Aneurysmal SAH and Cardiac Ischemia

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Background

- Pilot data from UT Southwestern at Dallas study done during my fellowship looking at cTnI in patients after SAH (showed 20% incidence of cTnI elevation)
- 33,000 aSAH/year in US
- Myocardial injury in 17-40%
- 46% of patients surviving aSAH have long term physical and neuropsychological disability
  - Why?
  - How?

Study

- **2004 – 2009 $2.7M NIH R01** sponsored prospective study at UPMC Presbyterian Hospital. Patients with aSAH underwent cTnI, EKG evaluations, catecholamine levels in CSF/urine, TCD. Selective patients underwent echocardiograms, cardiac catheterizations, Holter monitoring.
- N= 325 (84% of all aSAH admissions enrolled)

- **Primary Goals**
  - Determine the incidence and etiology of aSAH related cardiac injury
  - Determine the association between the magnitude of catecholamine release and the occurrence of myocardial ischemia in the first 5 days after aSAH
  - Determine whether the presence of myocardial ischemia within the first 5 days increases the risk of vasospasm

Findings

- **SAHMI is more prevalent than previously thought and is incrementally associated with aSAH severity**
  - 31% of our sample had a peak cTnI $\geq$0.3 ng/ml
  - Only 4% had prior history of CAD
  - History of CAD did not differ between those with elevated cTnI and those without cTnI
  - Elevated cTnI prevalence increases as aSAH severity increases
  - While cTnI rises proportionate to aSAH severity in a stepwise fashion not all cases fit this trend. This variation may be due to variation in individuals' sensitivities to catecholamines.

Findings

- **SAHMI represents myocardial injury, but it is NOT due to cardiac perfusion impairment**
  - The regional wall motion abnormality (RWMA) patterns seen in those with SAHMI do not favor a coronary artery distribution causation
    - RWMA is circumferential and diastolic in nature (diastolic dysfunction predominates in global cardiomyopathies, whereas ischemic cardiomyopathy is associated with systolic dysfunction)

Findings

- **There does not seem to be a strong relationship between SAHMI and risk for symptomatic vasospasm**
  - If poorer SAHMI neuro outcomes are not due to delayed cerebral ischemia, what is the cause for this finding?

Findings

- **Although cTnI increases along with aSAH severity, a cTnI level >1 ng/ml is the most sensitive and specific value associated with myocardial dysfunction after SAH**

Findings

- **Effects of SAHMI persists for longer than previously thought (similar to that seen with myocardial stunning)**
- **12 lead ECG, Holter monitor, Echocardiogram showed that arrhythmia and myocardial dysfunction persists throughout hospitalization (5-10 days)**
  - cTnI≥0.3ng/ml associated with:
    - prolonged QT interval on early (63% vs 30%, p<.0001) and late ECG (24% vs 7%, p=.024
    - VT/VF on Holter (22% vs 9%, p=.018)
    - EF on Echo <50% (44% vs 5%, p<.0001) persisted in 59% of affected patients
    - RWMA on Echo (44% vs 4%, p<.0001) persisted in 73% of affected patients

Findings

- **A relationship existed between SAHMI and 24 hour urine monoamine metabolite levels (metabolites from tyrosine and tryptophan)**
  - This fits with the theory that norepinephrine release from myocardial sympathetic fibers following aSAH causes myocardial necrosis and SAHMI.
  - Patients with cTnI$\geq$0.3 ng/ml were more likely to have elevated levels of endogenous catecholamine metabolites.
  - Higher metabolite levels were also associated with poorer 3 month GOS

Findings

- **SAHMI is associated with gross neurologic functional disability independent of aSAH severity (after controlling for bleed severity, race, gender and age)**
  - 47% with cTnI≥0.3 ng/ml had poorer 3 month GOS as compared to 22% of patients with cTnI≤0.3 ng/ml
  - 45% with cTnI≥0.3 ng/ml had poorer 3 month MRS as compared to 18% of patients with cTnI≤0.3 ng/ml
- SAHMI also predicted NP dysfunction in measures of verbal ability, executive function and verbal memory after controlling for age and aSAH severity

Findings

- Individual adrenergic receptor polymorphisms may be responsible for which patients develop SAHMI and which ones don't
- These polymorphisms may affect how receptors respond to local catecholamine surges

Future Directions

- **R01 Fall 2010 Submission:**
  - Determine the persistence and recovery of SAHMI over time (hospitalization, 4-6 weeks, 3 months)
  - Determine the influence of SAHMI upon cerebral perfusion and its association with short and long term outcomes by using noninvasive devices that measure continuous cerebral perfusion and cardiac output
    - NICOM technology for CO determination
    - Noninvasive Near Infrared Spectrometry (NIRS) for cerebral perfusion
- Explore genetic predisposition as a potential explanation of differential patient response to catecholamines and development of SAHMI
- More detailed cognitive evaluations since NP outcomes don't necessarily correlate with GOS and MRS scores
- More accurate and sensitive assays of catecholamine breakdown products

Future Directions

- **Copeland Grant 2011**
  - Goal to study myocardial dysfunction is patients with non aneurysmal intraparenchymal hemorrhages/hematomas
  - This data combined with data from the two NIH R01 studies on aSAHMI will possibly serve as pilot data for a third R01.