Aneurysmal SAH
and
Cardiac Ischemia
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Michael Horowitz, M.D
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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 > 0.3 ng/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 > 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 $\geq 0.3$ ng/ml had poorer 3 month GOS as compared to 22% of patients with cTnI $\leq 0.3$ ng/ml
  - 45% with cTnI $>0.3$ ng/ml had poorer 3 month MRS as compared to 18% of patients with cTnI $\leq 0.3$ 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 in 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.