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Impact of Operator and Site Experience on Outcomes after Angioplasty and Stenting in the SAMMPRIS Trial

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Disclosures

Colin Derdeyn MD serves on the Executive Committee of the Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial which is funded by the National Institute of Neurological Disorders and Stroke (grant number: U01 NS058728). He is a Co-PI on the SAMMPRIS trial and receives salary support from the SAMMPRIS grant. Dr. Derdeyn also receives other grant support from the NINDS (P50 55977; R01 NS051631). He is also on the Scientific Advisory Board for W.L Gore and Associates and is the Chair of the Scientific Advisory Board for Pulse Therapeutics.

David Fiorella MD, PhD serves on the Executive Committee of the Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial which is funded by the National Institute of Neurological Disorders and Stroke (grant number: U01 NS058728). He is a Co-PI on the SAMMPRIS trial and receives salary support from the SAMMPRIS grant. Dr. Fiorella has received institutional research support from Seimens Medical and Microvention, consulting fees from Micrus - Johnson and Johnson, EV3/Covidian, Vascular Simulators, NFocus, W.L. Gore and Associates, and Microvention, and royalties from Micrus - Johnson and Johnson.

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Abstract

Background and Purpose—To investigate the relationship between physician and site experience and the risk of 30-day hemorrhagic and ischemic strokes in the stenting arm of the SAMMPRIS trial.

Methods—Study records and an investigator survey were examined for physician and site-related factors, including: number of Wingspan and aneurysm stents submitted for credentialing, number of study procedures performed in SAMMPRIS, years in practice after training, primary specialty, and site enrollment. Bivariate and multivariate analyses were performed to determine if these factors were associated with the 30-day rate of cerebrovascular events after angioplasty and stenting.

Results—Two hundred and thirteen patients underwent angioplasty alone (n=5) or angioplasty and stenting (n = 208) with study devices by 63 interventionists at 48 sites. For credentialing, the median number of Wingspan and similar aneurysm stent cases submitted by study interventionists were 10 and 6, respectively. Interventionists with higher numbers (≥ 10) of wingspan cases submitted for credentialing tended to have higher rates of 30-day events (19.0% versus 9.9%) than those with < 10 cases. High enrolling sites in the trial tended to have lower rates of hemorrhagic stroke (9.8% at sites enrolling < 12 patients versus 2.7% at sites enrolling ≥ 12 patients).

Conclusion—Interventionists credentialed with less Wingspan experience were not responsible for the high rate of peri-procedural stroke in SAMMPRIS. Hemorrhagic stroke may be related to low enrollment in the trial but not previous Wingspan experience.

Keywords

Intracranial stenosis; angioplasty and stenting; clinical trial

INTRODUCTION

Enrollment in the Stenting and Aggressive Medical Management for the Prevention of Recurrent Ischemic Stroke (SAMMPRIS) trial was stopped early, after randomization of 451 patients (planned 764), owing to the higher than expected 30-day rate of stroke or death after percutaneous transluminal angioplasty and stenting (PTAS) relative to the medical arm [1]. Of the 224 patients randomized to PTAS, 33 (14.7%) suffered a stroke within 30 days of randomization compared to 13 (5.8%) in the medical arm.

Given the higher than expected rate of stroke after PTAS in SAMMPRIS, it is important to determine if technical factors including previous experience with the Wingspan stent, training background, and the metrics chosen for the credentialing process may have contributed to the high complication rate. The purpose of the present study is to examine the relationships between factors that reflect interventionist and site experience and the risk of cerebrovascular events within 30 days (termed peri-procedural events).

METHODS

The SAMMPRIS trial is a randomized, prospective, multi-center, National Institutes of Health funded, blindly-adjudicated trial of PTAS with aggressive medical management versus aggressive medical management alone. PTAS in the trial was performed with the Gateway PTA Balloon Catheter and Wingspan Stent System (both manufactured by Boston Scientific Corporation, now Stryker Neurovascular). Details of the study design have been published, as well as the 30-day outcomes with follow up out to one year in approximately half of the enrolled subjects [1, 2]. Medical treatment and follow up of enrolled patients will continue until March 2013.

Credentialing process

Interventionists interested in participating in the trial were required to submit operative reports and documentation of short-term outcome (discharge summary or follow up clinic notes) from 20 consecutive intracranial stenting or angioplasty alone cases. If the physician had not done 20 cases with the Wingspan stent, the remainder of the 20 cases could be, in order of preference, coronary stents for intracranial atherosclerotic disease, stent-assisted coiling of brain aneurysms, and angioplasty alone for intracranial atherosclerotic disease. A minimum of three cases with the Wingspan stent was required for consideration.

The order of preference of non-Wingspan procedures was chosen based on the rationale that experience and documented success with placement of coronary balloon-expandable stents for intracranial stenosis would predict good performance with the Wingspan stent for intracranial stenosis. Allowing self-expanding stents for stent-assisted coiling of aneurysms to be included in credentialing cases was based on the fact that these stents are deployed in a similar manner to the Wingspan stent. Finally, in the uncommon scenario that an experienced interventionist did not have 20 cases of Wingspan, coronary balloon-expandable stents, or self-expanding stents for the treatment of aneurysms but had experience and success with angioplasty alone for atherosclerotic intracranial stenosis, those cases were allowed for credentialing based on familiarity with the endovascular treatment of intracranial atherosclerosis and good technique with a fundamental aspect of the study procedure.

The submitted procedure notes and outcome documents for all 20 cases for every interventionist were reviewed by members of the credentialing committee (Barnwell, Derdeyn (Chair), Dion, Fiorella, Gobin, Meyers, Zaidat, Chimowitz (non-voting) and Lane (non-voting)) and abstracted for full review by the committee. Cases with complications

were flagged for discussion. Committee decisions fell into three categories: approval, rejection, or deferral until more experience or better outcomes with the Wingspan stent was documented. Approval was required to be a unanimous decision. The threshold for approval, in terms of numbers of cases with the Wingspan stent, for additional physicians at the same site as an approved physician was generally lower (though never less than 3), particularly if there was evidence from procedure notes of joint participation in cases.

Monitoring of Interventional Performance in the Trial

Performance of interventionists in the trial was closely monitored to ensure patient safety and adherence to protocol [2]. Notes for all procedures performed in SAMMPRIS were reviewed by the Neurointerventional PIs (if no procedural adverse event was reported) or the internal neurointerventionist safety monitor (if a procedural adverse event was reported). Interventionists were contacted by the co-principal interventional investigators if there were any questions raised regarding technique or protocol adherence. An interventionist was investigated if there was any suspicion by the safety monitor of poor judgment or technique, or if a safety threshold was crossed (any single occurrence of vessel rupture or more than one procedural-related serious adverse event or technical problem with the study device reported in the first 10 cases).

Data Used for Analyses

For the purpose of the present study, we collected data from the following sources: the SAMMPRIS credentialing data-base, a survey sent by email to all interventionists who participated in the trial, the SAMMPRIS trial data-base, and the two largest published multicenter Wingspan registries in the USA [3,4].

The following data were obtained from the credentialing data-base: the number of cases submitted by each interventionist for credentialing with the Wingspan stent, coronary stents, aneurysm stents, and angioplasty alone for intracranial atherosclerotic stenosis. Years in practice after neurointerventional training by the start of the trial and primary specialty were collected from the interventionists' survey.

Data derived from the SAMMPRIS trial included the number of patients enrolled in the trial at each site and the number of SAMMPRIS PTAS performed by each interventionist. Total site enrollment was used to divide the sites into high enrolling (the highest volume sites accounting for 50% of all enrolled patients) low enrolling (the remaining sites). An analysis of individual operator experience gained over the course of the trial was not feasible, owing to the large number of operators with very few cases.

Enrollment data from the two published Wingspan registries were used to determine if a SAMMPRIS site had a principal interventionist who had been the primary operator at one of the top five enrolling sites in either of the two Wingspan registries that had mutually exclusive participating sites [3, 4]. If so, that SAMMPRIS site was considered one of the top 10 enrolling sites in the Wingspan registries for this analysis. Between the close of the registries and the beginning of SAMMPRIS, three principal interventionists had moved from another institution participating in the registries to a SAMMPRIS site that had not participated in the registries. In those situations, the site that the interventionist moved to (rather than from) was considered as a high enrolling site in the registries because it is the interventionists' experience that we were most interested in for this analysis.

30-day Outcomes

Of the 224 patients randomized to PTAS in SAMMPRIS, 11 patients did not undergo PTAS. Therefore, 213 patients underwent angioplasty alone (n=5) or angioplasty and stenting (n =

208) with study devices. The analyses in this paper are confined to the 213 patients who underwent PTAS. Peri-procedural strokes were subcategorized as hemorrhagic and ischemic, and further broken down into primarily subarachnoid (SAH) or intraparenchymal (ICH) for hemorrhage, and occlusion of local perforators for ischemic strokes. The details of these subgroup categorizations have been reported [5]. Asymptomatic hemorrhagic strokes were included, as were cerebral infarctions with temporary symptoms (CITS) since mechanistically these were considered important events even though they were not primary endpoints.

Statistical Analysis

For each of the factors, patients were classified into categories and the percent of patients with an event was compared among the categories using Fisher's Exact Test. For the continuous factors (number of credentialing cases with Wingpan stents and aneurysm stents, number of years in practice, and number of SAMMPRIS PTAS cases) two categories were formed according to the median value among the interventionists. Exact unconditional 95% confidence intervals for the difference in percentages between groups were calculated using a score statistic [6]. For the factor with 3 categories (specialty of the primary interventionist) a Bonferroni correction to the alpha level was applied. Stepwise logistic regression analysis was done to relate the occurrence of an endpoint to multiple factors. To determine if the credentialing factors were significant when accounting for the clinical factors identified in a separate analysis [5], we report the results of an analysis in which the significant credentialing factors are included in a model with the clinical factors. The p-value for inclusion or removal from the model was 0.05. No adjustments were made for multiple comparisons in hypothesis tests. All analyses were done in SAS 9.3.

RESULTS

Experience with device and training background

Angioplasty alone (n=5) or angioplasty and stenting (n = 208) in the trial was done by 63 interventionists at 48 sites. Thirty nine interventionists were radiologists, 18 were neurosurgeons and 6 were neurologists. The median numbers of procedures submitted for credentialing were 10 (range 3 to 20) with the Wingspan stent, 1 (range 0 to 16) with coronary balloon-expandable stents, 6 (range 0 to 17) using aneurysm stents, and 0 (range 0 to 16 for angioplasty alone. Within the trial, the median number of PTAS procedures per interventionist was 3 (range 1 to 13)

Monitoring of Interventionists in Trial

No interventionists were suspended for safety or protocol concerns. One interventionist had two adverse events (one primary endpoint, one technical issue) in the first two PTAS cases; however that site was terminated for failing to meet enrollment goals before any additional patients were recruited.

All Cerebrovascular Events (n=34)

There were a total of 34 cerebrovascular events within 30 days of enrollment in patients undergoing PTAS. There were 19 ischemic strokes, 2 cerebral infarcts with temporary signs (CITS), 11 symptomatic hemorrhagic strokes, and 2 asymptomatic hemorrhagic strokes. The 34 events occurred at 25 investigational sites. Of 7 sites at which more than 1 of these events occurred, 5 were among the highest-enrolling sites. Table 1 shows the 30-day rates of any cerebrovascular event according to the various interventionist and site features that were evaluated. None of the interventionist or site features were significantly ($P < 0.05$) associated with any cerebrovascular event in bivariate analysis. The rates of any peri-

procedural cerebrovascular event were 9.9% for interventionists credentialed with < 10 Wingspan cases vs. 19.0% for interventionists credentialed with ≥ 10 Wingspan cases (p=0.11).

Hemorrhagic Strokes (n=13)

There were 13 hemorrhagic strokes. Of these, 7 were ICH, one of which was asymptomatic and not counted as a 30-day primary endpoint in the trial. All but one of the seven ICHs became evident or were identified within 12 hours after the procedure. The mechanism of these hemorrhages was attributed to reperfusion hemorrhage as they were intraparenchymal and delayed and therefore considered unlikely to be related to wire perforation or vessel rupture. There were six SAHs. Four of the six were definite wire perforations and one was a vessel rupture. One of the six SAH patients was asymptomatic. One of the wire perforations was treated with coil occlusion of the injured branch which resulted in an ischemic stroke. This event was counted as an ischemic stroke in the primary paper but for the purpose of this analysis focusing on the initial causative mechanism, it is counted as a symptomatic SAH.

The comparisons of operator and site variables with total and subgroup hemorrhage categories are shown in table 2 The rates of any hemorrhagic stroke were 9.8% at low enrolling sites in SAMMPRIS vs. 2.7% at high enrolling sites (P=0.04). The rates of any hemorrhagic stroke were 2.8% for neurosurgeons, 6.1% for radiologists, and 15.4% for neurologists (P=0.07). The rates of any hemorrhagic stroke were not related to number of Wingspan stents credentialed with, years interventionists had been in practice, and whether a site was a high enrolling site in the Wingspan registries. In multivariate analysis the only variable that was associated with any hemorrhagic stroke was high versus low enrolling site in SAMMPRIS (p = 0.04, odds ratio 3.9; Wald 95% CL 1.05–14.6). When high versus low enrolling site and subspecialty are included in a model along with the clinical factors that were associated with an increased risk of hemorrhagic stroke (percent stenosis, modified Rankin score, and clopidogrel load associated with intraprocedural ACTs > 300 seconds - see accompanying paper by Fiorella et al.), the p-values are 0.058 for high versus low enrolling site and 0.70 for subspecialty.

In hemorrhagic subgroup analyses, the rates of SAH were 0% for neurosurgeons, 3.5% for radiologists, and 7.7%% for neurologists (P=0.08), 0.9% at high enrolling sites vs. 4.9% at low enrolling sites in SAMMPRIS (P=0.11), and 0.9% amongst interventionists in practice for ≥ 8 years vs. 4.8% amongst interventionist in practice < 8 years (P=0.11). There were no relationships between interventionist or site features and the risk of ICH.

Ischemic Infarcts (n = 21)

Twenty one ischemic infarcts (19 strokes, 2 CITS) occurred within 30 days of randomization in 213 patients undergoing PTAS. Of the 21 ischemic events, 15 occurred within 24 hours of PTAS, 5 occurred between 24 hours and 6 days after PTAS (of which two were definite or probable complete stent thromboses), and one (a CITS) occurred 3 weeks after PTAS. Fifteen of the 21 ischemic infarcts were categorized as involving a perforator territory. Table 3 shows the rates of any ischemic infarct and the subgroup with perforator infarct according to the various interventionist and site features that were evaluated. None of these features were significantly (P < 0.05) associated with any ischemic infarct. The rates of any ischemic infarct were 12.6% at high enrolling sites in SAMMPRIS vs. 6.9% at low enrolling sites (P=0.18).

DISCUSSION

Several important observations can be drawn from these data regarding the relationships between interventionist and site experience and cerebrovascular complications after PTAS in the SAMMPRIS trial. First, the lack of a relationship between more extensive previous experience with the Wingspan stent (as evidenced by number of Wingspan cases interventionists were credentialed with and whether a site was one of the highest enrolling sites in previous Wingspan registries) and a lower rate of peri-procedural events in SAMMPRIS support our decision to allow self-expanding aneurysm stents and coronary stents for credentialing in SAMMPRIS. Interventionists credentialed for SAMMPRIS with fewer Wingspan cases typically made up their 20 cases with either a self-expanding aneurysm stent (Neuroform, Stryker, Kalamazoo MI), which has a similar delivery system to Wingspan, or balloon mounted coronary stents. The results of this study support the fact that good performance and outcome with these other stents were acceptable surrogates for good performance with the Wingspan stent. It should be noted that the credentialing data was self-reported: cases with bad outcomes may not have been included with the submitted operative notes and discharge summaries, and complications may have been under-recognized. However, the total number of cases performed with the device is likely to be reasonably accurate.

Second, the credentialing process in SAMMPRIS was effective as evidenced by the fact that interventionists who submitted fewer Wingspan cases for credentialing for the trial had a lower rate of ischemic events (p=0.05) and a similar rate of hemorrhagic stroke compared with investigators credentialed with more Wingspan cases (tables 2 and 3). These findings, coupled with the fact that the vast majority of interventionists credentialed for SAMMPRIS had been in practice for several years, argues strongly against the suggestion that operator inexperience with the device or in general was responsible for the higher than expected 30-day rate of stroke after PTAS in SAMMPRIS [7]. While the association of less experience with the Wingspan stent prior to SAMMPRIS and a lower rate of cerebrovascular complications in SAMMPRIS seems paradoxical, it was not totally unexpected since the credentialing process was designed to include well trained, experienced, high-quality interventionists even if they had not had a large experience with Wingspan, as long as they had sufficient experience and good outcomes with another self-expanding stent or coronary stent.

Third, data from this study suggests a potential relationship between low enrollment and an increased risk for hemorrhagic stroke after PTAS. This was the only variable to reach statistical significance in bivariate analysis and it was nearly significant when included in a model that incorporated clinical factors associated with hemorrhage. We suspect that this association may, in part, be related to better familiarity and adherence to the PTAS protocol at high volume sites. Important components of the PTAS protocol to lower the risk of hemorrhagic stroke were maintaining an activated clotting time (ACT) between 250 – 300 seconds during the procedure and treating elevated blood pressure during and after the procedure with intravenous antihypertensive agents. While SAMMPRIS does show that high ACT levels associated with a loading dose of clopidogrel was an independent risk factor for peri-procedural hemorrhagic stroke [5], we did not collect data on peri-procedural blood pressures. As such, we cannot evaluate whether peri-procedural blood pressure control was a contributing factor to the high rate of peri-procedural hemorrhagic stroke in the trial.

On bivariate analyses, trends were seen between fewer years in practice and increased risk of SAH and between physician specialty and increased risk of SAH and any hemorrhagic stroke. However, neither of these features were associated with hemorrhagic stroke in a multivariate analysis. Additionally, when clinical covariates associated with hemorrhagic

stroke in SAMMPRIS [5] were included in a multivariate analysis, the p-values for subspeciality went from 0.07 in bivariate analysis to 0.70 in the multivariate analysis indicating that the higher hemorrhagic event rate amongst neurology interventionists is probably explained by the clinical covariates, i.e., the neurology interventionists treated patients with a higher prevalence of factors found to be related to the occurrence of a hemorrhage.

This study has important limitations: the analysis is post-hoc, the number of interventionists is high, the number of cases done by each interventionist is low, and the number of 30-day events is low. As such, the likelihood of both type 1 error (random chance associations because of multiple comparisons) and type 2 errors (concluding no relationship exists when one in fact does but the study has insufficient power) is very high in this analysis. Also, the confidence intervals for the difference between the percentages of patients with events show that with the small sample sizes we are unable to rule out that large differences may exist between groups for many of the factors. For these reasons, many of the findings in this analysis should be considered hypothesis generating.

Despite these limitations, the data from this analysis show unequivocally that: 1. The cerebrovascular complications from PTAS with the Wingspan system were widely distributed amongst many sites in the trial, i.e. could not be explained by the poor performance of a few interventionists or sites; 2. The credentialing process in SAMMPRIS was effective in ensuring that interventionists credentialed with lower numbers of Wingspan procedures performed at least as effectively as interventionists credentialed with high numbers of Wingspan procedures; and 3. The poor outcome after PTAS compared to medical therapy alone in SAMMPRIS cannot be attributed to inexperience with the study device. Rather, the higher than expected rate of cerebrovascular complications in SAMMPRIS is more likely attributable to restricting inclusion in the trial to patients with severe (70–99%) stenosis and qualifying events within 30 days of enrollment as well as prospective and independent end-point adjudication in SAMMPRIS. The original registries that reported much lower rates of peri-procedural stroke included patients with 50 to 99% stenosis and patients with prior symptoms beyond 30 days. Both factors may be associated with lower procedural risks. Finally, patients in the registries were not prospectively and independently assessed for end-point events and may have been under-reported as a consequence.

Given the unexpected and substantial decrease in the risk of stroke from aggressive medical therapy alone in SAMMPRIS, future endovascular approaches for this disease will need to focus on those subgroups in SAMMPRIS that had a high risk of stroke despite aggressive medical therapy. Perhaps patients with hemodynamic factors [8,9] will turn out to be one of those subgroups. In addition, improvements in patient selection (e.g., by imaging intracranial plaque using high resolution MRI [10–12]), reconsideration of less invasive endovascular approaches such as angioplasty alone [13], and improvements in devices will be necessary to substantially reduce the complication rate in order for endovascular therapy to be have a clearer role in the treatment of these patients.

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Table 1

Operator and Site Factors versus the Occurrence of a Hemorrhagic or Ischemic Event (n=34)

Factor	# Sites or Operators	# Patients	Hemorrhagic or Ischemic Event		
			n(%)	p-value*	Difference (95% CI) †
SAMMPRIS Site Enrollment					
High (≥ 12)	12	111	17 (15.3%)	0.85	−1.4% (−11.7% – 8.7%)
Low (< 12)	36	102	17 (16.7%)		
High-Enrolling Registry Site					
No	38	132	21 (15.9%)	0.99	−0.1% (−11.3% – 9.8%)
Yes	10	81	13 (16.0%)		
Primary Specialty of Interventionist					
Radiology	39	115	17 (14.8%)	0.28	1: 0.9% (−13.4% – 13.3%)
Neurosurgery	18	72	10 (13.9%)		2: −12.1% (−38.7% – 7.3%)
Neurology	6	26	7 (26.9%)		3: −13.0% (−39.5% – 7.9%)
Credentialing: # Study devices					
< 10	30	71	7 (9.9%)	0.11	−9.1% (−18.5% – 2.1%)
≥ 10	33	142	27 (19.0%)		
Credentialing: # Aneurysm Stents					
< 6	29	116	21 (18.1%)	0.45	4.7% (−5.8% – 14.7%)
≥ 6	34	97	13 (13.4%)		
# Years in Practice					
< 8	28	104	18 (17.3%)	0.71	2.6% (−7.5% – 12.9%)
≥ 8	35	109	16 (14.7%)		
# SAMMPRIS PTAS Cases					
< 3	31	43	7 (16.3%)	0.99	0.4% (−10.6% – 15.9%)
≥ 3	32	170	27 (15.9%)		

*P-value for Fisher's exact test comparing percentages among groups.

[†] Difference between percentages, calculated as first group – second group, except for Primary Specialty (1: Radiology – Neurosurgery, 2: Radiology – Neurology, 3: Neurosurgery – Neurology).

[≠] Total in both groups exceeds 63 interventionists because individual interventionists had patients in both groups.

PTAS = Percutaneous Transluminal Angioplasty and Stenting, CI = Confidence Interval.

Table 2

Operator and Site Factors versus the Occurrence of a Hemorrhagic Stroke (n=13)

Factor	# Sites or Operators	# Patients	SAH	ICH	SAH or ICH		
			n (%)	n (%)	n (%)	p-value	Difference (95% CI) †
SAMMPRIS Site Enrollment							
High (≥ 12)	12	111	1 (0.9%)	2 (1.8%)	3 (2.7%)	0.043	−7.1% (−14.9% – −0.6%)
Low (< 12)	36	102	5 (4.9%)	5 (4.9%)	10 (9.8%)		
High Enrolling Registry Site							
No	38	132	5 (3.8%)	5 (3.8%)	10 (7.6%)	0.38	3.9% (−4.0% – 10.5%)
Yes	10	81	1 (1.2%)	2 (2.5%)	3 (3.7%)		
Primary Specialty of Interventionist							
Radiology	39	115	4 (3.5%)	3 (2.6%)	7 (6.1%)	0.071	1: 3.3% (−6.6% – 11.7%)
Neurosurgery	18	72	0 (0%)	2 (2.8%)	2 (2.8%)		2: −9.3% (−34.3% – 4.8%)
Neurology	6	26	2 (7.7%)	2 (7.7%)	4 (15.4%)		3: 12.6% (−37.1% – 1.9%)
Credentialing: # Study devices							
< 10	30	71	2 (2.8%)	2 (2.8%)	4 (5.6%)	0.99	−0.7% (−7.3% – 8.1%)
≥ 10	33	142	4 (2.8%)	5 (3.5%)	9 (6.3%)		
Credentialing: # Aneurysm Stents							
< 6	29	116	3 (2.6%)	4 (3.4%)	7 (6.0%)	0.99	−0.2% (−7.7% – 6.8%)
≥ 6	34	97	3 (3.1%)	3 (3.1%)	6 (6.2%)		
# Years in Practice							
< 8	28	104	5 (4.8%)	3 (2.9%)	8 (7.7%)	0.40	3.1% (−3.8% – 10.8%)
≥ 8	35	109	1 (0.9%)	4 (3.7%)	5 (4.6%)		
# SAMMPRIS PTAS Cases							
< 3	31	43	2 (4.7%)	2 (4.7%)	4 (9.3%)	0.40	4.0% (−3.8% – 17.2%)
≥ 3	32	170	4 (2.4%)	5 (2.9%)	9 (5.3%)		

*P-value for Fisher's exact test comparing percentages among groups.

† Difference between percentages, calculated as first group – second group, except for Primary Specialty (1: Radiology – Neurosurgery, 2: Radiology – Neurology, 3: Neurosurgery – Neurology).

‡ Total in both groups exceeds 63 interventionists because individual interventionists had patients in both groups.

PTAS = Percutaneous Transluminal Angioplasty and Stenting, SAH = Subarachnoid Hemorrhage, ICH= Intraparenchymal Hemorrhage, CI = Confidence Interval.

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Table 3

Operator and Site Factors versus the Occurrence of an Ischemic Event (n=21)

Factor	# Sites or Operators	# Patients	Perforator Stroke or CITS	All Ischemic Stroke or CITS		
			n (%)	n (%)	p-value	Difference (95% CI) †
SAMMPRIS Site Enrollment						
High (≥ 12)	12	111	10 (9.0%)	14 (12.6%)	0.18	5.7% (−2.7% – 14.3%)
Low (< 12)	36	102	5 (4.9%)	7 (6.9%)		
High-Enrolling Registry Site						
No	38	132	7 (5.3%)	11 (8.3%)	0.35	−4.0% (−13.8% – 4.3%)
Yes	10	81	8 (9.9%)	10 (12.3%)		
Primary Specialty of Interventionist						
Radiology	39	115	9 (7.8%)	10 (8.7%)	0.76	1: −2.4% (−15.6% – 8.4%)
Neurosurgery	18	72	4 (5.6%)	8 (11.1%)		2: −2.8% (−27.9% – 10.3%)
Neurology	6	26	2 (7.7%)	3 (11.5%)		3: −0.4% (−25.1% – 15.5%)
Credentialing: # Study devices						
< 10	30	71	3 (4.2%)	3 (4.2%)	0.054	−8.5% (−15.94% – 1.1%)
≥ 10	33	142	12 (8.5%)	18 (12.7%)		
Credentialing: # Aneurysm Stents						
< 6	29	116	11 (9.5%)	14 (12.1%)	0.26	4.9% (−3.9%– 13.2%)
≥ 6	34	97	4 (4.1%)	7 (7.2%)		
# Years in Practice						
< 8	28	104	6 (5.8%)	10 (9.6%)	0.99	−0.5% (−8.9% – 8.1%)
≥ 8	35	109	9 (8.3%)	11 (10.1%)		
# SAMMPRIS PTAS Cases						
< 3	31	43	2 (4.7%)	3 (7.0%)	0.58	−3.6% (−11.5% – 9.6%)
≥ 3	32	170	13 (7.6%)	18 (10.6%)		

*P-value for Fisher's exact test comparing percentages among groups.

† Difference between percentages, calculated as first group – second group, except for Primary Specialty (1: Radiology – Neurosurgery, 2: Radiology – Neurology, 3: Neurosurgery – Neurology).

‡ Total in both groups exceeds 63 interventionists because individual interventionists had patients in both groups.

CITS = Cerebral Infarct with Temporary Signs, PTAS = Percutaneous Transluminal Angioplasty and Stenting, CI = Confidence Interval.