Carotid Stenosis - selecting the high risk patients for intervention

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Declaration of Interest

No conflicts of interests
Identifying people with asymptomatic carotid stenosis at higher risk of stroke

A novel clinical risk score

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University of Oxford
Carotid Artery Disease

- Important cause of ischaemic stroke (15-20%)
- Most (80%) carotid strokes have no warning symptoms
- Asymptomatic stenosis: important long-term stroke risk
- RCTs confirm Net benefit of CEA among asymptomatic patients
- Successful CEA ~halves long-term stroke risk
## Trial Characteristics

<table>
<thead>
<tr>
<th></th>
<th>VA</th>
<th>ACAS</th>
<th>ACST-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>444</td>
<td>1 662</td>
<td>3 120</td>
</tr>
<tr>
<td>Region</td>
<td>USA</td>
<td>USA</td>
<td>Europe</td>
</tr>
<tr>
<td>Follow-up, Median [IQR]</td>
<td>5.7 [4.5-7.0]</td>
<td>4.8 [3.7-5.0]</td>
<td><strong>9.0 [6.1-11.1]</strong></td>
</tr>
</tbody>
</table>

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CEA for Asymptomatic Carotid Stenosis: VA, ACAS, ACST-1 Trials

2291 Patients on triple therapy (ie, including statin) before stroke

A. Any stroke or perioperative death

B. Any non-perioperative stroke
Purpose of this Study

There is uncertainty as to which asymptomatic patients benefit most from carotid intervention

**AIM:** to develop a simple clinical risk score to identify patients with high risk asymptomatic carotid stenosis
Methods

• IPD of ‘medically treated’ patients from all 3 asymptomatic trials
  • VA (1/6 of total)
  • ACAS (1/3)
  • ACST-1 (1/2)

• Restricted to those with no CEA prior to stroke (ie, medically managed)

• Stroke risk ratios (RR) from Cox regression

• Most important factors then included in risk score (RR >1.3)
# Association of CV Risk Factors with Stroke (amongst medically managed)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Events / Person-years</th>
<th>Stroke RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of Diabetes</td>
<td>87/2433</td>
<td>1.32 (1.03-1.68)</td>
</tr>
<tr>
<td>Male Sex</td>
<td>260/8631</td>
<td>1.23 (0.97-1.55)</td>
</tr>
<tr>
<td>Total Cholesterol (per 2 mmol/L)</td>
<td>* 316/11665</td>
<td>1.16 (0.95-1.40)</td>
</tr>
<tr>
<td>Older Age (per 10 years)</td>
<td>* 365/13184</td>
<td>1.15 (1.00-1.33)</td>
</tr>
<tr>
<td>Systolic Blood Pressure (per 20 mmHg)</td>
<td>* 364/13147</td>
<td>1.09 (0.98-1.21)</td>
</tr>
<tr>
<td>History of Ischaemic Heart Disease</td>
<td>137/4625</td>
<td>1.03 (0.83-1.27)</td>
</tr>
</tbody>
</table>

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## 3 Important Stroke Risk Factors

<table>
<thead>
<tr>
<th>Events / Person-years</th>
<th>At Risk</th>
<th>Reference</th>
<th>Stroke RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain Infarct on Imaging</td>
<td>93/2435</td>
<td>158/6301</td>
<td>1.57 (1.21-2.03)</td>
</tr>
<tr>
<td>Prior Contralateral Event</td>
<td>133/3497</td>
<td>232/9687</td>
<td>1.57 (1.26-1.94)</td>
</tr>
<tr>
<td>History of Diabetes</td>
<td>87/2433</td>
<td>278/10751</td>
<td>1.32 (1.03-1.68)</td>
</tr>
</tbody>
</table>

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## Summative Risk Score

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes only</td>
<td>1</td>
</tr>
<tr>
<td>Prior cerebral ischaemia* only</td>
<td>2</td>
</tr>
<tr>
<td>Both</td>
<td>3</td>
</tr>
</tbody>
</table>

*Prior contralateral symptoms or brain infarct on imaging*
# Risk Prediction

## Risk Factors

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Participants</th>
<th>Events / Person-years</th>
<th>Stroke RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1597</td>
<td>78/4230</td>
<td>1.00 (0.80-1.25)</td>
</tr>
<tr>
<td>Diabetes Only</td>
<td>438</td>
<td>28/929</td>
<td>1.54 (1.06-2.24)</td>
</tr>
<tr>
<td>Prior Cerebral Ischaemia Only*</td>
<td>1145</td>
<td>113/2881</td>
<td>2.15 (1.79-2.59)</td>
</tr>
<tr>
<td>Both</td>
<td>328</td>
<td>32/697</td>
<td>2.39 (1.69-3.39)</td>
</tr>
</tbody>
</table>

*Prior contralateral symptoms or brain infarct on imaging
Risk Prediction

If the 10-year stroke risk is:

9% (no risk factors)  
10y Absolute gain from CEA ~5%

13%* (diabetes)  
10y Absolute gain from CEA ~7%

20% (prior ischaemia)  
10y Absolute gain from CEA ~10%

(1/3 of trial participants)

*Stroke risk of ACST-1 participants taking statin, BP and antithrombotic treatment

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Implications

- **Statins work:** With CEA or without CEA, modern statin ~halves stroke risk
- **And CEA works:** With a statin or without a statin, successful CEA ~halves stroke risk
- Risk of stroke ~**double with prior cerebral ischaemia**
- Those with **higher risk scores** should **derive greater absolute benefit** from CEA
Conclusion

Simple characteristics (ie, diabetes, prior ischaemia) can be used to identify high stroke risk patients who might benefit most from CEA (or be considered for ACST-2, comparing CEA vs CAS)
Acknowledgements

ACST, ACAS, VA Trialists and to the participants who took part

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- Volodos (innovation) and Janet Powell (evidence) Lectures
- Main Scientific Sessions with invited speakers, state of the art short talks, the top abstract and quick-fire presenters