Asymptomatic Carotid Stenosis is associated with Cognitive Impairment: Does Carotid Revascularization Reverse the Deficit?

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**Disclosures**
- Co-PI NIH: CREST 2
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- PI VA Merit: Exercise for thrombus resolution in DVT (EFFORT)
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**Microembolic brain injury**
- Increasing age is associated with “silent brain infarcts”
  Cardiovascular Health Study, JAMA 2006
- Silent brain infarcts lead to cognitive impairment
  Rotterdam Scan Study, Stroke 2008
- Asymptomatic carotid stenosis is associated with “silent brain infarcts”
  • Martini et al., Stroke 1992

**Cerebral hypoperfusion**
- Computer model for intracranial circulation
- Carotid stenosis results in reduced post-plaque perfusion pressure
- 44 patients undergoing carotid balloon test occlusion
  - CBF below 30 ml/100g/min resulted in impaired attentional performance

**Prior studies**
- Prior studies
  - Cardiovascular Health Study (n=32) decline in MMSE
  - Martini et al. (n=26) decline in MOCA
  - Benke et al. (n=20) decline in learning & mental speed
  - Framingham Study (n=35) decline in overall cognition
  - Tromso study (n=100) decline in memory & mental speed

- Existing information is equivocal:
  - Mixed asymptomatic with stroke patients
  - Incomplete/inadequate cognitive battery
  - No controls
  - No accounting for VCI from vascular risk factors

NIH Cognitive Harmonization Standards, Stroke 2010
Asymptomatic Carotid stenosis and COgnitive Function study (ACCOF)

- Prospective controlled natural history study
- 2 year enrollment, 2 year follow-up
- 90% power to detect a cognitive function decline of 0.4 SD, α=0.05
- VA Merit Funding

Age & risk factor matched controls, n=100
Asymp. carotid stenosis, n=100

Administrative Ctr
TCD Core Facility
Cognitive Function Core Facility
US Core Facility
Data Management Center

• To identify the isolated impact of asymptomatic carotid stenosis (ACS) on cognitive function
• To identify mechanisms impacting cognition in ACS

Results
- The stenosis group performed worse on the composite cognitive score and scores for learning/memory and processing speed
- Stenosis patients with low BHI performed worse on overall composite score (t=2.0; p<.05; d=.58), learning/memory (t=2.4; p<.05; d=.68) and processing speed (t=1.79; p<.09; d=.42)
- Stenosis patients with detectable microembolization (n=7) performed similar to non-embolization patients on all cognitive domains

Summary
- First study to demonstrate that asymptomatic carotid stenosis is associated with cognitive impairment independent of other factors
- Likely mechanism is reduced cerebrovascular reactivity/flow

Revascularization

Lal BK et al. VASCULAR Annual Meeting 2014
Background

- Cognitive function after CEA (n=28 studies)
  - N=16, improvement
  - N=8, decline
  - N=4, no change

- Cognitive function after CAS (n=9 studies)
  - N=5, improvement
  - N=3, decline
  - N=1, no change

- Cognitive function after CEA vs. carotid angioplasty
  - 2 studies: equivalent decline after both procedures

- Cognitive function after CEA vs. CAS
  - No studies

Objective

- Compare cognitive outcome in patients with asymptomatic high-grade carotid stenosis 6 months after undergoing CEA vs. CAS

Results

- Overall improvement in cognitive function after CEA and CAS
- Impaired psychomotor speed after CAS
- Impaired memory after CEA

Implications/Questions raised

- Cognitive function is an important endpoint in clinical trials for carotid stenosis
  - Included in CREST2

- Strong information suggests that stenosis impairs cognitive function
  - What happens in the long term? ACCOF

- Smaller studies suggest that revascularization may improve cognitive function

- Cognitive function is emerging as a new treatment target for carotid stenosis
  - Marker for high-risk asymptomatic carotid stenosis

- More studies needed to test optimal treatments to prevent/reverse this impairment
  - Cognitive rehabilitation, ACCOF 2
  - Aggressive medical management & revascularization, CREST2

- Strong argument in favor of wider screening for carotid stenosis (AHRQ vs. SVS)

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