ORIGINAL ARTICLE

Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis

Marc I. Chimowitz, M.B., Ch.B., Michael J. Lynn, M.S., Colin P. Derdeyn, M.D., Tanya N. Turan, M.D., David Fiorella, M.D., Ph.D., Bethany F. Lane, R.N., L. Scott Janis, Ph.D., Helmi L. Lutsep, M.D., Stanley L. Barnwell, M.D., Ph.D., Michael F. Waters, M.D., Ph.D., Brian L. Hoh, M.D., J. Maurice Hourihane, M.D., Elad I. Levy, M.D., Andrei V. Alexandrov, M.D., Mark R. Harrigan, M.D., David Chiu, M.D., Richard P. Klucznik, M.D., Joni M. Clark, M.D., Cameron G. McDougall, M.D., Mark D. Johnson, M.D., G. Lee Pride, Jr., M.D., Michel T. Torbey, M.D., M.P.H., Osama O. Zaidat, M.D., Zoran Rumboldt, M.D., and Harry J. Cloft, M.D., Ph.D., for the SAMMPRIS Trial Investigators*

ABSTRACT

BACKGROUND

Atherosclerotic intracranial arterial stenosis is an important cause of stroke that is increasingly being treated with percutaneous transluminal angioplasty and stenting (PTAS) to prevent recurrent stroke. However, PTAS has not been compared with medical management in a randomized trial.

METHODS

We randomly assigned patients who had a recent transient ischemic attack or stroke attributed to stenosis of 70 to 99% of the diameter of a major intracranial artery to aggressive medical management alone or aggressive medical management plus PTAS with the use of the Wingspan stent system. The primary end point was stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or stroke in the territory of the qualifying artery beyond 30 days.

RESULTS

Enrollment was stopped after 451 patients underwent randomization, because the 30-day rate of stroke or death was 14.7% in the PTAS group (nonfatal stroke, 12.5%; fatal stroke, 2.2%) and 5.8% in the medical-management group (nonfatal stroke, 5.3%; non–stroke-related death, 0.4%) (P=0.002). Beyond 30 days, stroke in the same territory occurred in 13 patients in each group. Currently, the mean duration of follow-up, which is ongoing, is 11.9 months. The probability of the occurrence of a primary end-point event over time differed significantly between the two treatment groups (P=0.009), with 1-year rates of the primary end point of 20.0% in the PTAS group and 12.2% in the medical-management group.

CONCLUSIONS

In patients with intracranial arterial stenosis, aggressive medical management was superior to PTAS with the use of the Wingspan stent system, both because the risk of early stroke after PTAS was high and because the risk of stroke with aggressive medical therapy alone was lower than expected. (Funded by the National Institute of Neurological Disorders and Stroke and others; SAMMPRIS ClinicalTrials.gov number, NCT00576693.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Chimowitz at the Medical University of South Carolina Stroke Program, 19 Hagood Ave., Harborview Office Tower, Suite 501, Charleston, SC 29425, or at mchimow@musc.edu.

*The investigators in the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial are listed in the Supplementary Appendix, available at NEJM.org.

This article (10.1056/NEJMoa1105335) was published on September 7, 2011, at NEJM.org.

N Engl J Med 2011;365:993-1003.
Copyright © 2011 Massachusetts Medical Society.

The New England Journal of Medicine
Downloaded from nejm.org at EMORY UNIVERSITY on December 5, 2011. For personal use only. No other uses without permission.
Copyright © 2011 Massachusetts Medical Society. All rights reserved.

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Medical-Management Group (N=227)	PTAS Group (N=224)
Age — yr	59.5±11.8	61.0±10.7
Male sex — no. (%)	145 (63.9)	127 (56.7)
Race — no. (%)†		
Black	50 (22.0)	55 (24.6)
White	161 (70.9)	160 (71.4)
Other	16 (7.0)	9 (4.0)
Hypertension — no. (%)	203 (89.4)	201 (89.7)
Diabetes — no. (%)	103 (45.4)	106 (47.3)
Lipid disorder — no. (%)	203 (89.4)	194 (86.6)
Smoking history — no./total no. (%)		
Never	78/227 (34.4)	90/223 (40.4)
Former	80/227 (35.2)	79/223 (35.4)
Current	69/227 (30.4)	54/223 (24.2)
History of coronary artery disease — no. (%)	59 (26.0)	47 (21.0)
History of stroke other than qualifying event — no. (%)	58 (25.6)	60 (26.8)
Qualifying event — no. (%)		
Stroke	152 (67.0)	142 (63.4)
TIA	75 (33.0)	82 (36.6)
Already receiving antithrombotic therapy at time of qualifying event — no. (%)	141 (62.1)	145 (64.7)
Time from qualifying event to randomization — days		
Median	7	7
Interquartile range	4–19	4–16
Symptomatic qualifying artery — no. (%)		
Internal carotid	49 (21.6)	45 (20.1)
Middle cerebral	105 (46.3)	92 (41.1)
Vertebral	22 (9.7)	38 (17.0)
Basilar	51 (22.5)	49 (21.9)
Stenosis of symptomatic qualifying artery‡		
Mean percentage stenosis	81±7	80±7
Distribution — no./total no. (%)		
70–79% stenosis	102/227 (44.9)	107/223 (48.0)
80–89% stenosis	97/227 (42.7)	92/223 (41.3)
90–99% stenosis	28/227 (12.3)	24/223 (10.8)

* Plus–minus values are means ±SD. Baseline characteristics of the two groups were compared with the use of either an independent groups t-test (for means) or a chi-square test (for percentages). None of the characteristics differed significantly between the groups (P>0.05 for all comparisons). PTAS denotes percutaneous transluminal angioplasty and stenting.

† Race was self-reported.

‡ Stenosis was quantified on the basis of a reading of the angiogram by the site interventionist.

The New England Journal of Medicine
Downloaded from nejm.org at EMORY UNIVERSITY on December 5, 2011. For personal use only. No other uses without permission.
Copyright © 2011 Massachusetts Medical Society. All rights reserved.

Table 2. Measures of Risk Factors at Baseline and 4 Months.*

Variable	Medical-Management Group (N=227)		PTAS Group (N=224)	
	Baseline	4 Mo	Baseline	4 Mo
Clinical factor				
Blood pressure				
No. of patients evaluated	227	179	220	173
Systolic — mm Hg	146.8±21.8	134.8±17.0	143.9±20.6	133.1±15.9
Diastolic — mm Hg†	82.3±12.0	77.3±10.0	77.9±10.7	76.2±9.7
Lipids‡				
No. of patients evaluated	226	175	219	174
LDL cholesterol — mg/dl	97.7±36.6	72.8±26.0	96.3±38.5	75.9±40.9
HDL cholesterol — mg/dl	38.8±10.1	41.9±11.4	37.8±10.6	43.2±13.3
Non-HDL cholesterol — mg/dl	116.6±40.3	90.9±30.8	116.6±43.9	94.3±50.2
Glycated hemoglobin in patients with diabetes§				
No. of patients evaluated	98	47	102	50
Level of glycated hemoglobin — %	8.3±2.3	7.5±2.0	7.9±2.1	7.8±2.4
Body-mass index¶				
No. of patients evaluated	227	180	224	170
Value	30.7±6.3	30.4±6.4	30.3±6.2	30.0±6.2
Lifestyle factor				
No. of patients evaluated	227	181	223	173
Current smoker — %	30.4	20.4	24.2	17.3
Moderate or vigorous exercise — %‖	29.1	56.6	34.2	56.1

* Plus–minus values are means ±SD. Risk-factor measures in both groups at 30 days and at 1 year are provided in Table 2 in the Supplementary Appendix. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586. PTAS denotes percutaneous transluminal angioplasty and stenting.

† The difference in diastolic blood pressure at baseline between the two groups is significant (P<0.001).

‡ Lipid levels at baseline and 4 months were measured at the Central Lipid Laboratory, with low-density lipoprotein (LDL) cholesterol levels measured directly. Non–high-density lipoprotein (non-HDL) cholesterol is total cholesterol minus HDL cholesterol, or the sum of LDL cholesterol and very-low-density lipoprotein cholesterol.

§ Levels shown are baseline and 6-month levels, rather than baseline and 4-month levels (the protocol did not require levels to be measured at 4 months). Diabetes was defined according to the 2010 criteria of the American Diabetes Association.

¶ The body-mass index is the weight in kilograms divided by the square of the height in meters.

‖ Moderate or vigorous exercise was defined as a score on the Physician-based Assessment and Counseling for Exercise (PACE) evaluation of 4 to 8, with 4 indicating vigorous exercise less than three times per week or moderate exercise less than five times per week and 8 indicating vigorous exercise at least 3 days a week for at least the previous 6 months. Examples of moderate exercise include brisk walking, gardening, and slow cycling for at least 10 minutes; examples of vigorous exercise include jogging, running, and fast cycling for at least 20 minutes. A total of 182 patients were included in the medical-management group at 4 months.

major hemorrhage were significantly higher in the PTAS group than in the medical-management group. The difference between the two groups in the rate of death or any stroke (16.3% vs. 23.2%) was not significant (P=0.06).

DISCUSSION

Contrary to what we hypothesized, the results of this trial showed that aggressive medical therapy was superior to PTAS with the use of the Wing-

The New England Journal of Medicine
Downloaded from nejm.org at EMORY UNIVERSITY on December 5, 2011. For personal use only. No other uses without permission.
Copyright © 2011 Massachusetts Medical Society. All rights reserved.