Published in final edited form as:

Stroke. 2015 November ; 46(11): 3282–3284. doi:10.1161/STROKEAHA.115.009846.

Does SAMMPRIS Support Stenting Over Medical Therapy for Subpopulations of Patients with Intracranial Arterial Stenosis?

Helmi L. Lutsep, MD,

Oregon Health & Science Univ

Michael J. Lynn, MS,

Emory Univ Rollins Sch of Public Health

George A. Cotsonis, MA,

Emory Univ Rollins Sch of Public Health

Colin P. Derdeyn, MD,

Washington Univ Sch of Med

Tanya N. Turan, MD,

Medical Univ of South Carolina

David Fiorella, MD, PhD,

State Univ of New York

L. Scott Janis, PhD,

Natl Inst of Health

Bethany F. Lane, RN,

Emory Univ Rollins Sch of Public Health

Jean Montgomery, RN, and

Emory Univ Rollins Sch of Public Health

Marc I. Chimowitz, MB, ChB

Medical Univ of South Carolina

for the SAMMPRIS Investigators

Abstract

Background and Purpose—While the SAMMPRIS trial showed that medical therapy alone was superior to stenting plus medical therapy for preventing recurrent strokes in patients with symptomatic intracranial stenosis, we determined whether SAMMPRIS supported the use of stenting in any subpopulations of patients with symptomatic intracranial arterial stenosis.

Helmi L. Lutsep, MD, Oregon Stroke Center, Oregon Health & Science University, 3181 SW Sam Jackson Park Rd, CR131, Portland, OR 97239, lutsep@ohsu.edu, Phone: 503-494-7225, Fax: 503-494-4690.

Disclosures: George Cotsonis, Michael Lynn, Tanya Turan, Colin Derdeyn, David Fiorella and Marc Chimowitz received grant support from SAMMPRIS.

L. Scott Janis is the Program Director, NINDS.

Helmi Lutsep, Bethany Lane and Jean Montgomery have no disclosures.

Clinical Trial Registration: URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT00576693.

Methods—The primary outcome, 30-day stroke and death and later strokes in the territory of the qualifying artery, was compared in those with and without baseline factors in the two treatment arms, percutaneous transluminal angioplasty and stenting (PTAS) plus aggressive medical therapy (AMM) vs. AMM alone. Baseline factors included gender, age, race, diabetes, hypertension, lipid disorder, smoking status, type of qualifying event, qualifying event hypoperfusion symptoms, use of antithrombotic or proton pump inhibitor at baseline, days to enrollment, old infarcts in the same territory, percent stenosis, other artery stenosis and location of the symptomatic artery.

Results—A total of 451 patients were enrolled, 227 randomized to AMM and 224 to PTAS. Of all variables evaluated, the observed 2-year event rates were higher with PTAS than with AMM in the vast majority and the interaction with treatment was not statistically significant for any of the factors.

Conclusions—The SAMMPRIS results do not provide evidence to support the use of PTAS using the Wingspan stent system compared to medical treatment in any examined subpopulation of patients with symptomatic intracranial stenosis, including those with qualifying event hypoperfusion symptoms.

Keywords

Intracranial stenosis; angioplasty and stenting; ischemic stroke

The Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis (SAMMPRIS) trial has shown that patients with a transient ischemic attack (TIA) or stroke within 30 days prior to enrollment that was attributed to 70-99% stenosis of a major intracranial artery had greater benefit from Aggressive Medical Management alone (AMM) than with Percutaneous Transluminal Angioplasty and Stenting with the Wingspan stent plus Aggressive Medical Management (PTAS) (1,2). The current study determined whether there were subpopulations of patients with symptomatic intracranial arterial stenosis in whom SAMMPRIS did support the use of PTAS compared to AMM alone.

Methods

The study design for the SAMMPRIS trial has been published previously (3). AMM included antiplatelet therapy with clopidogrel 75 mg per day for 90 days and aspirin 325 mg per day indefinitely, careful risk factor management and a lifestyle modification program (3). Stenting was performed using the Wingspan stent system and patients treated with PTAS received the same AMM. All patients gave written informed consent to participate and institutional review boards at all 50 participating sites in the USA approved the study protocol.

The primary outcome, 30-day stroke and death and later strokes in the territory of the qualifying artery, was compared in those with and without baseline factors in the two treatment arms, PTAS plus AMM versus AMM alone. Baseline factors are provided in the table. Qualifying event (QE) hypoperfusion symptoms were defined as related to either change in position, effort on exertion or recent change in antihypertensive. Seven of these subgroups indicated by * had been pre-specified.

The subgroup analyses were conducted by fitting a Cox proportional hazards regression model that included treatment, treatment by time to primary endpoint interaction (included because the proportional hazards assumption was not met for the treatments), the factor, and the treatment by factor interaction. P-values are reported for the treatment by factor interaction and p-values < 0.05 would indicate that the effect of treatment was different across the levels of the factor. Since the analysis results are intended to be exploratory, no adjustment was made for multiple subgroup comparisons. Kaplan-Meier estimates of the event rates by treatment at two years after randomization are reported for each of the factor levels.

Results

Of 451 patients enrolled in SAMMPRIS, 227 were randomized to AMM and 224 to PTAS. The observed 2-year event rates were higher with PTAS than with AMM in the vast majority of variables evaluated and the interaction with treatment was not statistically significant for any of the factors (table).

Discussion

The results showed no differential effect of treatment with PTAS or AMM in any subgroup of patients with intracranial stenosis compared with the patients overall.

Previous studies have shown higher stroke recurrence rates in certain patient groups on medical treatment, such as those with a higher degree of stenosis and earlier time to enrollment (4) or patients with clinical hemodynamic characteristics (5). Such risk groups did not show benefit with stenting in the current study. In the 14% (31/227) of patients in the current study that had QE hypoperfusion symptoms in the AMM group, the 2-year probability of an outcome event was only 7.0%.

While none of the baseline variables studied reached statistical significance for a treatment interaction, there was less of a numerical difference in the outcome between PTAS and AMM in some subgroups. These were patients with QE hypoperfusion symptoms, blacks, those without a lipid disorder, smokers and those with an old infarct in the territory of the stenotic vessel.

Limitations of the current study included its post- hoc nature and the small number of patients in some subgroups because SAMMPRIS did not reach its enrollment goal. These limitations raise the possibility of Type I or Type II errors for some subgroups (i.e., erroneously concluding that there are differences in outcome between the two treatment arms or failing to identify a subgroup that benefits from medical therapy or stenting).

Given the results of this analysis and the fact that SAMMPRIS was stopped primarily for safety, there currently is no evidence to support the use of the Wingspan stent system in any group of patients with intracranial stenosis. The results continue to support the use of AMM in all examined subpopulations of patients with symptomatic intracranial stenosis.

Acknowledgments

Sources of Funding: SAMMPRIS is funded by the National Institute of Neurological Disorders and Stroke (NINDS) U01 NS058728. Stryker Neurovascular provided study devices and supplemental funding for third party device distribution, site monitoring and study auditing and AstraZeneca donated rosuvastatin (Crestor) to study patients in the SAMMPRIS trial.

References

1. Chimowitz MI, Lynn MJ, Derdeyn CP, Turan TN, Fiorella D, Lane BF, et al. the SAMMPRIS Trial Investigators. Stenting versus aggressive medical therapy for intracranial arterial stenosis. *N Engl J Med*. 2011; 365:993–1003. [PubMed: 21899409]
2. Derdeyn CP, Chimowitz MI, Lynn MJ, Fiorella D, Turan TN, Janis LS, et al. Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis Trial Investigators. *Lancet*. 2014; 383:333–41. [PubMed: 24168957]
3. Turan TN, Lynn MJ, Nizam A, Lane B, Egan BM, Le NA, et al. Rationale, design, and implementation of aggressive risk factor management in the Stenting and Aggressive Medical Management for Prevention of Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial. *Circ Cardiovasc Qual Outcomes*. 2012; 5:e51–60. [PubMed: 22991350]
4. Kasner SE, Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, et al. Predictors of ischemic stroke in the territory of a symptomatic intracranial stenosis. *Circulation*. 113:555–563. 2—6. [PubMed: 16432056]
5. Mazighi M, Tanasescu R, Ducrocq X, Vicaut E, Bracard S, Houdart E, et al. Prospective study of symptomatic atherothrombotic intracranial stenosis: The GESICA Study. *Neurology*. 2006; 66:1187–1191. [PubMed: 16636236]

Observed 2-year event rate probabilities in the aggressive medical management and percutaneous transluminal angioplasty and stenting treatment groups for each of the variables

Factor	n Medical	2 Year Probability	n PTAS	2 Year Probability	p-value
* Age (years)					
<60	119	11.9% (7.2,19.2)	107	15.9% (10.2,24.4)	0.7429
60	108	16.5% (10.6,25.2)	117	24.8% (18.0,33.7)	
* Gender					
Male	145	10.7% (6.6,17.1)	127	18.2% (12.5,26.1)	0.4044
Female	82	20.1% (12.8,30.8)	97	23.7% (16.4,33.5)	
Race					
White	162	13.3% (8.8,19.6)	160	16.4% (0.9,29.2)	0.2152
Black	49	19.0% (10.3,33.3)	55	20.5% (11.9,34.0)	
Hypertension					
No	24	17.4% (6.9,39.9)	24	20.8% (9.2,43.0)	0.6168
Yes	203	13.7% (9.6,19.3)	200	20.6% (15.6,26.9)	
Lipid Disorder					
No	25	28.9% (14.9,51.3)	29	27.6% (14.9,47.7)	0.0843
Yes	202	12.2% (8.4,17.7)	195	19.5% (14.6,25.9)	
Diabetes					
No	124	10.6% (6.3,17.6)	119	14.3% (9.1,22.0)	0.9123
Yes	103	18.3% (11.9,27.4)	105	27.7% (20.2,37.4)	
Smoking					
Smoker	149	14.7% (9.8,21.6)	133	14.3% (9.4,21.5)	0.0678
Non-Smoker	78	13.0% (7.2,22.8)	90	30.1% (21.7,40.7)	
* Symptomatic artery					
Internal carotid	49	23.2% (13.6,38.0)	45	29.0% (18.0,44.7)	0.6266
Middle cerebral	105	12.8% (7.6,21.1)	92	14.2% (8.5,23.2)	
Vertebral	22	9.5% (2.5,33.0)	38	21.1% (11.1,37.7)	
Basilar	51	9.9% (4.3,22.2)	49	24.5% (14.7,39.1)	
Symptomatic artery					
Anterior	154	16.1% (11.1,23.1)	137	19.1% (13.4,26.8)	0.2392
Posterior	73	9.8% (4.8,19.4)	87	27.0% (18.8,37.9)	
Percent stenosis					
<80%	154	12.0% (7.7,18.3)	160	20.0% (14.6,27.1)	0.2624
80%	71	19.2% (11.6,30.7)	64	23.0% (15.5,33.3)	
* QE					
TIA	75	7.0% (3.0,15.9)	82	20.7% (13.4,31.2)	0.1206
Stroke	152	17.5% (12.3,24.7)	142	20.5% (14.7,28.2)	
* Days to Enrollment					
7	115	13.4% (8.3,21.2)	115	22.7% (16.0,31.5)	0.5524
>7	112	14.7% (9.3,22.9)	109	18.4% (12.3,27.1)	
* Old infarct in					
No	186	9.9% (6.3,15.2)	185	17.3% (12.6,23.6)	0.2082

Factor	n Medical	2 Year Probability	n PTAS	2 Year Probability	p-value
territory	36	34.7% (21.4,53.0)	30	33.3% (19.5,53.1)	
* Antithrombotic	87	11.6% (6.4,20.6)	80	18.8% (11.8,29.2)	0.6821
at QE	140	15.6% (10.5,22.9)	144	21.6% (15.7,29.30)	
Proton pump	191	12.9% (8.9,18.7)	192	20.4% (15.3,26.8)	0.5619
Inhibitor at QE	36	20.1% (10.1,37.7)	32	21.9% (11.1,40.5)	
QE	196	15.1% (10.8,21.0)	206	21.9% (16.8,28.2)	0.5780
Hypoperfusion symptoms	31	7.0% (1.8,25.3)	18	5.6% (0.8,33.4)	
symptoms					

* Indicates subgroup that had been prespecified. Qualifying event=QE; PTAS=percutaneous transluminal angioplasty and stenting; TIA=transient ischemic attack