POST STROKE COMPLICATIONS

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Disclosures

- I have no financial disclosures and will not be discussing any off-labeled use of medical therapies or interventions
non scholae, sed vitae discimus:

- We learn not for school, but for life

Impact of Stroke

- Stroke is the 4th leading cause of death
  - Over 128,842 people die each year from stroke in the United States (down from 140,000+/year)
- Stroke is the leading cause of serious, long-term disability in the United States
- Each year, about 795,000 people suffer a stroke. About 610,000 of these are first attacks, and 185,000 are recurrent attacks.
- Every 40 seconds someone has a stroke and every 4 minutes someone dies from stroke

Sources: U.S. Centers for Disease Control and Prevention and the Heart Disease and Stroke Statistics, 2012 Update
Age-Adjusted Stroke Death Rates (per 100,000 US standard population, age >=18 from ‘07-’09)

http://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm

Financial Burden of Cerebrovascular Disease

- “The conditions and disabilities associated with stroke cost the United States between $30 billion and $40 billion a year.”

- “The average cost of care for a patient up to 90 days post-stroke is $15,000.”
  - The University Hospital. "Stroke Statistics".

- “The mean lifetime cost of ischemic stroke in the U.S. is an estimated $140,048. This cost includes inpatient care, rehabilitation, and follow-up care.”
Case Presentation

- 61 yo wm with VRFs of afib (on aspirin) not anticoagulated 2/2 previous retroperitoneal hematoma, previous embolic ischemic stroke and hypertension who was admitted for workup and evaluation of syx bradycardia
- Last normal at 9am on day of presentation
- At 10am he was noted to have right hemiparesis and decreased output of speech
- Stroke alert was called

Initial Exam

- NIHSS 24
- globally aphasic (only said “yeah” and would only follow simple midline commands)
- L gaze deviation
- R arm and leg hemiplegia
- R facial droop
- R homonymous hemianopsia
Localize the Lesion

- 1. Anterior Circulation (Internal Carotid Artery)
  - Dominant hemisphere
  - Nondominant hemisphere
- 2. Posterior Circulation (Vertebrobasilar System)
- 3. Can’t Tell

Anterior Circulation, Dominant Hemisphere

- Findings specific to anterior circulation
  - Gaze preference
  - Aphasia (dominant hemisphere)
- Is he a tPA candidate?
What did his vessels look like?

Plain Head CT

Is he an IV tPA candidate?
IV tPA Contraindications

- Recent stroke within 3 months
- Obvious hypodensity of significant size on initial plain head CT
- Previous history of retroperitoneal hematoma (not an absolute contraindication)

How did he do neurologically?

- He was admitted to MICU and given IVFs and PR aspirin and monitored closely
- Repeat HCT the following day showed expected evolution of ischemic stroke
- Repeat HCT the following day showed evidence for hemorrhagic transformation into the area of ischemia, likely from recanalization of the previously noted thrombus
- Decision was made to make him comfort measures at the families request
Objectives

- Understand some frequently encountered post-stroke complications
- Identify ways that medical providers can decrease the risk of these complications
- Learn ways in which these complications can be treated
- Take what is learned today and utilize this new information daily to optimize patient care in the future

Post-stroke Complications: Why bother?

- Incidence?
  - Up to 40-96% of all patients after stroke have some complication reported by 90 days
- Do they REALLY affect patient outcomes?
  - Several studies have shown that although deaths within a few days of stroke are usually the direct consequence of brain damage, those occurring over the following weeks are mainly due to potentially preventable problems such as infection, venous thromboembolism, or cardiac disease
  - Admission to stroke units has been shown to reduce complication rates and improve outcomes
What Constitutes a Post-stroke Complication?

- **Neurologic Complications**
  - Recurrent Stroke
  - Hemorrhagic Transformation
  - Dysphagia
  - Post-stroke epilepsy
  - Spasticity
  - Dementia

- **Cardiovascular Complications**
- **Infections**
  - Urinary Tract Infection
  - Respiratory infection

- **Complications of immobility**
  - Falls
  - DVT/PE

- **Psychiatry**
  - Depression
  - Anxiety
  - PTSD
Neurologic Complications

- **Recurrent Stroke**
  - 2-18% of all stroke patients
  - Odds ratio (OR) of 7.5 for a worsened outcome and an OR of 10.5 for major disability or death
  - Early work-up for transient ischemic attack or minor stroke reduced the 90-day recurrent stroke rate from 10.3% to 2.1% in the Oxford Vascular Study
  - Large artery disease, previous MI, and atrial fibrillation seem to be the factors predisposing toward early recurrence and should be actively sought after

Neurologic Complications

- **Hemorrhagic Transformation (HT*)**
  - Two types:
    - Hemorrhagic Transformation (HT1 and HT2)
    - Parenchymal Hemorrhage (PH1 and PH2)
  - In one study incidence of early HT* of about 9%
  - PH1/2 seen in about 3% of the patients, was associated with an adverse outcome at 3 months
  - HT1/2 not associated with adverse outcome at 3 months
Neurologic Complications

- **Hemorrhagic Transformation**
  - The size of the ischemic lesion and cardioembolism were independent predictors of early HT*
  - High levels of fasting blood glucose on admission and thrombolytic treatment were independently associated with the development of PH1/2
  - Prophylactic doses of either unfractionated or low molecular weight heparin administered to prevent deep venous thrombosis (DVT), with or without concomitant aspirin, was **NOT** associated with HT*
  - Generally higher levels of blood pressure and the presence of severe white matter disease are both predictors of the development of HT*
  - Tight BP and BS control and appropriate use of thrombolytics remain the mainstay of hemorrhagic transformation prevention

Neurologic Complications

- **Dysphagia**
  - Reported frequencies are widely discrepant, ranging between 19% and 81%
  - The presence of dysphagia has been associated with an **increased risk for pulmonary complications and even mortality**
  - There is emerging evidence that early detection of dysphagia in patients with acute stroke reduces not only these complications but also reduces length of hospital stay and overall healthcare expenditures
  - Cerebral, cerebellar, or brain stem strokes can impair swallowing physiology
Neurologic Complications

**Dysphagia (cont)**
- The reported incidence for dysphagia in studies enrolling acute stroke patients regardless of lesion location was lowest with screening identification (37% to 45%), higher with clinical testing (51% to 55%), and highest with instrumental testing (64% to 78%).
- In one study there was a 3-fold increase in pneumonia risk among stroke patients with dysphagia and an 11-fold increase in risk among a subset of more severely impaired patients with confirmed aspiration, suggesting that these are 2 important predictors for the development of pneumonia.

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**Post-stroke Epilepsy**
- In a large epidemiological project, cerebrovascular diseases represented the most commonly identified etiology of secondary epilepsy (11%).
- In another study stroke accounted for 30% of newly diagnosed seizures in patients 60 years old.
- There was a 2% rate of poststroke epilepsy over a median of 9 months in another study and a 4% rate over a median of 2 years in another.
- In the Oxfordshire Community Stroke Project, the cumulative actuarial risk of having a seizure after ischemic stroke was 4.2 (95% CI, 2.2 to 6.2) at 1 year and 9.7% at 5 years (95% CI, 3.7 to 15.7).
Post-stroke Epilepsy

Early seizures have been defined as those first occurring within 24 to 48 hours, 1 week, 2 weeks, or 1 month.

Late seizures have most commonly been described as occurring at least 2 weeks after stroke.

Overall rate is 2-4%.

Up to 33% of all post-stroke seizures occur “early” with 50% to 78% occurring within the first 24 hours after stroke.

One population-based study found that patients with early postischemic seizures were nearly 8 times (95% CI, 2.8 to 21.7) more likely to develop late postischemic seizures, and approximately 16 times (95% CI, 5.5 to 49.2) more likely to develop epilepsy as compared with patients without early seizures.

Another prospective study found seizure recurrences in 55% (34 of 62) of patients with late postischemic seizures, similar to that observed in other studies with longer follow up periods and higher than that reported for the general population experiencing a first unprovoked seizure.

Multivariate analysis has also shown that late-onset (2 weeks) postischemic seizures are an independent risk factor for epilepsy (hazard ratio [HR] 12.37; 95% CI, 4.74 to 32.32; P < 0.001).
Neurologic Complications

- **Post-stroke epilepsy**
  - Approximately **50% to 90%** of early onset seizures appear to be **simple partial seizure**
  - **<1%** of all stroke patients with seizures will develop **status epilepticus**
  - Results of clinical and autopsy studies have suggested that seizures are more common with cardioembolic infarction than other types of ischemic stroke but other studies refute this
  - **Cortical location** is the best-characterized risk factor for early seizures after ischemic stroke and is supported by studies with widely differing designs
  - They may also occur in the setting of subcortical ischemic stroke, a possible consequence of a substantial release of glutamate from axonal terminals arising from **injured thalamocortical neurons**

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Neurologic Complications

- **Post-stroke epilepsy**
  - At least 1 prospective cohort study found a **higher mortality at 48 hours** among patients with early seizures (30.8%) versus those without early seizures (7.4%; P 0.01)
  - But the difference in mortality rates was **no longer significant at hospital discharge or at follow-up after 27 months**
  - More recently, a large population-based study found that new onset postischemic seizures were **independent predictors of mortality** but did not look at early or late onset seizures separately
Neurologic Complications

- **Post-stroke epilepsy**
  - Patients who develop recurrent early or late postischemic stroke seizures generally **require pharmacological treatment**
  - An observational hospital-based study and a prospective cohort study showed that 54% and 67% of patients with cerebral infarction and epilepsy were seizure-free for at least 1 year with the majority of patients being treated with **a single drug**.
  - **Prophylactic AEDs are NOT recommended** at this time

Neurologic Complications

- **Dementia**
  - In the Framingham study, stroke patients had a **2-fold increased risk for dementia** compared with controls
  - The majority of stroke subjects developed either VaD or mixed dementia (AD with VaD).
  - The large proportion of subjects with mixed dementia after stroke (37%) suggests that a **combination of vascular and degenerative pathologies** may underlie the development of dementia after stroke
  - Some studies suggest **diabetes mellitus** to be an **independent predictor** for the development of poststroke dementia
  - Stroke preventative measures may limit further stroke and preserve cognition
Neurologic Complications

- **Spasticity**
  - Up to **39%** of all stroke patients will develop some degree of post-stroke spasticity after 12 months.
  - Three months after stroke, the patients who were nonspastic had statistically significantly better motor and activity scores than patients who were spastic.
  - However, the correlation between muscle tone and the motor and activity scores was overall low, and severe motor and activity problems were seen in almost the same number of nonspastic as spastic patients.
  - Botox can limit the tone and spasticity but has not been shown to improve motor function.
  - Medications like baclofen, tizandidine, dantrolene, BDZs all have some role in treatment of spasticity but have frequent ADRs.

Cardiovascular Complications

- **Myocardial Infarction**
  - Literature reports a frequency of MI or cardiac failure of **2% to 7%** in patients post-stroke.
  - In one study, despite being associated with a high-rate of disability and mortality in the unadjusted analysis, this serious event, which occurred mainly in older patients, was not independently associated with a reduction in functional outcome.
  - There is a correlation with poor outcome with MI post-stroke.
  - Aggressive cardiac workup including EKG, cardiac enzymes, echocardiogram and telemetry during admission.
    - Troponins of >3 are not likely explained by brain injury.
Infections

- **Pneumonia**
  - Incidence of 10% to 22% in various studies and known to be associated with high-mortality
  - Adjusted OR of 3.3 and 2.5 for worsened outcome and for dependency and death, respectively.
  - In a study of 14,293 US Medicare patients admitted for stroke, pneumonia was identified in 6.9% of patients and conferred a 3-fold increase in 30-day mortality
  - Pathophysiology: reduced swallowing ability, reduced mobility and thereby lung mechanics, and central nervous system injury-induced immune depression.

Infections

- **Pneumonia (cont.)**
  - Performing a swallowing evaluation before any oral-intake has been shown to decrease the incidence of aspiration pneumonia 3-fold
  - Early initiation of antibiotic therapy is generally recommended and seems to be one of the interventions that make SU care so effective
    - Prophylactic antibiotic use is NOT currently recommended
  - Greater emphasis on patient-mobilization is likely another important preventive aspect of SU care
    - Unclear exactly when to begin this mobilization
  - Incentive spirometry, commonly used in the postoperative management of patients, could be an accessory measure in those patients, which cannot be mobilized to a standing position.
Infections

- **Urinary Tract Infections**
  - Incidence has been estimated from **7-28%**
  - Not independently associated with a reduction in 90-day function in one study
  - Removal of Foley catheters and early mobilization are important
  - Prophylactic antibiotics are not recommended

Complications of Immobility

- **Falls**
  - Incidence varies between **2.2-26%**
  - A minority (3%) of patients sustained a concomitant serious soft tissue injury or fracture.
  - Falls conferred an OR of 1.43 for worsened outcome and an OR of 1.41 for disability or death.
  - Appropriate interventions to reduce falls should increase the patient’s coping ability and concomitantly reduce his/her fear of falling to counteract the downward spiral of fear, less physical activity, decline in physical ability and further increase in the risk of falling.
Complications of Immobility

- **DVT/PE**
  - Incidence approximately 10% DVT (3% of which are symptomatic)
  - Stocking Compression Devices (SCDs) have been shown to be an effective means of ppx but despite their use post-stroke DVT and subsequent PE remains common
  - Prophylactic anticoagulation has been shown to be superior to SCDs but carries with it a risk of hemorrhagic transformation
  - At MUSC we found asymptomatic DVTs in approximately 20% of all ICH and ischemic stroke patients admitted to the NSICU
  - Mobilize early and often

Psychiatric Complications

- **Depression/Anxiety/PTSD**
  - pooled estimate indicates that depressive symptoms are present in 33% (95% CI, 29% to 36%) of all stroke survivors at any time during follow-up (34% in the “long term” phase of recovery)
  - **OR of 2.52 for depression at 3 months** when compared to controls
  - Some patients recovered within the first few months of stroke but others had their depression persist for more than a year
  - Personal or family history of depression is thought to predispose patients to depression after stroke
  - **FLAME study** showed use of fluoxetine from day 5 post stroke to 3 month post stroke improved motor recovery in the paretic arm and leg
Timing of symptomatic complications after stroke.

Cumulative proportion (% of patients experiencing complication)

- Pain
- Falls
- Depression
- Chest infection
- UTI
- Pressure sore
- Recurrent stroke

DVT

Time (weeks) from index stroke

Distribution of modified Rankin Scale (mRS) scores at 90 days.

- Whole Cohort N=244
- Recurrent Stroke N=12
- Myocardial Infarction N=17
- Chest Infection N=42
- Urinary Tract Infection N=68
- Other Infection N=31
- Pain N=140
- Falls N=70

mRS 0=light green, 1=dark green, 2=yellow, 3=orange, 4=red, 5=light blue, 6=dark blue

Gitta Rohweder et al. Stroke. 2015;46:65-70
## Frequency of Complications and Distribution of Outcomes in Terms of mRS90

<table>
<thead>
<tr>
<th>Complication</th>
<th>n</th>
<th>% of Cohort</th>
<th>Age, y</th>
<th>Earlier mRS, Mean±SD</th>
<th>mRS90, Mean±SD</th>
<th>mRS90, 0–3, %</th>
<th>mRS90, 4–6, %</th>
<th>mRS90, 6, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole cohort</td>
<td>244</td>
<td>100</td>
<td>77±9</td>
<td>1.6±1.1</td>
<td>3.0±1.8</td>
<td>66</td>
<td>34</td>
<td>17</td>
</tr>
<tr>
<td>Recurrent stroke</td>
<td>12</td>
<td>5</td>
<td>78±6</td>
<td>1.6±1.1</td>
<td>4.7±1.6</td>
<td>23</td>
<td>75</td>
<td>42</td>
</tr>
<tr>
<td>MI</td>
<td>17</td>
<td>7</td>
<td>84±6</td>
<td>2.1±1.4</td>
<td>4.8±1.6</td>
<td>23</td>
<td>77</td>
<td>33</td>
</tr>
<tr>
<td>Chest infection</td>
<td>42</td>
<td>17</td>
<td>82±7</td>
<td>2.0±1.2</td>
<td>4.7±1.6</td>
<td>19</td>
<td>81</td>
<td>45</td>
</tr>
<tr>
<td>UTI</td>
<td>68</td>
<td>28</td>
<td>81±9</td>
<td>2.0±1.1</td>
<td>3.9±1.5</td>
<td>40</td>
<td>60</td>
<td>19</td>
</tr>
<tr>
<td>Other infection</td>
<td>31</td>
<td>13</td>
<td>78±9</td>
<td>1.4±0.9</td>
<td>3.4±1.6</td>
<td>48</td>
<td>52</td>
<td>13</td>
</tr>
<tr>
<td>Falls</td>
<td>70</td>
<td>29</td>
<td>76±10</td>
<td>1.4±0.9</td>
<td>3.1±1.2</td>
<td>69</td>
<td>31</td>
<td>4</td>
</tr>
<tr>
<td>Pain</td>
<td>140</td>
<td>57</td>
<td>77±10</td>
<td>1.5±1.1</td>
<td>3.9±1.6</td>
<td>66</td>
<td>34</td>
<td>12</td>
</tr>
</tbody>
</table>

### OR for Worsened Outcome (Ordinal Logistic Regression) and Bad Outcome (mRS>3 at Day 90)

<table>
<thead>
<tr>
<th>Complication</th>
<th>OR (95% CI) for Worsened Outcome</th>
<th>P Value</th>
<th>OR (95% CI) for mRS&gt;3</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent stroke</td>
<td>7.45 (2.83–20.96)</td>
<td>&lt;0.0001</td>
<td>10.45 (1.03–38.93)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MI</td>
<td>1.83 (0.62–5.36)</td>
<td>0.272</td>
<td>1.89 (0.42–8.53)</td>
<td>0.408</td>
</tr>
<tr>
<td>Chest infection</td>
<td>3.28 (1.16–9.29)</td>
<td>0.025</td>
<td>2.52 (1.14–5.54)</td>
<td>0.022</td>
</tr>
<tr>
<td>UTI</td>
<td>1.19 (0.63–1.74)</td>
<td>0.323</td>
<td>1.33 (0.91–1.93)</td>
<td>0.137</td>
</tr>
<tr>
<td>Other infection</td>
<td>1.59 (1.12–2.24)</td>
<td>0.009</td>
<td>2.09 (1.15–3.80)</td>
<td>0.015</td>
</tr>
<tr>
<td>Falls</td>
<td>1.43 (1.06–1.93)</td>
<td>0.021</td>
<td>1.41 (1.06–1.88)</td>
<td>0.019</td>
</tr>
<tr>
<td>Pain</td>
<td>1.00 (0.92–1.09)</td>
<td>0.961</td>
<td>0.94 (0.80–1.10)</td>
<td>0.439</td>
</tr>
</tbody>
</table>
In Summary...

- Complications following stroke should be expected and carefully monitored for.
- Recurrent stroke, MI and Respiratory infections are correlated with more poor outcomes.
- When complications are identified, aggressive treatment of these can strongly influence long term outcome.

Questions?