Spontaneous embolisation on TCD and carotid plaque features

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I have the following potential conflicts of interest to report:

- Consulting: Amgen
- Stockholder of a healthcare company: Vascularis Inc.
- Lecture fees: BMS, Pfizer
Risk of CAS vs. CEA from 21 registries
- Asymptomatic stenosis; average risk patients

- Most patients with asymptomatic stenosis cannot benefit from intervention
- A 3% risk threshold is too high!

1. Paraskevas K et al. Eur J Vasc Endovasc Surg (2015) online, 1e-10
How can we identify the ~10-15% who might benefit from intervention?

- TCD microemboli
- Ulceration on 3D ultrasound
- Echolucency/juxtaluminal “black plaque”
- Intraplaque hemorrhage on MRI
- Plaque composition/texture on ultrasound
- Neovascularization on ultrasound
- Plaque inflammation on PET/CT
- Plaque roughness on ultrasound

TCD microembolus detection

319 ACS patients between 2000 and 2004
10% had microemboli

1-year Stroke Risk
No Emboli  Emboli
1% 15.6
95% CI (1.01 -1.36) (4.1-79)
p<0.0001

Stroke risk over 2 years by baseline microembolic status

Survival free of stroke

Days to event

Spence JD et al. Stroke 2005;36:2373-2378
Emboli decline with medical therapy

<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>Year 1</th>
<th></th>
<th></th>
<th>Year 2</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TCD−</td>
<td>TCD+</td>
<td>P</td>
<td>TCD−</td>
<td>TCD+</td>
</tr>
<tr>
<td>Emboli at Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Event, n (%)</td>
<td></td>
<td>287</td>
<td>32</td>
<td>P</td>
<td>205</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emboli at follow-up</td>
<td></td>
<td>4</td>
<td>11</td>
<td>&lt;0.0001</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4%</td>
<td><strong>34.4%</strong></td>
<td></td>
<td>1.0%</td>
<td><strong>9.4%</strong></td>
</tr>
</tbody>
</table>

Spence JD et al. Stroke 2005;36:2373-2378
Decline of microemboli with more intensive medical therapy

< 5% can now benefit from intervention based on microemboli

Kaplan-Meier Survival free of stroke, death, MI

logrank test p<0.0001

Microemboli predict risk despite intensive medical therapy

Paraskevas K, Veith F, Spence JD. SVN 2018;3: e000129
Asymptomatic carotid emboli study (ACES)

Risk is lower with repeated TCD embolus detection, but still greater than the risk of intervention
Ulceration vs. microemboli in ACS

Madani A, ...Spence JD. Neurology 2011;77:744–750
Ulceration vs microemboli in ACS

- Almost no overlap – only 1 patient had both ulcers and emboli
- So ulceration adds another ~ 5% to those who could benefit
Juxtaluminal “black plaque”
The Future

Imaging vulnerable plaque
CAIN Project 2
Histological validation of preoperative imaging of vulnerable plaque in patients scheduled for carotid endarterectomy

3D US ulceration

Plaque composition by MRI and 3D US

3D US plaque roughness

3D histology

Plaque inflammation by PET/CT
Plaque inflammation on PET/CT correlates with inflammation on histology.

CD 45 staining correlates with FDG uptake: $R = 0.88$, $p < 0.001$

Cocker M, Spence JD et al. Intl J Cardiol 2018;271: 378-386
Plaque inflammation on PET/CT by time since event

Cocker M, Spence JD et al. Intl J Cardiol 2018;271: 378-386
Plaque composition by MRI

Clarke SE et al. Stroke 2006;37:93-97
Intraplaque hemorrhage on MRI

N=91
37% had intraplaque hemorrhage
2 strokes, 4 TIA’s all with IPH
HR=3.59;
95% CI 2.48, 4.71; P=.001
### Carotid Plaque Features in Patients with and without Symptoms

<table>
<thead>
<tr>
<th>Variable</th>
<th>Symptomatic Group ( n = 35 )</th>
<th>Asymptomatic Group ( n = 69 )</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque thickness (mm)*</td>
<td>2.86 ± 0.96</td>
<td>3.00 ± 0.88</td>
<td>.45</td>
</tr>
<tr>
<td>Plaque ulceration</td>
<td>8 (23)</td>
<td>11 (16)</td>
<td>.43</td>
</tr>
<tr>
<td>Plaque echogenicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft</td>
<td>26 (74)</td>
<td>26 (38)</td>
<td>.001</td>
</tr>
<tr>
<td>Hard</td>
<td>2 (6)</td>
<td>6 (9)</td>
<td>.71</td>
</tr>
<tr>
<td>Calcified</td>
<td>2 (6)</td>
<td>9 (13)</td>
<td>.33</td>
</tr>
<tr>
<td>Mixed</td>
<td>5 (14)</td>
<td>28 (40)</td>
<td>.007</td>
</tr>
<tr>
<td>Contrast enhancement</td>
<td>28 (80)</td>
<td>21 (30)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Enhanced intensity in plaque (dB)*</td>
<td>13.9 ± 6.4</td>
<td>8.8 ± 5.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Ratio*†</td>
<td>0.54 ± 0.23</td>
<td>0.33 ± 0.19</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*\( P \) values are based on statistical significance between groups.

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Plaque neovascularularity/vasa vasorum

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- Xiong L et al. Radiology 2009; 251: 583-9
Some of these will overlap

• So maybe 10-15% of patients with ACS could benefit from intervention
• Still work to be done
• Without such evidence of high risk, ACS patients should not be subjected to intervention