
- Discussion Forums

Three new language options @ HeartHub.org