Will guidelines and clinical practice for asymptomatic stenosis change in the near future?

M Storck, MD, PhD
Director Dept. Vascular and Thoracic Surgery
Klinikum Karlsruhe
Academic Teaching Hospital, University of Freiburg
Germany
Disclosure

Speaker name:  
M. Storck, MD, PhD

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

X I do not have any potential conflict of interest
Guideline updates

• Guideline recommendations are generally based on scientific evidence
• Best evidence is created by RCT’s and metaanalyses
• For asymptomatic carotid stenosis, RCT’s are still ongoing (ACST II, CREST II, other)
• Until these trials are not finished, no new level I evidence will be available
Clinical practise

- Is not only based on guidelines
- Large registries can provide valuable information and influence clinical practice
- For asymptomatic stenosis, the role of BMT is increasing
- The improved selection of patients will be the key issue in the (near) future
5year Results ACT-1: Survival and Freedom from stroke

Planned: n= 1658
Included: n= 1453

Sample size not reached due to slow enrollment…

Stent noninferior?

Comment from the editor of the NEJM:

What has not been resolved, however, is the issue of the generalizability of randomized-trial findings into routine clinical practice, and, more importantly, the vexed question of how best to treat the asymptomatic patient. No one should harbor any illusions that ACT I and CREST have resolved the latter issue.
### Study characteristics and endpoints of RCTs investigating long-term results of CAS vs. CEA in asymptomatic carotid artery stenosis

<table>
<thead>
<tr>
<th>Characteristics of trials</th>
<th>SAPPHIRE</th>
<th>CAVATAS</th>
<th>CREST</th>
<th>Brooks (Lexington II)</th>
<th>ACT-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total randomized</td>
<td>334</td>
<td>505</td>
<td>2502</td>
<td>189</td>
<td>1453</td>
</tr>
<tr>
<td></td>
<td>symptomatic (28,7%) asymptomatic (71,3%)</td>
<td>symptomatic (90%) asymptomatic (10%)</td>
<td>symptomatic (52,4%) asymptomatic (47,6%)</td>
<td>symptomatic (55%) asymptomatic (45%)</td>
<td>symptomatic (0%) asymptomatic (100%)</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>CAS</td>
<td>CEA</td>
<td>overall</td>
<td>CAS</td>
<td>CEA</td>
</tr>
<tr>
<td></td>
<td>14,4%</td>
<td>29,9%</td>
<td></td>
<td>k.A.</td>
<td>k.A.</td>
</tr>
<tr>
<td>Follow-up (median, years)</td>
<td>3,0</td>
<td>5,0</td>
<td>7,4</td>
<td>10 †</td>
<td>5 †</td>
</tr>
<tr>
<td>Embolic protection device</td>
<td>95,6%</td>
<td>0,0%</td>
<td>96,1%</td>
<td>0,0%</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Study endpoints of asymptomatic study participants

<table>
<thead>
<tr>
<th>Combined endpoint (death, myocardial infarction or any stroke within 30 days or death or ipsilateral stroke between 31 and 1080 days)</th>
<th>CAS</th>
<th>CEA</th>
<th>P-value</th>
<th>CAS</th>
<th>CEA</th>
<th>P-value</th>
<th>CAS</th>
<th>CEA</th>
<th>P-value</th>
<th>CAS</th>
<th>CEA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>21,4 % 29,2% 0,27</td>
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<tr>
<td>Combined endpoint (any stroke, myocardial infarction or periprocedural death or postprocedural ipsilateral stroke)</td>
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<tr>
<td>Any stroke and periprocedural death</td>
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<tr>
<td>Any stroke -incl. periprocedural period</td>
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<tr>
<td>-only periprocedural</td>
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<tr>
<td>Any stroke after 48 months incl. periprocedural period</td>
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<tr>
<td>Ipsilateral stroke and lethal and non-lethal myocardial infarction incl. periprocedural period</td>
<td>-</td>
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<tr>
<td>Primary combined endpoint (death, any stroke or myocardial infarction within 30 days or ipsilateral stroke after 1 year)</td>
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<tr>
<td>Periprocedural death or major stroke</td>
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<tr>
<td>Periprocedural minor stroke</td>
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</tbody>
</table>
Primary endpoint and its individual components investigated in 1181 asymptomatic CREST patients

<table>
<thead>
<tr>
<th>endpoint</th>
<th>periprocedural period</th>
<th>4-year period (incl. periprocedural period)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAS</td>
<td>CEA</td>
</tr>
<tr>
<td></td>
<td>no. of patients (%±SE)</td>
<td>percentage points</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic patients</td>
<td>7 (1,2±0,4)</td>
<td>13 (2,2±0,6)</td>
</tr>
<tr>
<td>Any periprocedural stroke or postprocedural ipsilateral stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic patients</td>
<td>15 (2,5±0,6)</td>
<td>8 (1,4±0,5)</td>
</tr>
<tr>
<td>Any periprocedural stroke or death or postprocedural ipsilateral stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic patients</td>
<td>15 (2,5±0,6)</td>
<td>8 (1,4±0,5)</td>
</tr>
<tr>
<td>Primary endpoint (periprocedural stroke, myocardial infarction or death or ipsilateral stroke)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic patients</td>
<td>21 (3,5±0,8)</td>
<td>21 (3,6±0,8)</td>
</tr>
</tbody>
</table>
Temporal trends in CAS and CEA – Impact of clinical trials on daily practise

Hussain M et al. Stroke 2016;47:2923-2390
Temporal trends in CAS and CEA – Male vs. Female

Hussain M et al. Stroke 2016;47:2923-2390
Temporal trends in CAS and CEA – Symptomatic vs. Asymptomatic

Hussain M et al. Stroke 2016;47:2923-2390
Influence of age –
Metaanalysis of 4 RCT’s (CEA)

Age not an important factor in CEA

Carotid Stenting Trialist’s Collaboration.
The Lancet 2016; 387:1305-311
Influence of age – Metaanalysis of 4 trials (CAS)

Age dependent differences in outcome in CAS

Carotid Stenting Trialist’s Collaboration.
The Lancet 2016; 387:1305-311
Influence of procedure type and age – Peri- and postprocedural events

Figure 4: CAS versus CEA hazard ratio for events by age group and for the periprocedural and postprocedural periods
Hazard ratios (95% CIs) were adjusted by study. Events during the periprocedural period included stroke in either hemisphere plus deaths, whereas events in the postprocedural period included ipsilateral strokes only. CEA = carotid endarterectomy. CAS = carotid artery stenting.
Worldwide: CEA vs CAS over time

Medicine Baltimore 2015; Jul 94(26): e1060
CEA vs. CAS depending on continent
Carotid stenting in dialysis patients

Carotid stenting dialysis patients – does it make sense?

Fig 2. All-cause mortality after carotid artery stenting (CAS) comparing symptomatic and asymptomatic patients.

What should be considered in asymptomatic stenosis in 2017?

• Careful indication for CAS in patients > 70 years (Evidence level IA)

• Poor indication in hemodialysis patients and transplant patients (Evidence level IIB)

• Poor indication with simultaneous ACBG (Evidence level GCP)
What influences our daily practice in 2017?

• Evidence
• Experience
• Quality management
• Patient preference (?)

Cave:
Reimbursement systems
Hospital economy aspects
Definition of Best Medical Treatment in Asymptomatic and Symptomatic Carotid Artery Stenosis

Kosmas I. Paraskevas, MD, PhD, Dimitri P. Mikhailidis, MD, FFPM, FRCPath, FRCP, Frank J. Veith, MD, FACS, and J. David Spence, MD, FRCP, FAHA

Abstract
Implementation of best medical treatment (BMT) is the cornerstone of the management of patients with either asymptomatic or symptomatic carotid artery stenosis. We review the literature to define the components of BMT. Smoking cessation, maintaining a healthy body weight, moderate exercise, and a Mediterranean diet are essential lifestyle measures. Moderate alcohol consumption may also be beneficial but recommending it to patients may be hazardous if they consume too much. The importance of lifestyle measures is largely underestimated by both physicians and patients. Blood pressure and diabetes control, antiplatelet agents, and lipid-lowering treatment with statins/ezetimibe comprise the pharmacological components of BMT. Initiation of an intensive regimen of BMT is a sine qua non for patients with carotid artery stenosis whether or not they are offered or undergo an invasive revascularization procedure.

Keywords
best medical treatment, carotid stenosis, asymptomatic, symptomatic, stroke
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