Impact of CREST 2 on CEA&CAS in Asx CS Patients: Predictions for the Future

“Garbage In...Garbage Out”

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Disclosure Statement of Financial Interest
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>Grant/Research Support</td>
<td>Canon Med</td>
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<tr>
<td>Consulting Fees/Honoraria</td>
<td>None</td>
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<td>Boston Scientific, Ocular, Silk Road, Imperative Care, Cerebrotech, Medtronic, Endovascular, Ventriclus</td>
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<td>Royalty Income</td>
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<td>Ownership/Founder</td>
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<td>Intellectual Property Rights</td>
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<td>Other Financial Benefit</td>
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69 yo M sent by PCP for elevated dopplers on screening. Asymptomatic.
Doppler 276 systolic, MRI negative for DWI hits
Afib on Eliquis, HTN, DM, HLD, aortic aneurysm post stenting now on plavix.
This is a common problem without a clear answer.

To treat or not?
Randomize or not?

75 YO Asymptomatic WM
PMD heard a bruit on right Doppler 250
CT Normal
HTN controlled with meds
This is a common problem without a clear answer.

To treat or not?
Randomize or not?

CREST 1 Refresher (2010 Brott et al)
- 2502 patients followed x 2.5 years.
- Conclusion: Primary composite endpoint did not differ between CAS and CEA for symptomatic or asymptomatic patients.
- Periprocedural minor stroke higher w/ CAS, and peri-procedural MI higher w/ CEA.

CREST 2 TRIAL, In a nutshell.
- RCT (multicenter double arm) comparing:
  - 21st century intensive medical therapy to CAS or CEA w/ intensive therapy
  - Asymptomatic patients harboring >70% stenosis.
  - December 2020 completion date, 2480 participants.
  - Primary outcome: stroke or death at 44 days to 4 years.
  - Secondary outcomes: cognitive outcomes, major stroke differences, and effect modification base on age, sex, severity, risk level, duration of asymptomatic period.
We have learned much about Carotid disease
Perhaps the most studied disease & treatment in the world

Remember the Cerebral Bypass Trial!

- That was “Garbage In, Garbage Out”
- We randomized the patients with mild stenosis
- We bypassed the patients with severe disease
- The result...
  - “No Benefit”
  - No reimbursement!!
  - The end of a good operation!!
  - All we really learned was who did not benefit from bypass

Important for treatment decisions...
What defines Asymptomatic status?

Asymptomatic in CREST II
- No DWI hits
- No TIA or symptoms of stroke in the last 180 days

Findings not considered symptomatic:
- Micro embolic HIT counts positive on TCD
- Cognitive decline
- Plaque morphology
- US, MRI
- Vascular reserve
- % stenosis

Medicare Impact of Crest 2

CREST 2 will likely change policy on reimbursement if favorable

Future Predictions: CREST2 results for CAS

1. CREST 2 will likely change Medicare reimbursement for asymptomatic CAS if positive.
2. CREST 2 cognitive outcomes may change the way we define asymptomatic.
3. Positive trial... Number of carotid stents for asymptomatic disease will likely increase
   - In the UK 62% drop in CEA for asymptomatic disease between 2011-2017 possibly due to changing attitudes toward asymptomatic disease.
4. We will be a step closer to determining the “asymptomatic” high stroke risk patients who may benefit from revascularization from those who will not. (micro emboli, plaque morphology, vascular reserve, stenosis rate etc).
5. We will know finally how good best medical therapy (21st century) is in compliant patients

A negative result for CEA may have a huge impact for asymptomatic patients


Gupta et al., What is the future of asymptomatic carotid artery disease?, American College of Cardiology, 2015

A negative result for CEA may have a huge impact for asymptomatic patients