2017 Update in Diagnosis and Management of Stroke

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The speaker has no disclosures

Case 1
• A 69 year-old right handed man with a history of HTN and smoking presented to the ED after the sudden onset of right sided weakness.
• Exam shows a dense expressive aphasia, R face and arm plegia and L gaze deviation.
• She was last seen normal at 1 p.m., and it is now 3:45 pm

UCSF “Stroke Protocol” CT
• Obtained at UCSF in suspected acute stroke and TIA patients hours from onset
  1. Non-contrast CT of the head
  2. CT Angiography from aortic arch to the top of the head
  3. CT Perfusion study
  4. Post-contrast CT of the head

What treatment should this patient likely receive?
A. IV t-PA alone
B. IV t-PA followed by embolectomy
C. Embolectomy alone
D. IV heparin
E. Antiplatelets
The 2017 Acute Stroke Timeline

- **Time of onset**: last time seen normal
  - 0-4.5 Hours: IV-tPA
  - 0-6* Hours: Mechanical Embolectomy
  - Greater than 6* hours: Anticoagulants or Antiplatelets

* = Basilar occlusions to 12 hours

Intravenous t-PA

- Pivotal IV t-PA NINDS trial (0-3 hours)
  - 30% increase in minimal or no disability at 90 days, not the Lazarus effect
  - Symptomatic hemorrhage risk increased 0.6 to 6.4%, half were serious and fatal
  - No change in mortality
  - Multiple recent studies confirm this result in diverse settings
  - **THE EARLIER THE BETTER!!!**

Speed Matters:
Time is Brain

- Examination of the Get With the Guideline Registry in the U.S. over the last decade
  - 1400 hospitals, nearly 59,000 patients
  - Mean time to treatment was 144 minutes
    - Earlier on weekdays, more severe stroke, arrival in ambulance
  - For every 15 min earlier administration…
    - Significantly lower in-house mortality
    - Significantly lower rates of ICH
    - Significantly more independent ambulation at d/c
    - Significantly higher rate of d/c to home

**Note:** Saver J et al. JAMA 309:2480, 2013

Intravenous t-PA: Broad Success

**Note:** Emberson, J et al. *Lancet* 2014
The 2015 Endovascular Revolution

- Five major positive trials of endovascular therapy all published in 2015 in NEJM
- Trial design somewhat differed, but common to each:
  - 1. Used newer-generation devices
  - 2. Selected patients who were eligible via CTA (less commonly perfusion)
  - 3. IV t-PA in those who were eligible followed by embolectomy
  - 4. At least 6 hour time window

- 90-day functional outcomes significantly improved with endovascular treatment (nearly doubled odds of good outcome)
- No increased risk of hemorrhage
- First time a mortality benefit has been shown in an acute stroke trial (1 trial)

What do we do given this data?

- 1. All patients eligible for IV t-PA should receive it (quickly)
- 2. Patients within 6* hours (for now) should receive a CTA to look for a large vessel occlusion (LVO)
- 3. If LVO present, endovascular therapy should occur, even following IV t-PA
- Fundamental shift in hospital protocols including transfer protocols

What’s coming!

2017-2018

- DAWN and DEFUSE3 Trials
- Select patients with LVO treated up to 24 hours based on perfusion selection
  - Automated CT perfusion software
- Will lead to reexamination of triage and ED/hospital protocols once again, this time in a major way, including perfusion
Case 2

- A 65 year-old man with a history of HTN presents with 3 days of R arm weakness
- Examination shows a R pronator drift and mild weakness in the extensors of the R hand and arm
- The patient takes aspirin 81mg daily as well as HCTZ

Which of the following is not part of the standard embolic stroke workup?

A. Echocardiogram
B. Extended cardiac telemetry
C. Lipid panel
D. B12, TSH, RPR, ESR
E. Carotid evaluation

Standard Large-Vessel Stroke Workup

- Cardioembolic: afib, clot in heart, paradoxical embolus
  - 1. Telemetry
  - 2. TEE with bubble study
- Aortic Arch
  - 2. TEE with bubble study
- Carotids
  - 3. Carotid Imaging (CTA, US, MRA, angio)
- Intracranial Vessels
  - 4. Intracranial Imaging (CTA, MRA, angio)

And evaluate stroke risk factors

TEE vs. TTE

- 231 consecutive TIA and stroke patients of unknown etiology underwent TTE and TEE
- 127 found to have a cardiac cause of emboli, 90 of which (71 percent) only seen on TEE
- TEE superior to TTE for: LA appendage, R to L shunt, examination of aortic arch
- Recent study: TEE found additional findings in 52% and changed management in 10%

Atrial Fibrillation Detection

• EKG
• 48 Hours of Telemetry
• Long-term cardiac event monitor (>21d)
  – 15-20% of patients with cryptogenic stroke otherwise unexplained had afib detected
  – Clearly changes management
  – Probably cost effective


Approach to Stroke Treatment

Acute Stroke Therapy?
  No

Anticoagulants?
  No

Antiplatelets

Shrinking Indications for Anticoagulation in Stroke

1. Atrial Fibrillation
2. Some other cardioembolic sources
   – Thrombus seen in heart
   – ?PFO WARCEF 2012
   – ?PFO with associated Atrial Septal Aneurysm
3. Vertebral or Carotid dissection CADISS 2015
4. Rare hypercoagulable states: APLS

The “Absolute Mess” of PFO in Stroke


• Around 20% of all patients have a PFO
• PFO alone is not necessarily associated with higher risk of recurrent stroke
  – High risk: Large PFO, associated atrial septal aneurysm
• Three previous negative trials of closure devices but cardiologists still performing these procedures widely
• New data coming in 2017-18: select closures probably work but choose carefully
Heparin in Acute Stroke

- Study examined the largest trials of heparin, heparinoids, LMWH in acute stroke
- Could find no benefit even in those patients with highest risk of recurrent ischemia and lowest risk of hemorrhage
- Considering use of heparin for “selected patients” therefore seems unwise


Case 3

- A 70 year-old woman with a history of DM, smoking presents 10 hours after the onset of slurred speech and right arm and leg weakness.
- The patient is taking ASA 81mg daily

Stroke workup is unrevealing. your Treatment?
A. Increase ASA to 325mg daily
B. Add Plavix to ASA
C. Stop ASA, start Plavix
D. Stop ASA, start Aggrenox
E. Anticoagulate

Approach to Stroke Treatment

Acute Stroke Therapy?
No

Anticoagulants?
No

Antiplatelets
Antiplatelet Options

• 1. ASA
  – 50mg to 1.5g equal efficacy long-term
• 2. Aggrenox
  – 25mg ASA/200mg ER Dipyridamole
• 3. Clopidogrel (Plavix)
  – Multiple secondary prevention studies (CHARISMA, SPS3) show no long-term benefit in combination with ASA

Antiplatelet Options

• If on no antiplatelet medication
  – Plavix vs. Aggrenox (or ASA)
• If already on ASA
  – Switch to Plavix vs. Aggrenox
• If already on Plavix or Aggrenox
  – ???

Clopidogrel + ASA: Ever A Winning Combination?

• CHANCE trial
  – 5170 TIA or Minor Stroke patients assigned to daily ASA + Placebo versus daily ASA + Clopidogrel following 300mg load
  – Primary outcome was stroke at 90 days
    • NNT=29 to prevent 1 stroke
    • Similar safety endpoints
• Generalizability?
  – Await POINT trial results
• Not all patients benefit
  – CYP2C19 loss of function

Other Acute Stroke Management

• Statins for (almost) all patients with stroke or TIA
  – 80mg atorvastatin if LDL>100 for at least 5 years
• Tight Glucose and Fever control in acute period
• Enoxaparin for DVT prophylaxis
  – Beats compression stockings
  – Beats unfractionated heparin
Permissive Hypertension

- National Guidelines
  - To at least 220/120
  - After IV tPA: less than 185 systolic for 24 hours
- We typically stop all meds except half-dose β-blockers and maybe clonidine

Permissive Hypertension

- When to stop remains controversial
- Situations where more important
  - Large Vessel Occlusion
  - Fluctuating Symptoms
- We begin a medicine before discharge (~72h) and aim for normotension over a matter of weeks
  - Choose thiazides and ACEI first

Case 4

- A 73 year-old woman with HTN comes to the ED after a 5 minute episode of right arm weakness that has since resolved.
- Exam is normal except blood pressure is elevated at 176/97

Other than TIA, what is the most common neurologic diagnosis here?

A. Conversion disorder
B. Migraine
C. Focal Seizure
D. UTI
E. Cervical spine lesion
TIA versus Stroke

• Up to 30-50% of TIA have infarct on MRI
• Conceptually the same disorder
  – Same workup, same treatment
• Pendulum swing
  – Pre-2001: Much more aggressive with stroke
  – 2002-2007: TIA and stroke equally aggressive
  – 2008-present: A more aggressive approach with TIA outside of the acute treatment window

Risk of Future Stroke with TIA: ABCD² Score

• 7-day risk overall 8.6-10.5 percent
• Age
  – >60 =1 point
• Blood Pressure
  – SBP>140 or DBP>90 =1 point
• Clinical Features
  – Unilateral weakness =2 points
  – Speech disturbance without weakness =1 point
• Duration
  – >60 minutes =2 points
  – 10-59 minutes =1 point
• Diabetes=1 point


Aggressive Therapy for TIA

• 1. SOS-TIA trial
  – 1085 patients with TIA admitted to a 24-hour center
  – All treated with standard therapy
    • 74 percent discharged on same day, stroke risk reduced 80 percent from ABCD² prediction
• 2. EXPRESS study
  – 80 percent reduction in risk with urgent TIA clinic visit versus usual primary care visit in 1278 patients

Lancée PC et al: J Stroke Cerebrovasc 13:552, 2005

TIA Aggressive Therapy: A Modern Look

• 2009-2011 TIA registry of nearly 5000 patients
• Population at baseline was high risk as with historical cohorts
• 78% saw a stroke specialist within 24 hours
  – Hospitalists not mentioned in this European study
• 1-year stroke rate was 5.1%
• Rates at 2d, 7d, 30d, 90d, 1y were all less than half of that in historical cohorts

When to Fix the Carotid?

- NASCET in early 1990s
  - Benefit of endarterectomy 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
- In stroke management don’t miss carotid disease or atrial fibrillation

How to Fix the Carotid?

- Stenting vs. CEA: CREST Trial
  - 4-year study of 1321 symptomatic and 1181 asymptomatic patients randomized to CEA vs. carotid stenting
  - Combined endpoint of stroke, MI, death not significantly different
    - More strokes in first 90 days in stenting group, more MIs in surgical group
    - After 90 days, similar endpoints


Result confirmed over 5 years in a 2015 trial