The Role of Cerebral Protection in TAVR and Other Transcatheter Procedures
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Implications of ‘Silent’ Cerebral Ischemia for Neurocognitive Function

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<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
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<td>Core Lab/Equity</td>
<td>Claret Medical, Inc</td>
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Vascular Cognitive Impairment


- Language
- Memory
- Praxis, Copying

\{ Focal Stroke \}

- Attention, Working Memory
- Executive Function
- Reasoning
- Processing Speed

\{ Multiple Stroke, Silent Infarction, Diffuse White Matter Disease, Hemodynamic Compromise \}
Cerebral Hypoperfusion

Hemodynamic Failure
Stage 1        Stage 2

Auto Regulation                  Critical Perfusion          Ischemia

Decreasing Cerebral Perfusion Pressure

Test Balloon Occlusions in the Internal Carotid Artery

Lazar et al, JNNP, 1996
Recovery of Brain Function During Induced Cerebral Hypoperfusion

**Cellular**
- protein synthesis inhibition
- anaerobic glycolysis
- glucose metabolism, acidosis, edema, K+ / Ca++ transients
- electrical failure
- membrane failure

**Clinical**
- higher cerebral dysfunction
  - hemiparesis
  - EEG change in anesthetized patients
  - ischemic penumbra?
  - ischemic core

CBF
- 50
- 40
- 30
- 20
- 10
- 0
Heart Disease and Neurocognition

- Cardiac Arrest
- Heart Failure
- CABG
- TAVR

Perfusion Failure

Embolism

Both?
Factors Associated With Decreased Cerebral Blood Flow in Congestive Heart Failure Secondary to Idiopathic Dilated Cardiomyopathy

Choi et al. Am J. Cardiol, 2006

- N=52
- EF $\leq 35$
- CBF: SPECT
Association of low ejection fraction with impaired verbal memory in older patients with heart failure

Festa et al. *Arch Neurology*, 2011
• RCT of patients with ICA occlusion and increased OEF (113%) on PET. (Ancillary to COSS)

• Compared neurocognition in 43 PET Positive (↑ EOF but no stroke) vs 28 who met clinical/imaging (no stroke) without OEF asymmetry (PET Negative).

• Results: PET Positive Composite Cognition Z-Score = -1.4 SD below mean PET Negative Composite Cognition Z-Score= -.76 SD below mean (p=0.04)
Results:

- Patients with new DWI lesions had a larger postoperative z score change on neurocognitive testing than those without DWI abnormalities ($p=0.04$).

- The number of multiple new DWI lesions was associated with a larger decline in composite z score ($p=0.046$).
Cerebral Ischemic Lesions on Diffusion-Weighted Imaging Are Associated with Neurocognitive Decline after Cardiac Surgery

N=40
25: AVR
Baseline & 6 weeks
16/37: + Image
16/16: ↓Cognition
21/37: - Image
7/21: ↓Cognition
The proposed battery and its variants have been validated and used in both NIH-funded (NHLBI, NINDS) and industry-sponsored studies, assessing neurocognitive sequelae in end-stage heart failure and LVAD support, carotid artery disease, and recently piloted in the PARTNER II study.

Assessments will be by Core Lab trained and certified study neuropsychologist or technician under the direct supervision of a neuropsychologist.
Silent Brain Infarction: Future Risk
Population-Based Studies

- Presence of silent brain infarcts increases risk of future stroke 2 – 4x (Bernick et al, 2001; Vermeer et al, 2003; Vermeer et al, 2007)

- Stroke risk is highest with silent brain infarction and severe white matter disease (Kuller et al, 2004)

- Silent infarcts unmask underlying Alzheimer’s disease, especially with new infarcts after baseline (Vermeer, 2003)

- Rotterdam Scan Study showed that presence of silent infarction doubled risk of dementia (Vermeer, 2003)

Lazar, TCT 2014
Silent Brain Infarction

Silent?

- Silent brain infarction from embolism or perfusion failure affects broadly distributed, more complex cognitive processes (executive function, processing speed, attention).
- Cognition is more sensitive to vascular pathology than other neurological functions.
- Patients incurring silent brain infarcts after cardiac intervention are more likely to have cognitive impairment.
- The presence of silent brain infarction increases risk for stroke and dementia.

Lazar, TCT 2014