



# **Detailed Analysis of Periprocedural Strokes in Patients Undergoing Intracranial Stenting in Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS)**

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## Detailed Analysis of Peri-Procedural Strokes in Patients Undergoing Intracranial Stenting in SAMMPRIS

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## Abstract

**Background and Purpose**—Enrollment in the SAMMPRIS trial was halted due to the high risk of stroke or death within 30 days of enrollment in the percutaneous transluminal angioplasty and stenting (PTAS) arm relative to the medical arm. This analysis focuses on the patient and procedural factors that may have been associated with peri-procedural cerebrovascular events in the trial.

**Methods**—Bivariate and multivariate analyses were performed to evaluate whether patient and procedural variables were associated with cerebral ischemic or hemorrhagic events occurring within 30 days of enrollment (termed peri-procedural) in the PTAS arm.

**Results**—Of 224 patients randomized to PTAS, 213 underwent angioplasty alone (n=5) or with stenting (n=208). Of these, 13 had hemorrhagic strokes (7 parenchymal, 6 subarachnoid), 19 had ischemic stroke, and 2 had cerebral infarcts with temporary signs (CITS) within the peri-procedural period. Ischemic events were categorized as perforator occlusions (13), embolic (4), mixed perforator and embolic (2), and delayed stent occlusion (2). Multivariate analyses showed that higher percent stenosis, lower modified Rankin score, and clopidogrel load associated with an activated clotting time above the target range were associated ( $p < 0.05$ ) with hemorrhagic stroke. Non-smoking, basilar artery stenosis, diabetes, and older age were associated ( $p < 0.05$ ) with ischemic events.

**Conclusions**—Peri-procedural strokes in SAMMPRIS had multiple causes with the most common being perforator occlusion. Although risk factors for peri-procedural strokes could be identified, excluding patients with these features from undergoing PTAS to lower the procedural risk would limit PTAS to a small subset of patients. Moreover, given the small number of events, the present data should be used for hypothesis generation rather than to guide patient selection in clinical practice.

## Keywords

Intracranial stenosis; angioplasty and stenting; clinical trial

## Introduction

Enrollment in the Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial was stopped due to the high rate of stroke and death within 30 days of enrollment in the stenting arm compared to the medical arm<sup>1</sup>. In this paper, we report the technical outcomes after PTAS in the trial, the types of peri-procedural strokes that occurred, and a detailed analysis of the patient, lesion, and procedural characteristics that may have been associated with peri-procedural cerebral ischemic and hemorrhagic events.

## Methods

### Study Design and Patient Population

SAMMPRIS is an investigator-initiated, randomized, clinical trial funded by the National Institute of Neurological Disorders and Stroke that is being conducted at 50 sites in the United States<sup>1, 2</sup>. Medical treatment and follow up of enrolled patients will continue until March 2013. Details of the study design have been published previously<sup>1, 2</sup>. Eligible patients had TIA or non-disabling stroke within 30 days prior to enrollment attributed to angiographically-verified 70% to 99% stenosis of a major intracranial artery.

### PTAS Procedure

PTAS in the trial was performed with the Gateway PTA Balloon Catheter and Wingspan Stent System (both manufactured by Boston Scientific Corporation). Details of the PTAS procedure, post-procedure care, and aggressive medical management (same in both arms of the trial) have already been published<sup>2</sup>. Patients randomized to PTAS were required to undergo the procedure within three business days of randomization. Patients not on daily clopidogrel (75 mg) for five days prior to PTAS were given a 600 mg loading dose between 6 – 24 hours before PTAS. IV heparin was administered during PTAS to achieve an activated clotting time (ACT) of between 250 and 300 seconds.

### Follow-up and Assessment of Outcome

Patients were evaluated at study entry, four days (by study coordinator), 30 days after enrollment, and continue to be seen every four months. If a peri-procedural stroke was suspected, the patient was examined by a study neurologist and brain imaging was typically performed. All potential study endpoints were adjudicated centrally as described previously<sup>1,2</sup>

Ischemic stroke was defined as a new focal neurological deficit of sudden onset, lasting at least 24 hours that was not associated with a hemorrhage on brain CT or MRI. Cerebral infarct with temporary signs (CITS) was defined as a new infarct on brain imaging associated with neurological signs that lasted < 24 hours. Symptomatic hemorrhagic stroke was defined as parenchymal, subarachnoid, or intraventricular hemorrhage detected by CT or MRI that was associated with new neurological signs or symptoms lasting ≥ 24 hours or a seizure. Hemorrhagic stroke associated with symptoms or signs (but no seizure) that lasted < 24 hrs was defined as an asymptomatic hemorrhagic stroke.

### Subtype Classification of Events

All peri-procedural (within 30 days after randomization) ischemic strokes, CITS and hemorrhagic strokes were categorized by consensus of the three primary investigators (DF, CD, MC) based on an assessment of the available imaging and clinical data. Hemorrhagic strokes were classified as subarachnoid hemorrhages (SAH) when the bleeding was predominantly subarachnoid and the presentations were evident immediately after the procedure, or as reperfusion hemorrhages when the bleeding was predominantly intraparenchymal (ICH) and within the vascular distribution of the stented vessel. Ischemic strokes were categorized as perforator occlusions if the infarct(s) could be localized to the distribution supplied by perforating vessels arising within the margins of the stent, or embolic if the infarct was in a territorial distribution distal to the treated lesion. When more than one mechanism contributed to the clinical findings, the stroke was described as mixed. Delayed stent occlusion was diagnosed if there was imaging or other presumptive evidence of stent occlusion.

## Statistical Methods

In the analyses of risk factors for peri-procedural events, we separated the ischemic events (stroke, CITS) from the hemorrhagic strokes. Even though CITS and asymptomatic hemorrhagic strokes were not primary endpoints, we included these events because we were primarily interested in the underlying mechanism of ischemic and hemorrhagic injury after PTAS rather than the clinical outcome.

Bivariate associations between patient, lesion, and procedural factors and ischemic and hemorrhagic events were assessed using Fisher's exact test (for categorical factors) and the independent groups t-test or Wilcoxon rank-sum test (for continuous factors). Stepwise logistic regression analysis was done to relate the occurrence of an endpoint to multiple clinical factors. Factors were included as candidates for inclusion in the model if the p-value for the bivariate association with the endpoint was  $< 0.2$ . The p-value for inclusion or removal from the model was 0.05. The Hosmer-Lemeshow goodness of fit test was used to assess the fit of the model. No adjustments were made for multiple comparisons. All analyses were done in SAS 9.2.

## RESULTS

### Technical Results of PTAS

Of the 224 patients randomized to PTAS, four patients declined the procedure after randomization. The procedure was initiated in the other 220 patients a median of 9 days after the qualifying event (range 1 – 34 days). In these 220 cases, general anesthesia was performed in 217 (98.6%) and the ACT was maintained between 250–300 seconds throughout the procedure in 101 of 206 cases (49.0%) in which ACT was measured. The procedures were aborted in six cases without attempting PTAS owing to factors identified on angiography at the time of the planned procedure (interval occlusion of artery (n=3), resolution of stenosis to  $< 50\%$  (n=1), incidental adjacent aneurysm (n=1), or dissection rather than atherosclerosis (n=1)). In another case, attempts to cross the lesion with a wire were unsuccessful. On a per patient basis (excluding the six patients that PTAS was not attempted and two patients in whom stenting was performed without pre-dilation), an angioplasty balloon was successfully positioned across the lesion and inflated in 211 of 212 patients (99.5%). Stents were positioned and deployed across the lesion in 208 of 214 patients (97.2%) in whom PTAS was attempted (i.e., 5 patients had angioplasty alone, 1 lesion could not be crossed).

Of the 213 procedures in which angioplasty alone or stenting was done, the number of balloons used for pre-dilation were one in 187 cases (87.8%), two in 23 cases (10.8%); three in one case, and none in two cases. Of the 226 stents introduced into a guiding catheter, 208 (92.0%) were successfully navigated across the lesion and deployed. Post-stenting balloon dilation was performed in 21 of 208 (10.1%) patients who had a stent placed. Stent success (i.e., the lesion was accessed and a stent was placed across the stenosis resulting in less than 50% residual stenosis by local reading) was achieved in 197 of 214 patients (92.0%) in whom PTAS was attempted. Procedural success (i.e., placement of the last stent used with less than 50% stenosis at the end of the procedure and without stroke or death within 24 hours of the procedure) was achieved in 174 of 214 patients (81.3%). The mean percent stenosis at the various stages of the PTAS procedures was 79.7% pre-PTAS, 40.2% post-angioplasty, and 27.0% at the end of the procedure.

### Types of Peri-Procedural Strokes

A total of 33 peri-procedural strokes (14.7%) occurred among the 224 patients assigned to the PTAS arm. Ten were hemorrhagic and 23 ischemic. Three of the ischemic strokes

occurred in patients in whom PTAS was not done because of findings on angiography at the time of the planned PTAS procedure. One occurred immediately after an angiogram that showed the stenosis had decreased to < 50%. Two others occurred in patients whose previously stenotic artery had progressed to complete occlusion. Both had strokes in the territory of the occluded artery – one at three days and one at four days after angiography. Since PTAS was not performed in these patients, these events were omitted from the risk factor analysis. One stroke that was adjudicated as ischemic in the primary paper<sup>1</sup> was the result of intentional coil occlusion of an artery that had been perforated by a wire during the procedure. In this analysis, this event was counted as a hemorrhage yielding 19 ischemic strokes and 11 symptomatic hemorrhagic strokes.

The 19 peri-procedural ischemic strokes were classified as predominantly perforator occlusions in 12, embolic in three, mixed perforator and embolic in two, and delayed stent occlusion in two. The two strokes associated with stent occlusion occurred four and six days after the procedures and both were large ipsilateral hemisphere strokes. In addition to these ischemic strokes, there were two CITS – one perforator occlusion and one embolic.

Of the 11 symptomatic hemorrhagic strokes, six were parenchymal brain hemorrhages (ICH) and five were subarachnoid hemorrhages (SAH). Of the six ICHs, one was evident immediately after the procedure and five were noted when neurological signs developed 4 hours after PTAS. All ICHs were distributed within the vascular territory of the treated artery. Of the six ICHs, four were fatal, one resulted in a modified Rankin score (mRS) of 5, and one resulted in a mRS of 2 at 90 days. Of the five SAHs, all were recognized during or immediately after the procedure, none were fatal, and the resulting mRSs at 90 days were 0, 2, 3, 4 and 5 respectively.

In addition to the 11 symptomatic hemorrhagic strokes, one patient with transient post-operative nausea had a cerebellar ICH on CT (categorized as an asymptomatic reperfusion hemorrhage). A second patient had two syncopal events after angioplasty that prompted a CT demonstrating SAH. By definition, these two hemorrhages were considered asymptomatic and, together with the symptomatic hemorrhages, comprised 13 hemorrhagic strokes. Of the 34 events (21 ischemic events, 13 hemorrhagic strokes), 33 (97%) occurred within six days of PTAS and one CITS occurred three weeks later.

### **Risk Factors for Peri-Procedural Hemorrhagic Stroke**

The data for all variables evaluated in the bivariate analyses for an association with hemorrhagic stroke (n=13) are provided in tables A and B in the on-line appendix. Tables 1 and 2 show those factors that were associated with a  $p < 0.2$  in the bivariate analyses. A stepwise logistic regression analysis involved 201 patients, including all 13 patients with hemorrhagic strokes (12 patients were excluded from the analysis because of missing data). Three factors were associated with hemorrhagic stroke in the multivariate analysis: higher percent stenosis, low modified Rankin score (0 vs 1–3), and clopidogrel load associated with intraprocedural ACTs > 300 seconds. Table 3 shows the adjusted results from the model with the odds ratio for hemorrhagic stroke for these 3 significant variables. The model did not have a significant lack of fit ( $p = 0.42$ ).

Bivariate analyses for the reperfusion hemorrhages alone (n = 7) showed that mean percent stenosis was higher in patients with hemorrhages ( $86.3 \pm 5.6\%$  vs  $79.5 \pm 6.7\%$ ,  $p = 0.009$ ) and that patients with a loading dose of clopidogrel associated with high ACTs were at higher risk ( $4/43=9.3\%$  vs  $3/165 = 1.8\%$ ,  $p = 0.03$ ). All seven reperfusion hemorrhages occurred after PTAS of lesions with both 80% stenosis and diameter at the site of stenosis of <0.6 mm. Bivariate analyses for the SAHs alone (n = 6) showed that higher mean percent

stenosis immediately pre-PTAS ( $86.5 \pm 8.3\%$  with SAH vs.  $79.5 \pm 6.6\%$  without SAH;  $p=0.01$ ) was a risk factor.

### Risk Factors for Peri-Procedural Ischemic Events

The data for all variables evaluated in the bivariate analyses for an association with ischemic stroke or CITS ( $n=21$ ) are provided in tables A and B in the on-line appendix. Tables 4–5 show those factors that were associated with a  $p < 0.2$  in the bivariate analyses. Of note, patients with basilar stenosis had a 20.8% rate of ischemic events versus 6.7% for other arteries ( $p = 0.01$ ). Smoking status was a highly significant variable ( $p = 0.002$ ), with higher rates of ischemic events amongst never-smokers (18.1%) than former smokers and current smokers (4.7%). Patients with qualifying events of TIA (8.9%) or non-perforator stroke on baseline imaging (14.3 %) had higher rates of ischemic events than patients with a perforator stroke on baseline imaging (0%;  $p = 0.01$ ).

A stepwise logistic regression analysis relating clinical factors to the occurrence of an ischemic event included 198 patients among whom there were 19 events (15 patients were excluded from the multivariate analysis because of missing data, 2 of whom had a stroke or CITS). The factors associated with an increased risk of an ischemic event in the multivariate analysis were never smoked, basilar stenosis, diabetes, and older age. Table 6 shows the adjusted results from the model with the odds ratio for ischemic events for these significant variables. The model did not have a significant lack of fit ( $p = 0.23$ ).

Bivariate analyses for ischemic events involving perforator territories ( $n = 15$ ; 12 perforator strokes, 2 mixed perforator /embolism, 1 CITS) showed that older age ( $p=0.03$ ), never smoked ( $p=0.01$ ), old infarcts on baseline imaging ( $p=0.03$ ), and basilar stenosis ( $p=0.007$ ) were associated with an increased risk of perforator infarcts post-PTAS. Of 48 patients with basilar artery stenosis, 8 (16.7%) had a perforator infarct post-PTAS. No relationship was found between qualifying event type (TIA vs. acute perforator territory infarct vs. acute non-perforator territory infarct on baseline imaging) and perforator infarct post-PTAS. Of 45 patients who had an acute infarct in a perforator territory on baseline imaging, none (0%) had a new perforator territory infarct after PTAS.

### Time from Qualifying Event and Peri-procedural Stroke

The time between the qualifying event and PTAS had no impact on the risk of a hemorrhagic event ( $p=0.26$ ). In the six patients with SAH, the times from qualifying event to PTAS were 4, 9, 11, 22, 24 and 27 days. In the 7 patients with ICH, the times from qualifying event to PTAS were 3, 5, 6, 8, 20, 26, and 32 days. No relationship was found either between the proximity of PTAS to the qualifying event and the risk of an ischemic event (see table B in appendix). The rates of ischemic stroke, symptomatic hemorrhagic stroke, or any death at 30 days were 15.7% in the PTAS arm and 7% in the medical arm in patients enrolled within 7 days of their qualifying event ( $p=0.02$ ), and were 13.8% in the PTAS arm and 4.5% in the medical arm ( $p=0.14$ ) in patients enrolled beyond 7 days of their qualifying event.

### Discussion

SAMMPRIS provides the only large prospective cohort of patients undergoing PTAS for symptomatic intracranial atherosclerosis by credentialed interventionists at multiple sites with all potential endpoints evaluated by site neurologists and central blinded adjudicators. As such, the trial provides unique data to evaluate the technical success of PTAS, as well as the causes and risk factors for the cerebrovascular complications of PTAS.

Use of the Wingspan system in SAMMPRIS was associated with high rates of technical success confirming previous reports that the system is sufficiently flexible and of a low enough profile to allow for reliable intracranial navigation and deployment by experienced operators<sup>3-5</sup>. Peri-procedural strokes in SAMMPRIS had multiple causes with perforator occlusion being by far the most common cause of ischemic stroke and hemorrhagic stroke nearly evenly divided between SAH and reperfusion hemorrhage.

Peri-procedural ischemic events were associated with never smoked, basilar stenosis, diabetes, and older age. Smokers had dramatically lower peri-procedural ischemic events in SAMMPRIS than non-smokers. This “smokers paradox”, which has also been observed after coronary interventions<sup>6-10</sup>, may be related to the fact that non-smokers in SAMMPRIS were more likely to be female, diabetic, and hypertensive, which may have increased their risk of peri-procedural stroke compared to smokers. . Additionally, smokers tend to be more responsive to clopidogrel than non-smokers because smoking induces the hepatic cytochrome p450 system that is involved in the conversion of clopidogrel to its active metabolite<sup>11-13</sup>. This “smokers paradox” may, in part, account for the lower risk of peri-procedural stroke following PTAS that has been reported in regions of the world where smoking is more prevalent<sup>14-16</sup>.

Occlusion of perforators was the most common cause of ischemic events after PTAS, especially after basilar PTAS, as reported previously<sup>3</sup>. This may be the result of atherosclerotic debris being displaced or “snow-plowed” over the perforator origins during angioplasty or stent deployment. Of note, however, is that the perforator-rich MCA was associated with the lowest rate of peri-procedural ischemic stroke of all arteries stented in the trial (see Table A in on-line appendix). Advanced techniques such as high resolution MR imaging of the arterial wall may be useful to identify plaque features that could lead to better selection of patients for intracranial PTAS<sup>17,18</sup>. Importantly, SAMMPRIS showed no relationship between perforator stroke presentation and the risk of perforator stroke post-PTAS, i.e., including patients with perforator stroke presentations in SAMMPRIS does not explain the high peri-procedural stroke rate in the trial, as has been suggested previously<sup>19</sup>.

Hemorrhagic strokes were associated with higher percent stenosis, low modified Rankin score, and clopidogrel load associated with high intra-procedural ACTs. Higher percent stenoses, especially in vessels with small diameters, are typically more difficult to cross with a microwire, conceivably with a higher risk of perforation. In addition, these higher grade stenoses may also be associated with more severe hemodynamic impairment, which could increase the risk of reperfusion hemorrhage when flow is restored. A higher risk of hemorrhagic stroke with a clopidogrel load and high ACTs is not surprising and attests to the challenge of balancing the risk of thrombosis and hemorrhage during the procedure. Meticulous attention to keeping the ACT range in target throughout the procedure is important but is difficult as illustrated by the fact that this was only achieved in about half the patients undergoing PTAS. The association between low modified Rankin score and hemorrhagic stroke post-PTAS is difficult to explain and could be a type I error.

The original Wingspan HDE pilot study<sup>20</sup> did not allow stenting within seven days of a qualifying stroke presumably because of concerns about reperfusion hemorrhage, however, it has been suggested that stenting may offer the highest benefit in patients as soon as possible after a TIA or stroke<sup>19</sup>. We found no relationship between time from qualifying event to PTAS and the risks of peri-procedural ischemic events or hemorrhagic stroke. Additionally, the benefit of medical therapy over PTAS at 30 days after enrollment was similar in patients enrolled within 7 days of their qualifying event compared with patients enrolled beyond 7 days. As such, these data do not suggest that a 2–3 week “waiting period”



after the qualifying event would have benefitted those patients in the stenting arm of SAMMPRIS.

Although SAMMPRIS is the largest available prospective series of intracranial PTAS to date, the overall number of events is still relatively small. Correspondingly, it is possible that significant relationships between patient and procedural variables and the risk of peri-procedural stroke could have been missed or underestimated (Type II error). Another consequence of the small number of events is that the factors identified in the regression modeling are sensitive to small changes in the data. Given the large number of analyses performed, it is also possible that some of the significant relationships between individual variables and procedural outcomes could be false positives (Type I error). Also, as evidenced by the wide confidence intervals, the estimates for the odds ratios are imprecise. As such, these data should be used for hypothesis generation only.

In summary, peri-procedural strokes in SAMMPRIS encompassed all putative mechanisms of angioplasty and stenting complications. While we identified some factors associated with an increased risk of peri-procedural stroke, these factors are highly prevalent in the SAMMPRIS population (see tables A and B in the on-line appendix). Therefore, excluding patients with high-risk features from undergoing PTAS to lower the risk of peri-procedural stroke would limit the procedure to a very small subset of patients with intracranial stenosis. Moreover, given the limitations of the present analysis, particularly the small number of events, the results should be viewed with caution and not utilized as the basis for clinical treatment without further confirmatory studies.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1**

Continuous Baseline Factors versus the Occurrence of Hemorrhagic Stroke

Factor	Patients without Event		Patients with Event		p-value*
	n	Statistic	n	Statistic	
Percent arterial stenosis (%) – mean ± sd	200	79.3 ± 6.6	13	86.4 ± 6.6	0.0002
Diameter of artery at site of stenosis (mm) – median (IQR)	199	0.6 (0.4 – 0.8)	13	0.4 (0.3 – 0.5)	0.001
Balloon diameter (mm) – median (IQR)	198	2.5 (2.0 – 3.0)	13	2.0 (2.0 – 2.5)	0.09
Baseline HDL (mg/dl) – median (IQR)	197	35.6 (30.2 – 42.8)	13	30.9 (27.4 – 38.7)	0.19

\* The p-value for the independent groups t test comparing means or the Wilcoxon rank sum test comparing medians.

IQR = interquartile range

**Table 2**

Categorical Baseline Factors versus the Occurrence of Hemorrhagic Stroke

Factor	n	Patients with Event n (%)	p-value*
Modified Rankin score			
0	80	9 (11.2%)	0.03
1 – 3	132	4 (3.0%)	
Qualifying event			
TIA	79	8 (10.1%)	0.08
Stroke	134	5 (3.7%)	
Clopidogrel loading and high ACT			
No	165	8 (4.9%)	0.15
Yes	43	5 (11.6%)	

\* The p-value for Fisher's exact test comparing the percent of patients with an event.

ACT – activated clotting time

**Table 3**

Logistic Regression Results for Hemorrhagic Stroke (n = 201)

Factor	p-value	Odds Ratio (Wald 95% CI)
Pre-angio % stenosis	0.002	(5% increase): 2.1 (1.3 – 3.4)
Modified Rankin Score	0.028	(0 vs 1–3): 4.2 (1.2 – 15.4)
Clopidogrel Load and High ACT	0.05	(Loading Done and ACT High vs Others): 3.7 (1.0 – 13.5)

ACT – activated clotting time

**Table 4**

Continuous Baseline Factors versus the Occurrence of an Ischemic Event

Factor	Patients without Event		Patients with Event		p-value*
	n	Statistic	n	Statistic	
Age (yrs) – median (IQR)	192	60.3 (53.3 – 68.7)	21	65.5 (60.5 – 74.2)	0.01
Maximum balloon pressure (atm) – median (IQR)	189	6.0 (6.0 – 8.0)	20	7.0 (6.0 – 8.0)	0.07
Length of lesion (mm) – median (IQR)	192	6.6 (5.4 – 9.0)	21	8.0 (6.0 – 10.6)	0.12
Baseline glucose (mg/dL) – median (IQR)	188	108 (95 – 137)	21	126 (99 – 148)	0.17

\* The p-value for the independent groups t test comparing means or the Wilcoxon rank sum test comparing medians.

IQR = interquartile range



**Table 5**

Categorical Baseline Factors versus the Occurrence of an Ischemic Event

Factor	N	Patients with Event n (%)	n (%) p-value *
Smoking			
Current and Former	129	6 (4.7%)	0.002
Never	83	15 (18.1%)	
Diabetes			
No	113	5 (4.4%)	0.006
Yes	100	16 (16.0%)	
Symptomatic Artery			
ICA, MCA, or VA	165	11 (6.7%)	0.01
Basilar	48	10 (20.8%)	
Qualifying Event			
TIA	79	7 (8.9%)	0.01
Non-Perforator Stroke on Baseline Imaging	84	12 (14.3%)	
Perforator Stroke on Baseline Imaging	45	0 (0.0%)	
Old Infarcts on Baseline Imaging			
No	135	8 (5.9%)	0.02
Yes	65	11 (16.9%)	
Length of Last Predilation Balloon Inflated in Artery (mm)			
9	90	6 (6.7%)	0.09
15	104	11 (10.6%)	
20	17	4 (23.5%)	
Stent Thrombosis			
No	206	19 (9.2%)	0.11
Yes	6	2 (33.3%)	
Clopidogrel Loading and High ACT			
No	165	13 (7.9%)	0.14
Yes	43	7 (16.3%)	
Gender			
Male	124	9 (7.3%)	0.16
Female	89	12 (13.5%)	
Stenosis or Occlusion of Other Intracranial Artery			
No	161	13 (8.1%)	0.18
Yes	52	8 (15.4%)	

\* The p-value for Fisher's exact test comparing the percent of patients with an event.

ICA – Internal Carotid Artery, MCA – Middle Cerebral Artery, VA – Vertebral Artery ACT – activated clotting time

**Table 6**

Logistic Regression Results for an Ischemic Event (n=198)

Factor	p-value	Odds Ratio (Wald 95% CI)
Smoking	0.0008	(Never Smoked vs Others): 8.8 (2.5 – 31.8)
Symptomatic artery	0.004	(Basilar vs Others): 6.2 (1.8 – 21.0)
Diabetes	0.02	(Yes vs No): 4.5 (1.3 – 16.1)
Age	0.03	(10 yr increase): 1.9 (1.1 – 3.5)