The SAMMPRIS Trial: Implications for Cerebral and Carotid Trial Design and Patient Management

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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>Toshiba</td>
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<tr>
<td>Consulting Fees/Honoraria</td>
<td>Boston Scientific, Cordis, Abbott Vascular, Silk Road</td>
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<tr>
<td>Major Stock Shareholder/Equity</td>
<td>Boston Scientific, AccessClosure, Valor Medical, Claret Medical, Augmenix, Ocular Therapeutics, Ostial Corp</td>
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<td>Board/Trustee/Officer Position</td>
<td>AccessClosure, Claret Medical</td>
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<td><strong>Speakers Bureau</strong></td>
<td>Abbott Vascular</td>
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<tr>
<td>Honorarium</td>
<td>Boston Scientific, Cordis, Memorial Healthcare System, Complete Conference Management, SCAI, Cleveland Clinic</td>
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Major findings:
1. Higher than expected 30 day stroke rate in the stent + medical therapy arm (14.7%)
2. Lower than expected 30 day stroke rate in the medical therapy alone arm (5.8%).

• Beyond 30 days, the rates of stroke in the territory of the stenotic artery were similar in the two groups, but fewer than half the patients had been followed for 1 year

SAMMPRIS Conclusions

Based on SAMMPRIS results:

1. Medical therapy was more effective than anticipated *(earlier WASID data which showed recurrent stroke risk of 18% per year when taking aspirin alone)*

2. Intracranial stenting was less effective and more risky than anticipated *(based on earlier registries which demonstrated lower complication risk)*

3. **Conclusion:** patients with intracranial stenosis should be treated with medical therapy alone and should not be stented

**SAAMPRIS stopped intracranial stenting**
Stent Arm Complications

Mostly Technical

- Most major complications were hemorrhagic
- Of the 33 strokes in the angioplasty/stenting group, the majority of the strokes (n=25) occurred within 1 day of the procedure
- Reminiscent of the CAS trials …
Timing of Stroke After Carotid Revascularization: CAS vs. CEA

\[ P = 0.0008^{**} \]

- Day 0: CAS > CEA
- Day 1-7: CAS > CEA
- Day 8-30: CAS > CEA

Circulation 2012;126:3054-3061
Lessons from CAS Trials
Technology and Experience Matters!

Experience
SAMMRPIS required that 20 intracranial procedures had to be submitted. However, experience with other stent systems, angioplasty alone or even stent-assisted coiling of aneurysms was ok.

Medication COMPLIANCE
Medical arm lifestyle compliance coach every two weeks

Lessons from CAS:
Operator experience is critical in reducing periprocedural complications

*Example: CREST*
Outcomes of CAS Trials Over Time

- CAS results have vastly improved over time due to: (1) more experienced operators; (2) better patient selection and; (3) a wider spectrum of technology
- CAS outcomes have evolved over time similarly to CEA

(Enrollment: 2000-2008) CREST – 5.7%

(Enrollment: 2000-2008) CREST – 1.1%
Death or Major Stroke Rates in CAS Decrease for Symptomatic Patients

- 2.5% (2000-2004, N=160)
- 3.6% (2005, N=111)
- 0.8% (2006, N=131)
- 0.0% (2007, N=120)
- 0.0% (2008, N=77)

50% Symptomatic Patients Enrollment March 2006
Negative Results of Trials Have Taught Us Much

“Mistakes are the portals of discovery”

<table>
<thead>
<tr>
<th>CAS EXPERIENCE is Critical</th>
<th>ICAD</th>
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<tbody>
<tr>
<td>Learning who NOT to stent</td>
<td>Experience counts</td>
</tr>
<tr>
<td>Improved technique</td>
<td>Do not stent “Hot Plaques”</td>
</tr>
<tr>
<td>Strokes peri procedure</td>
<td>Submaximal angioplasty</td>
</tr>
<tr>
<td>Minor stroke resolve</td>
<td>Med compliance important</td>
</tr>
<tr>
<td></td>
<td>Wingspan stent 1st gen</td>
</tr>
<tr>
<td></td>
<td>Gateway balloon semi compliant</td>
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Our Alternate Approaches

Phase I Trial

Q: submaximal angioplasty alone (instead of stenting) provide safer results?

*Technique: Balloon is undersized to 50-75% of the nominal diameter of the vessel*

**Advantages:**
- Lower risk (vessel injury, embolization)
- Unlike intracranial stenting, no need for long-term dual antiplatelet therapy

**Disadvantages:**
- High rate of restenosis
- 3 month f/u... stent if severe restenosis
Submaximal Balloon Angioplasty

M1 stenosis

angioplasty

final result
## Summary of Submaximal Angioplasty Results at Different US Centers

<table>
<thead>
<tr>
<th>author/year</th>
<th>n</th>
<th>30 day stroke/death</th>
</tr>
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<tbody>
<tr>
<td>SAMMPRIS (stenting arm), 2011</td>
<td>224</td>
<td>33 (14.7%)</td>
</tr>
<tr>
<td>SAMMPRIS (medical arm), 2011</td>
<td>227</td>
<td>13 (5.8%)</td>
</tr>
<tr>
<td>Marks, 2006</td>
<td>120</td>
<td>6 (5.0%)</td>
</tr>
<tr>
<td>Nguyen, 2011</td>
<td>59</td>
<td>3 (5.0%)</td>
</tr>
<tr>
<td>UB experience , 2007-2011 (unpublished)</td>
<td>42</td>
<td>2 (4.8%)</td>
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Retrospective
Submaximal Angioplasty for Symptomatic Intracranial Atherosclerosis: A Phase 1 Trial

T Dumont, M Mokin, G Sorkin, K Snyder, A Siddiqui, E Levy, L Hopkins

• Ongoing prospective registry
• Preliminary results presented at the Congress of Neurological Surgeons Annual Meeting 2013

Demographics:
• 17 patients, 11 men, 6 women
• Mean age 66 yrs ± 11 yrs (range 48-80yrs)
• 12 white, 5 African-American
Procedure

- **Stenosis pre-angioplasty**
  - Mean 79% (range 70-86%)

- **Stenosis post-angioplasty**
  - Mean 52% (range 32-69%)
  - Mean reduction of stenosis
    - 34% ± 13%
  - Theoretical increase in flow by 200-400%
Outcomes: Perioperative

- No complications
- 1 Perioperative event (CASE 10)
  - TIA related to prolonged inflation of balloon in MCA
    - Symptoms resolved within minutes after deflation and removal of balloon
    - No permanent deficit
- Angioplasty is SAFE
Outcomes: Follow-up

• Two TIAs
  - Case 09: 36 days postop
  - Case 12: 126 days postop

• ZERO stroke in 86 months of follow-up among all 17 patients
Conclusion From Preliminary Results:

- Submaximal angioplasty is SAFE
- Efficacy in stroke prevention remains unclear
- Goal: Prospective study comparing best medical management to submaximal angioplasty
  - Ideal to select patients with matching perfusion deficit
Future Directions in Treatment of ICAD - Yet to be Determined

- Initial angioplasty and delayed stent prn
- Improve medical therapies (new agents)
- Different stent design (closed vs. open cell, balloon mounted stent …)
- Improve patients selection – CT perfusion, MRI plaque study