Subarachnoid Hemorrhage and Myocardial Injury

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Background

- 33,000 aSAH in US per year (6-8/100,0000)
  - Death in up to 50% of those who suffer aSAH
  - 10-15% die before reaching medical care
  - 8-10% die from progressive deterioration from initial hemorrhage
  - Vasospasm kills another 7-10%
  - Disability in 30-50% of survivors
  - **66% of patients who have their aneurysm treated successfully never return to the same quality of life they had prior to their bleed**

Study Goals and Methodology

- **Purpose**
  - to prospectively evaluate the incidence of myocardial ischemia and infarct in the aSAH population, and determine whether the presence of myocardial ischemia and infarct within the first 5 days of aSAH significantly increases the risk of symptomatic vasospasm.
  - to determine the association between the magnitude of catecholamine release and the occurrence of myocardial ischemia and infarct in the first 5 days after aSAH
- Prospective longitudinal observational design with 309 aSAH patients enrolled. All received cTnI measurements (7 samples over 5 days) as opposed to just patients with a clinical suspicion of cardiac injury as was done in prior studies at other centers

Findings

- SAHMI in 31% (elevated peak CTnI ≥ 0.3 ng/ml)
- Only 4% of patients had prior CAD symptoms
  - Prior CAD symptoms did not differ between patients with and without elevated cTnI; suggests SAHMI has a non-coronary artery based etiology
- 22% incidence of VT/VF
- SAHMI patients require greater amounts of vasopressor and inotrope medications to maintain adequate cerebral perfusion

Findings

- Echocardiograms performed in ? patients between days x and y.
  - ? % incidence of echocardiographic abnormalities found within ?h of bleed
  - 30% of patients with cTnI >1 ng/ml had regional wall motion abnormalities (RWMA)
  - 6% of patients with cTnI <1 ng/ml had RWMA

Findings

- While it was previously surmised that SAHMI was due to catecholamine induced coronary artery vasospasm, this study indicates that SAHMI represents myocardial injury that does not relate to cardiac perfusion impairment since the RWMA seen in our patients did not favor a coronary artery distribution.
  - Circumferential dysfunction in middle segments and diastolic ventricular dysfunction favors a catecholamine induced injury (subendocardial contraction band necrosis) rather than an ischemic cause.
  - Diastolic dysfunction predominates in global cardiomyopathies as opposed to ischemic cardiomyopathy which is more often associated with systolic dysfunction

Findings

- On late echo (mean 7d, range 5-12) 68% of patients with RWMA improve but only 26% have normalized (similar to myocardial stunning)
  - This complication of aSAH has potential long term patient care implications

Findings

- SAHMI persists for longer than was previously thought based on:
- Early and late ECG (first 72 h and 5-10 d) abnormalities
- Holter monitoring (5 days duration) abnormalities
- Early and late echos
  - In patients with cTnI ≥ 0.3 ng/ml prolonged QTc was seen 63% early($p<.001$) and 24% late ($p<.024$) vs 30% and 7% in those without elevated cTnI.
  - In patients with cTnI ≥ 0.3 ng/ml VT/VF was seen in 22% vs. 9% in those without elevated cTnI ($p<.018$)
  - In patients with cTnI ≥ 0.3 ng/ml EF<50% and RWMA was seen in 44% vs. 4% in those without elevated cTnI ($p<.001$)
  - RWMA persisted at second echo in 73% while EF<50% persisted in 59%

Findings

- cTnI rises proportionate to aSAH severity in a stepwise fashion in most but not all patients
  - cTnI <0.3 ng/ml group included 16% with HH 4-5
  - cTnI >0.3 ng/ml group included 20% with HH <4
    - May be due to a variation in catecholamine sensitivity to cause myodardial injury in some patients
- Elevated cTnI predicted gross functional disability and neurocognitive impairment after controlling for aSAH severity

Findings

- Neuropsych battery in 117 patients with SAHMI predicted NP dysfunction in measures of verbal ability (p=.004), executive function (p=.02), and verbal memory (p=.043) after controlling for age and SAH severity

- Of 239 subjects in a substudy controlled for bleed severity, race, gender, and age
  - 47% with cTnI>0.3 ng/ml had poorer functional recovery based on GOS compared to 22% with cTnI <0.3 ng/ml (p<.001)
  - 45% with cTnI>0.3 ng/ml had poorer functional recovery based on MRS compared to 18% with cTnI <0.3 ng/ml (p<.001)
  - cTnI > 0.3 ng.ml also predicted poorer GOS and MRS at 3m

Findings

- A statistically significant relationship was found between SAHMI and monoamine elevations that persisted over time
- It is surmised that local norepinephrine release from myocardial sympathetic chains at the time of aneurysm rupture leads to myocardial necrosis

Finding

- aSAH patients with adrenergic polymorphisms (beta-AR polymorphysm) are more likely to develop SAHMI (136 patients studied in a subgroup using Genotyping Assays)

Finding

- aSAHMI does not correlate with incidence of vasospasm

Findings Summary

- SAHMI is more common than previously appreciated
- SAHMI echocardiographic abnormalities are more common than previously appreciated
- Cardiac abnormalities are likely not ischemic in nature but rather necrotic
- SAHMI not associated with cerebral vasospasm
- SAHMI is associated with poorer neurocognitive outcomes
- SAHMI is associated with increased catecholamine levels
- SAHMI is not correlated with incidence of vasospasm

Goals for Next R01 Study (submitted July 2010)

- Determine the persistence and recovery trajectory of SAHMI over time by extending the study period to 4-6 w and 12 w after SAH using ECG, Holter, Echo
- Determine the influence of SAHMI on systemic and cerebral perfusion and its association with short and long term neuropsychologic and functional outcomes using a non-invasive continuous cardiac output measurement surface electrode system (NICOM) and non-invasive cerebral blood flow near infra-red spectrometry (NIRS InSpectra)
- Determine whether genetic predisposition can increase the risk of SAHMI based on genetic changes in adrenergic sensitivity and expression
- Measure endogenous catecholamine levels separate from administered inotropes and vasoactive medications by using high-pressure liquid tomography coupled with a colorimetric multi electrode array system to measure endogenous catecholamine metabolites.