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Estimation of numbers of people with cognitive impairment

The growth in numbers of people with dementia (millions) in high-income (HI) and low and middle-income countries (LMIC)

- 46.8 million people worldwide are living with dementia in 2015
- This number will almost double every 20 years


Association of carotid disease with cognitive impairment = Vascular Dementia

Simple regression model

<table>
<thead>
<tr>
<th>Test</th>
<th>B</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed word recall test</td>
<td>-1.97</td>
<td>0.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Category fluency test</td>
<td>-3.24</td>
<td>0.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Trail making test</td>
<td>81.23</td>
<td>10.90</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Cognition Tests → CIMT

Carotid artery intima-media thickness (CIMT) is inversely associated with memory function


Vascular dementia is a highly prevalent disease

M²OVE-AD
A $30million initiative by NIH May 2016

Can CEA / CAS improve cognitive function?

- Problems with Language
- Problems with Abstract Thinking
- Loss of Initiative
- Memory Loss
- Disorientation
- Personality Changes
- Poor Judgement
- Difficulty Performing Familiar Tasks

Normal
MCI cognitive impairment
Alzheimer's disease
Effects of CAS on Vascular Dementia: 
Angiographic performance

Recanalised RICA and improved perfusion postprocedural

Yun T. et al. Neuroradiology, 2013

Effects of CAS on Vascular Dementia: 
Increase in Cerebral Blood Flow

Improved Cerebral blood flow (CBF) after CAS 
using MRI arterial spin labeling (ASL)

Yun T. et al. Neuroradiology, 2013

The clinical assessment of cognitive function 
is usually difficult to perform

Confounding factors

- Various timing of assessment after CEA / CAS
- Different types of cognitive tests used
- Different population ages
- Symptomatic/asymptomatic status
- Contralateral carotid or vertebral artery disease
- Severity of carotid stenosis
- Use of protection devices

Neurocognitive functions in pts with minor stroke 
CEA vs BMT


Mini Mental (MMSE) scores were significantly 
improved only after CEA

CEA, n=40

Controls, n=40

Cognition in asymptomatic patients 
CEA (n=116) vs BMT (n=45)

Kojima et al. Neurological Research 2016

6 domains of cognitive function 
were studied before and after CAS:
1) global cognition
2) memory
3) attention/psychomotor speed
4) executive function
5) language ability
6) functional ability


Meta-analysis

The Impact of Carotid Artery Stenting on Cognitive Function in Patients with Extracranial Carotid Artery Stenosis

16 studies were eligible, including 626 CAS patients

Pooled weighted mean differences (WMDs)
Standardized mean differences (SMDs)
The Impact of Carotid Artery Stenting on Cognitive Function in Patients with Extracranial Carotid Artery Stenosis

**Meta-analysis**

<table>
<thead>
<tr>
<th>Cognitive Domain</th>
<th>Result</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global cognition</td>
<td>WMD=0.67, P&lt;0.001</td>
<td>Improved</td>
</tr>
<tr>
<td>Memory</td>
<td>SMD=0.33, P&lt;0.01</td>
<td>Improved</td>
</tr>
<tr>
<td>Attention/psychomotor speed</td>
<td>SMD=0.31, P&lt;0.02</td>
<td>Improved</td>
</tr>
<tr>
<td>Executive function</td>
<td>SMD=0.08, P=0.39</td>
<td>Not improved</td>
</tr>
<tr>
<td>Language ability</td>
<td>SMD=0.24, P=0.10</td>
<td>Not improved</td>
</tr>
<tr>
<td>Functional ability</td>
<td>SMD=0.08, P=0.63</td>
<td>Not improved</td>
</tr>
</tbody>
</table>

- **Improvement** in global cognition, memory and attention/psychomotor speed
- **No effect** on executive function, language and functional ability
- **CAS was not associated with a decline** in any area of cognitive function


Comparison of cognitive function after CEA vs. CAS vs. BMT

CREST-2 includes cognitive function at 4 years in the Secondary Outcome Measures but not as safety issue

RCT comparing neurological outcomes after CEA and CAS

- ICA >70%
- Randomized (CEA, n=73 – CAS, n=77)
- Neurological examination, cognitive function tests and MRI before and 24 h after intervention

1) New infarctions on MRI were found more frequently after CAS than CEA (49% vs. 25%; P=0.002)
2) Lesion volume was also significantly greater after CAS (P=0.010)
3) No significant differences were found in cognitive test results between the groups

Kolm et al. BJS, 2014

Microemboli Volume Correlates to Long-term Cognitive Change

n = 120 patients (46% symptomatic)

In 81.7% of CAS and 36.4% of CEA patients 587 emboli were identified by 3-T MRI with an accumulative volume of 29,327 mm³.

54 emboli were found in CEA patients and 533 emboli in CAS patients. 5% of patients had transient neurologic symptoms.

CAS was a significant independent predictor of microembolization. There was a trend of improved RAVLT scores overall after carotid revascularization, embolic volume significantly correlated to worst results.

Zhou Wei, SVS VAM June 2016

CEA and CAS Lead to Improved Cognitive Performance in Patients with Severe ICA Stenosis

**MMSE Cognitive test**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BNI Value</th>
<th>Post-angiography (%)</th>
<th>t-Value</th>
<th>df (df numerator, denominator)</th>
<th>P-Value</th>
<th>A-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>26.78±4.29</td>
<td>27.80±4.39</td>
<td>0.697</td>
<td>15 (15, 16)</td>
<td>0.514</td>
<td>0.514</td>
</tr>
<tr>
<td>CAS (n=65)</td>
<td>23.97±4.10</td>
<td>26.71±13.02</td>
<td>0.686</td>
<td>15 (15, 16)</td>
<td>0.514</td>
<td>0.514</td>
</tr>
<tr>
<td>Pre-treatment</td>
<td>26.38±4.65</td>
<td>26.30±4.17</td>
<td>0.787</td>
<td>15 (15, 16)</td>
<td>0.460</td>
<td>0.460</td>
</tr>
</tbody>
</table>

**Improvement** after CAS

NO improvement for controls

**Improved cognition after CEA**


Microemboli Volume Correlates to Long-term Cognitive Change
Perioperative Embolization Load and S-100b Do Not Predict Cognitive Outcome after Carotid Revascularization

<table>
<thead>
<tr>
<th>Cognitive domain</th>
<th>t-value</th>
<th>df</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term memory</td>
<td>2.31</td>
<td>19</td>
<td>0.12</td>
</tr>
<tr>
<td>Reversibility</td>
<td>0.62</td>
<td>19</td>
<td>0.51</td>
</tr>
<tr>
<td>Executive functioning</td>
<td>0.42</td>
<td>19</td>
<td>0.67</td>
</tr>
<tr>
<td>Fluid mental abilities</td>
<td>0.54</td>
<td>19</td>
<td>0.60</td>
</tr>
<tr>
<td>Visuospatial functioning</td>
<td>1.04</td>
<td>19</td>
<td>0.30</td>
</tr>
</tbody>
</table>

In the 3 treatment groups similar transient increases in S-100b values were observed

Increase in S-100b may be caused by impairment in the blood-brain barrier during intervention, and not due to cerebral infarction

It appears to be difficult to predict which patients will show postoperative cognitive decline

Conclusions I

- The effect of CEA and CAS on neurocognitive functions in patients with extracranial carotid disease is still controversial
  - There are various possible confounding factors making the clinical assessment of cognitive function difficult to perform

Conclusions II

- Many studies have evidenced an improvement in cognitive function as a result of normalization of blood flow in brain after CEA and CAS
- Several reports have documented a significant number of microemboli during CAS
- However cognitive function studies failed to show clear superiority of CEA over CAS

Conclusions III

- Cognitive function is being increasingly recognized as an important outcome measure that affects patient’s well-being and functional status
- Cognitive Tests should be included in all carotid studies.
- The long-term effect of BMT, CEA and CAS on cognitive function needs evaluation in large groups of patients.