

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

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Disclosure Statement of Financial Interest

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Affiliation/Financial Relationship

- Grant/Research Support
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- Major Stock Shareholder/Equity

- Board/Trustee/Officer Position
- **Speakers Bureau**
- Honorarium

Company

Toshiba

Boston Scientific, Cordis, Abbott Vascular, Silk Road

Boston Scientific, AccessClosure, Valor Medical, Claret Medical, Augmenix, Ocular Therapeutics, Ostial Corp

AccessClosure, Claret Medical

Abbott Vascular

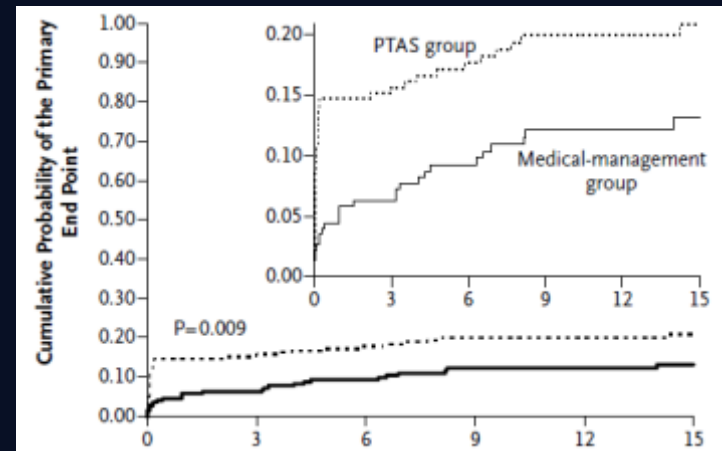
Boston Scientific, Cordis, Memorial Healthcare System, Complete Conference Management, SCAI, Cleveland Clinic



Stenting & Aggressive Medical Management for
Preventing Recurrent stroke in Intracranial Stenosis

SAMMPRIS

— on NIH-funded, multi-center clinical trial —



N Engl J Med, 2011. **365**(11)

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

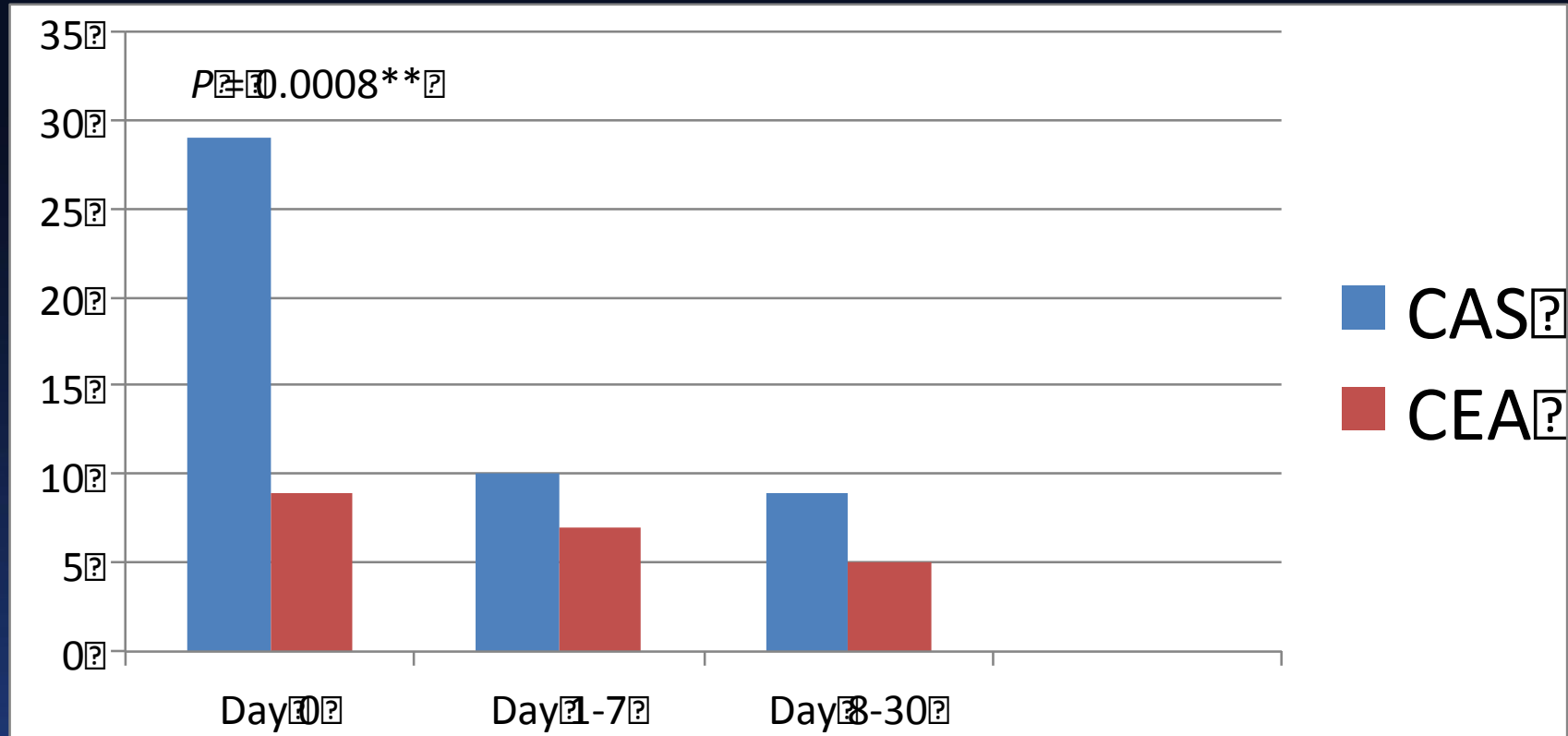
SAAMPRIS stopped intracranial stenting

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



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**

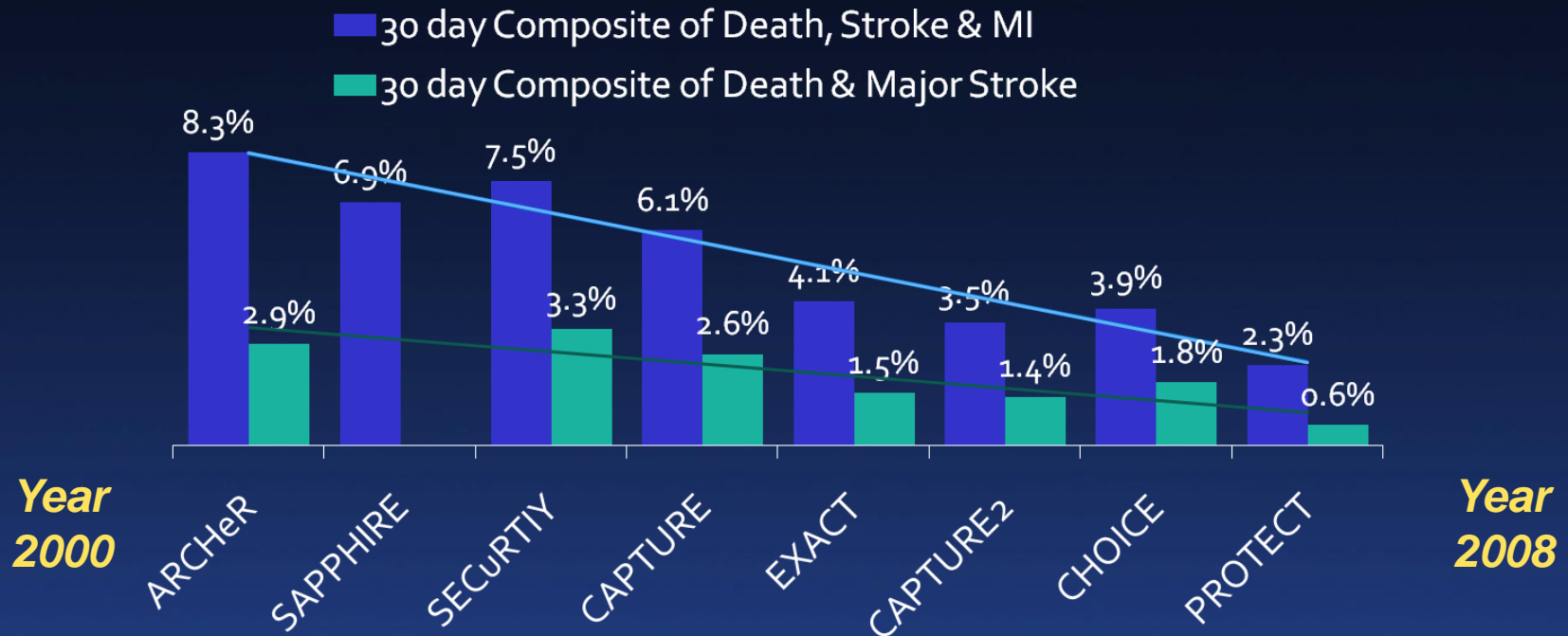
Lessons from CAS:

Operator experience is critical in reducing periprocedural complications

Example: CREST

Outcomes of CAS Trials Over Time

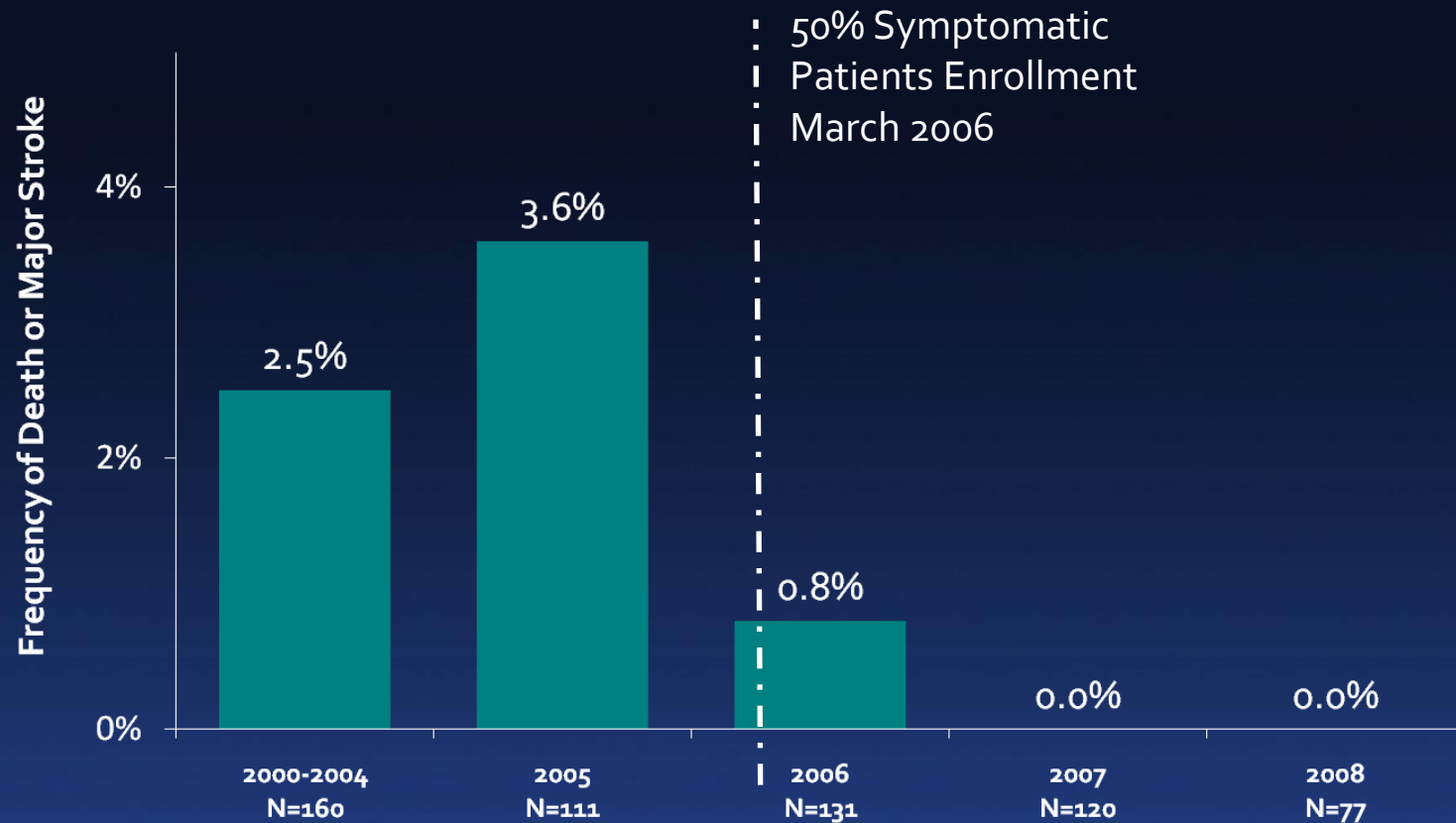
- CAS results have vastly improved over time due to: (1) more experienced operators; (2) better patient selection and; (3) a wider spectrum of technology
- CAS outcomes have evolved over time similarly to CEA



(Enrollment: 2000-2008) CREST – 5.7%

(Enrollment: 2000-2008) CREST – 1.1%

Death or Major Stroke Rates in CAS Decrease for Symptomatic Patients



Negative Results of Trials Have Taught Us Much

“Mistakes are the portals of discovery”

CAS

CAS EXPERIENCE is Critical

- Learning who NOT to stent
- Improved technique
- Strokes peri procedure
- Minor stroke resolve

ICAD

- Experience counts
- Do not stent “Hot Plaques”
- Submaximal angioplasty
- Med compliance important
- Wingspan stent 1st gen
- Gateway balloon semi compliant

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

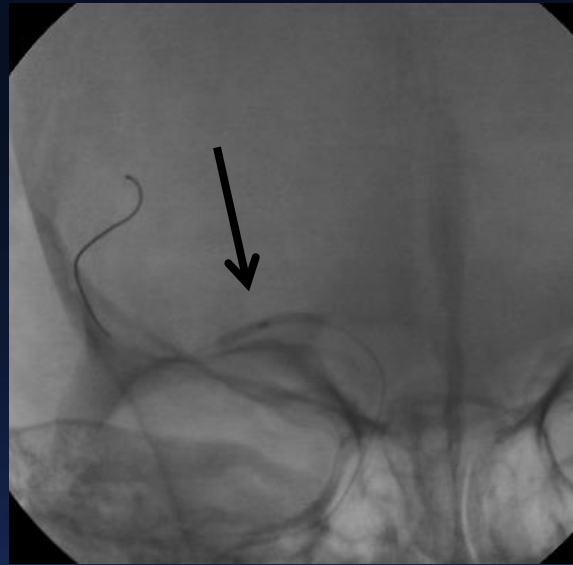
Disadvantages:

- 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

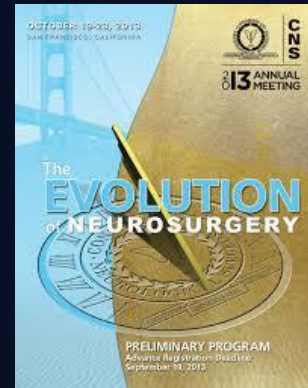
author/year	n	30 day stroke/death
SAMMPRIS (stenting arm), 2011	224	33 (14.7%)
SAMMPRIS (medical arm), 2011	227	13 (5.8%)
Marks, 2006	120	6 (5.0%)
Nguyen, 2011	59	3 (5.0%)
UB experience , 2007-2011 (unpublished)	42	2 (4.8%)



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*

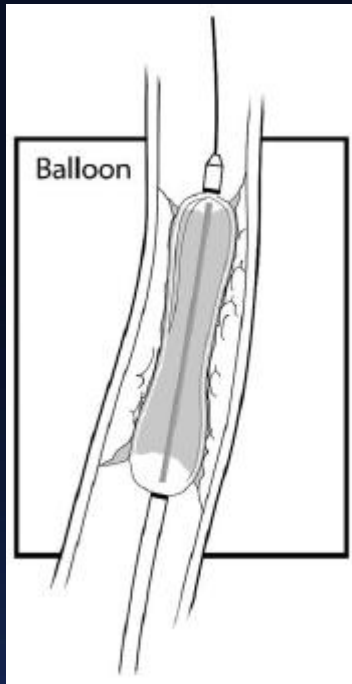


- Ongoing prospective registry
- Preliminary results presented at the Congress of Neurological Surgeons Annual Meeting 2013

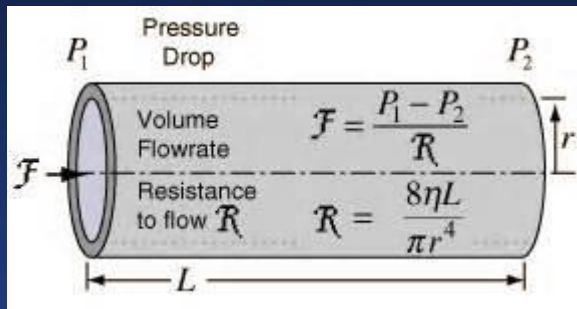
Demographics:

- 17 patients, 11 men, 6 women
- Mean age 66 yrs \pm 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
 - $34\% \pm 13\%$
 - 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

