Published in final edited form as:

Surg Neurol. 2009 March ; 71(3): 311–318. doi:10.1016/j.surneu.2007.12.027.

Pre-hemorrhage statin use and the risk of vasospasm following aneurysmal subarachnoid hemorrhage

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Abstract

Background and Purpose—Aneurysmal subarachnoid hemorrhage (SAH) is often followed by delayed ischemic deficits attributable to cerebral vasospasm. Recent studies suggest a positive impact of statin therapy on the incidence of vasospasm. This study was designed to assess whether a history of prior use of statin therapy was associated with a lower risk of vasospasm in patients with SAH.

Methods—We performed a comprehensive retrospective review of patients with aneurysmal SAH between 1997 and 2004. Clinical demographics and imaging data for all patients were reviewed and a logistic regression analysis was performed to identify the predictors of cerebral vasospasm, defined as a combination of clinical signs with radiographic confirmation.

Results—308 patients were included. Mean age was higher in the group receiving statins (64 +/- 12 versus 54 +/- 12 years). Hunt and Hess scores and treatment modality were not significantly different between the groups. Vasospasm was observed in 31% of patients not taking a statin (n=282) versus 23% taking a statin (n=26), without achieving statistical significance. Discontinuation of the statin did not affect risk of vasospasm.

Conclusions—Use of a statin prior to an aneurysmal SAH trended to reduce the incidence of subsequent vasospasm, without achieving statistical significance.

Keywords

aneurysm; delayed cerebral ischemia; HMG-CoA reductase inhibitor; statin; vasospasm

Introduction

Subarachnoid hemorrhage (SAH) from the rupture of a cerebral aneurysm is often followed by delayed spasm of cerebral vasculature. This vasospasm is associated with ischemia and infarction, resulting in significant morbidity and mortality (22). Prediction and treatment of

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vasospasm are critical areas for improvement in clinical outcome, and has been increasingly explored with the growing understanding of underlying pathophysiologic mechanisms.

One mechanism proposed to contribute to vasospasm is inadequate nitric oxide production and function. Nitric oxide is a complex and integral modulator of blood flow in several organ systems, functioning as a potent vasodilator, free radical scavenger, inhibitor of platelet activation, and mediator of inflammation. In the setting of subarachnoid hemorrhage, these mechanisms may all be altered with resultant cerebral vasospasm (17). Interference of the nitric oxide system has been a proposed therapeutic method to mitigate vasospasm. In animal models, pharmacologic donors (3,18) of nitric oxide can reduce vasospasm. Similarly, the safety and efficacy of intrathecal nitroprusside for vasospasm has been shown in clinical studies (16,23, 24). In the setting of SAH, nitric oxide synthases (NOS) are down-regulated and activity is suppressed. Pharmacologic and genetic upregulation of these enzymes reduces vasospasm in animal models of SAH (4).

Hydroxymethylglutaryl CoA reductase inhibitors (statins) are commonly used as anti-hypercholesterolemia medications. There is growing evidence that there are pleiotropic benefits to statins in coronary artery disease, independent of the reduction in low density lipoproteins. Statins promote antioxidant effects and reduce inflammation (20). Systemic use of statins interferes with nitric oxide function, as evidenced by increased nitrosylation byproducts of normal endothelial proteins (5,20) and activation of endothelial nitric oxide synthase, an enzyme integral to vasomotor tone (2,13,26).

The enhancement of nitric oxide pathways by statins has been employed in the setting of SAH to reduce vasospasm. Recent trials demonstrated benefit to acute use of statins to reduce vasospasm (11,25) and retrospective studies suggest that prior use of statins confers a similar advantage (12,13,15). In the retrospective studies, limited data was reported to address whether discontinuation of the statin impacted the risk of vasospasm. In this study, we review our experience and additionally investigated whether discontinuation of the statin affected the risk of vasospasm.

Methods

Study design

IRB approval was obtained prior to commencement of this study. A retrospective review of the hospital records and imaging of patients with subarachnoid hemorrhage between 1997 and 2004 was performed. Patients were excluded for traumatic and non-aneurysmal causes of subarachnoid hemorrhage based on standard cerebral angiography. 310 patients formed the study group during this time period. Two patients were excluded for incomplete medical records. The medical records of the remaining 308 patients were reviewed for information regarding age, gender, history of hypertension, smoking history, aneurysm location, Fisher score and Hunt and Hess grade at presentation, as these variables have been associated with risk of vasospasm (6). Additional data included method of definitive treatment, including microneurosurgical clipping and endovascular coiling, treatment with nimodipine, presence of hydrocephalus, and need for endovascular treatment of vasospasm. Patient characteristics are described in Table 1.

Historical medications were routinely reviewed on hospital admission. We identified statin-class medication use in the admitted patients, including atorvastatin, fluvastatin, lovastatin, pravastatin, simvastatin, and rosuvastatin. Information was collected regarding frequency, dosing, and continued use following admission.

Routine surveillance of vasospasm was performed via clinical examination continuously and every other day transcranial Doppler ultrasonography of cerebral blood vessels was performed. Diagnostic angiography was performed as clinically indicated. Vasospasm was defined with a combination of clinical and radiographic criteria. Clinical symptoms was defined as onset of a new focal or global neurological deficit not explained by hydrocephalus, hemorrhage, surgical complications, fever, infections, or metabolic abnormalities. Radiographic confirmation included either diagnostic angiography, or transcranial ultrasonography demonstrating absolute velocities greater than 120cm/s in any primary cerebral vessel.

Endovascular intervention for vasospasm included either intra-arterial vasodilator administration or balloon angioplasty, and was employed at the discretion of the interventionalist. Severity of vasospasm was suggested by the need for endovascular intervention. Medical therapies, including hypertension, hypervolemia and hemodilution, were employed for all patients with evidence of vasospasm.

Statistical analysis

Data was analyzed using a two-tailed Student's t-test to compare continuous variables between groups and chi-square tests to compare categorical variables. Univariate analysis was performed to determine the variables that predicted our outcome, vasospasm. To control for potential interaction among variables, a logistic regression model was created. P values of <0.05 were considered statistically significant. Additional analyses were performed comparing patients with and without microsurgical repair, and patients taking or not taking a statin.

Results

Overall patient group

The study group was comprised of 308 patients harboring 321 aneurysms. Patient characteristics and the correlation of these variables to vasospasm are described in Table 1. There were 101 men (33%) and 207 women (67%). The mean age was 55 +/- 13 years. Almost 65% of patients were smokers and 49% had chronic hypertension. Of the aneurysms, 209 (65%) were in the anterior circulation and 112 (35%) in the posterior circulation. Hydrocephalus occurred in 50% of patients. Definitive treatment was surgical in 57% and endovascular in 48%. The total sum exceeded 100% because both treatments were not mutually exclusive, as 17 patients required staged endovascular and surgical treatments. Additionally, aneurysms were left unsecured in three patients.

Vasospasm occurred in 30% and endovascular intervention was required in 17% of patients. Vasospasm was significantly ($p<0.05$) more frequent with hydrocephalus, microsurgical repair, higher Fisher score and Hunt and Hess grade, and less frequent for increasing age and endovascular repair. Intervention for vasospasm was expected to significantly correlate with the development of vasospasm.

Statin and vasospasm

Patients were grouped by the use of statins to elucidate the impact on the development of vasospasm. Twenty-six patients were taking a statin medication on presentation (8%, Group 1), and 282 patients were not (92%, Group 2). The specific statin medication and doses are listed in Table 2. A comparison between the demographics of the two groups is described in Table 3. Patients taking a statin were significantly older (64 +/- 12 versus 54 +/- 12 years; $p<0.0001$), and more likely to have chronic hypertension (69% versus 48%; $p=0.03$). Gender and cigarette use were not different between the groups. On presentation, Hunt and Hess grade ($p=0.48$) and Fisher score ($p=0.52$) was not different between the groups. Following hemorrhage, the incidence of hydrocephalus was similar (Group 1, 42% versus Group 2, 51%;

p=0.42). Definitive treatment of the aneurysms was different between the groups, with more patients taking statin undergoing endovascular coiling. In group 1, 69% of aneurysms were coiled and 38% were clipped, and in group 2, 46% were coiled and 59% were clipped (p=0.02 for coiling, p=0.048 for clipping).

Occurrence of vasospasm was markedly different between these two groups though did not achieve statistical significance. Vasospasm occurred in 23% (6 of 26 patients) in group 1 and in 31% (86 of 282 patients) in group 2 (p=0.43). Severity of vasospasm, as suggested by a need for endovascular intervention, was not different between the groups (15% of group 1 versus 17% of group 2).

Multivariate analysis

In order to control for multiple variables with an influence on vasospasm, a logistic regression model was used to predict the risk of vasospasm. Variables were chosen from among those that were significant in the univariate analysis. The presence of endovascular coiling was removed from the regression model, as it almost mirrored microsurgical repair. Additionally, the need for endovascular intervention was removed from the model, as intervention cannot be a meaningful clinical predictor of vasospasm. All other variables were incorporated in the logistic regression model, including age, hydrocephalus, Fisher score, Hunt and Hess grade, microsurgical repair, and statin use (Table 4; c-statistic=0.716).

Vasospasm was independently predicted by lower age (p<0.0001; odds ratio 0.95 less per year, confidence interval 0.93 – 0.97). Patients with microsurgical repair were 1.8 times less likely to develop vasospasm (p=0.038, confidence interval 1.03-3.13). Higher Hunt and Hess grade predicted vasospasm (p= 0.044, odds ratio=1.33, confidence interval 1.01-1.76). Using this model, statin use (p=0.78) did not predict vasospasm. This suggests that higher-grade SAH and younger age independently predicts vasospasm. Despite the marked reduction in absolute frequency of vasospasm in patients using statins, multivariate analysis also did not demonstrate statistical significance.

In our data, Fisher score and Hunt and Hess grade were highly correlated with each other (r=0.47, Spearman coefficient). This resulted in a lack of significance for both variables when simultaneously included in the multivariate analysis. Therefore, a logistic regression analysis was performed for Hunt and Hess grade and Fisher score independently with identical results for both analyses.

Microsurgical repair and vasospasm

Microsurgical repair independently predicted a lower risk for vasospasm in the logistic regression model. To clarify the benefit, patients treated with surgery were compared with those not treated with surgery (Table 5). The mean age of the patients who had a microsurgical repair was qualitatively similar to those who did not (53 versus 56 years; p=0.038). Additionally, the overall health prior to hemorrhage was better in the surgically treated group, as suggested by a lower rate of hypertension (44% versus 56%; p=0.031) and lower frequency of statin use (6% versus 12%; p=0.048). In addition, the clinical presentation was better, as the mean Hunt and Hess score was lower for those treated surgically (2.3 versus 2.7 for those treated without surgery; p=0.035), and the rate of hydrocephalus was lower (39% versus 63% for those treated without surgery; p<0.0001). Vasospasm occurred less frequently in the surgical group (25% versus 37%; p=0.020), though was not likely to result in an intervention (15% versus 20%; p=0.34). Since the impact of the other predictive variables is controlled for in the logistic regression model, the selection bias younger patients with lower surgical morbidity and better clinical presentation cannot fully explain the reduction in vasospasm.

Discontinuation of statins and vasospasm

The discontinuation has been suggested to influence the effect on vasospasm (21). Statins were only continued in 7 of 26 patients following admission (Table 6). As compared to those patients in which the statin was discontinued, these patients were not different in age (67 versus 63 years; $p=0.43$, Student's t-test), Hunt and Hess score (2.0 versus 2.5; $p=0.38$, chi square analysis), Fisher score (2.9 versus 3.1; $p=0.49$ chi square analysis), frequency of microsurgical repair (43% versus 37%; $p=1$, chi square analysis), and in frequency of vasospasm (29% versus 21%; $p=1$, chi square analysis). There was no difference between drug or dose between those that were continued and those that were discontinued.

Discussion

Delayed cerebral vasospasm is a significant contributor to the neurologic injury associated with aneurysmal SAH. Statin-class medications have been demonstrated to reduce the frequency of delayed vasospasm and secondary neurologic injury. This study examines the potential impact of statins used prior to SAH. A logistic regression model was utilized to clarify the role of additional variables which are known to impact the frequency of vasospasm. An insignificant reduction in frequency of vasospasm was seen in patients with a prior use of a statin, from 31% to 23% within the whole study group. This trend did not, however, achieve statistical significance. The lack of statistical significance, despite substantial difference in frequency of vasospasm is possibly due to the small number of patients who were taking a statin-class medication at the time of SAH. A properly powered study, designed to detect an 80% difference between the vasospasm rates of 31% and 23%, should include over 4000 patients. This calculated study size is based upon an 8% prevalence of statin use, as was seen in our study. An increased prevalence would reduce the number of patients necessary to demonstrate statistical significance, as was seen in McGirt et al (12) reporting statin use in 13% of patients,. Since the prevalence of statin use in the general population is increasing in response to the enhanced understanding of their benefits in cardiovascular disease, future studies with due attention to the effect of discontinuation of the statin may demonstrate statistical significance with a more reasonable study population size. Alternatively, a higher total number of patients could be accrued by extending the study longitudinally or as a multi-center study. The pleiotropic protective benefits (20) of statin use may be more profound in the setting of subarachnoid hemorrhage, with positive effects on outcome beyond incidence of vasospasm alone. In studies that capture broader outcome measures, the benefit may be greater than 8% and the number of included patients may be lower as well, as was needed in other studies exploring the benefits of acute statin use (11,25). Nonetheless, the large difference in frequency of vasospasm is highly suggestive and warrants further investigation.

Other studies

This study is consistent with previous reports of an increased risk of vasospasm with decreased age and increased Fisher score and Hunt and Hess grade. This study also demonstrated an increased risk of vasospasm for patients treated with endovascular coiling. Unlike decreased age and higher clinical grade, surgical treatment of ruptured aneurysms has not been described to increase the risk of subsequent vasospasm (8,19). In our analysis, however, the predicted risk is likely due to an imbalance in treatment selection. The group of patients treated with coiling had a worse medical condition as reflected by the increased pre-morbid rate of hypertension and statin use, and worse neurologic condition as reflected by the higher Hunt and Hess grade. Microsurgical repair was utilized more frequently in better grade patients, whereas endovascular embolization was more frequently employed for patients with a poorer clinical grade. While the logistic regression model eliminates the potential impact of age and clinical grade from the analysis of surgery and vasospasm, an increased risk of vasospasm in patients treated with coiling suggests an overall selection bias in the treatment modality of

ruptured aneurysms. Perhaps direct reduction in the volume of subarachnoid clot at the time of microsurgery may play a role in this difference between treatment modalities. Nevertheless, the exact nature of the relationship between surgery and vasospasm in our study population is not addressed by our study.

There are several clinical reports that evaluate the impact of statin use on cerebral vasospasm. In two small randomized prospective studies, acute use of a statin following SAH reduced the severity of vasospasm, preserved cerebrovascular autoregulation, and improved serologic markers and radiographic evidence of vasospasm (11,25). Outcome measures beyond discharge were not evaluated. Though these prospective studies excluded the prior use of a statin, vasospasm would be expected to occur less frequently or with reduced severity independent of patient age when monitoring patients following a SAH.

Three retrospective studies have been performed to address the role of prior statin use on delayed vasospasm, with conflicting findings. In an age- and grade-matched cohort study of twenty SAH patients with a history of statin use, Parra *et al* found a significantly reduced highest mean TCD velocity and improved clinical outcome at fourteen days post-hemorrhage. This benefit in clinical outcome was more significant in the subpopulation with higher Hunt and Hess grades (15). McGirt *et al* found that vasospasm and delayed neurologic deficits was similarly reduced in the 15 patients taking a statin in the group of 115 patients (12). In contrast, Singhal *et al* demonstrated that prior statin use increased the risk of vasospasm in 36 statin-users of 514 total patients, and discontinuation further increased the risk (21). However, there was no increased morbidity or mortality for these patients, which is in contradistinction to the well-established experience with vasospasm. Our findings are more consistent with the findings of Parra *et al* and McGirt *et al*, demonstrating a large absolute reduction in frequency of vasospasm, with greater benefit in higher grade patients, and no difference in the need for intervention for vasospasm (12,15). Unlike other studies, we more clearly define the impact of discontinuation of the statin.

Discontinuation of statins and vasospasm

The effect of discontinuation of statins on delayed vasospasm following SAH has not been well elaborated by the retrospective studies that investigate the historic use of statins. McGirt *et al* did not report whether patients were routinely maintained on the statin therapy, the frequency of statin discontinuation or effect on vasospasm (12). Parra *et al* reported on 20 patients who were taking statin as a historic medication (15). Only 11 had records available for review and only 64% of these continued statins following the hemorrhage. No analysis was reported for this, preventing any conclusions regarding the potential impact of discontinuing the statin. In Singhal *et al*, 36 patients were taking a statin on presentation and discontinued in 19 (21). They report that the use of a statin increased the risk of vasospasm and was mitigated by its discontinuation. Their primary finding is contrary to our and other studies, and therefore it is difficult to interpret the risk of discontinuing the statin. We found that the discontinuation of the statin did not result in an increase in the frequency of vasospasm (21% for those discontinued versus 28% for those continued). The statistical analysis with this small number of patients has a large chance of a type II error, in which a significant difference is missed between the discontinued and continued statin therapy. Since acute treatment with a statin following the hemorrhage is beneficial (11,25), an expected finding is that discontinuation would increase the risk of vasospasm. This however should be addressed in a prospective manner with a larger number of patients.

Statin choice

The patients in this study were taking variable medications within the statin-class of drugs. There is no strong evidence to suggest a benefit to a specific medication for prevention of

vasospasm following an aneurysmal subarachnoid hemorrhage. Since there is a limited understanding of the mechanisms that underlie its neuroprotective properties, it is possible that any statin-class medication might confer the same benefit. The retrospective nature of this study and small number of patients taking any specific medication prevents a further sub-analysis. While such an analysis would be interesting, the choice of statin was independently made by primary care providers prior to the hemorrhage, and is subject to the evolution in management of hypercholesterolemia.

Underlying mechanisms

Statins have been hypothesized to reduce cerebral vasospasm via stimulation of the nitric oxide pathways. The positive impact of statin therapy on the nitric oxide system has been explored in *in vitro* systems (1,2,7,9,10,13) and in clinical studies (14,20). This may be through a direct neuroprotective mechanism or through a shift in vascular tone toward dilation. The use of statins would be expected to enhance NOS activity and counteract the deficiency of nitric oxide which underlies cerebral vasospasm. Various studies have addressed this hypothesis in both animal models and small clinical trials. McGirt *et al* described a mouse model of SAH with a two-week pretreatment with simvastatin (13). Middle cerebral artery (MCA) diameter and cerebral endothelial NOS expression were increased, and early neurologic function was improved, compared to vehicle-treated SAH mice. When mice treated with simvastatin only following the experimental SAH, a similar pattern was seen with a less dramatic protective benefit in MCA diameter and neurologic function. Endothelial NOS expression was not enhanced following the SAH when simvastatin was not used prior to the SAH. This may suggest that statins maximally impact NOS expression and MCA diameter only when present at the time of aneurysmal rupture.

Limitations

In our patients, all historical medications were reviewed with the patient and family at admission, though compliance and accurate dosing was not consistently available. The retrospective nature of this study and extent over several years prevents clarification, and is a limitation of this study.

The definition of vasospasm in the literature varies widely. The management of vasospasm in our institution is guided by clinical symptomatology, including focal and systemic neurologic findings, with confirmatory radiographic findings, including TCD and angiography. This represents a limitation in this study in that a less or more rigid definition may alter our findings.

Conclusions

The role of statin use prior to aneurysmal SAH is proposed to reduce the frequency of delayed cerebral vasospasm, via multiple mechanisms. We demonstrate that vasospasm is reduced, though without achieving statistical significance, in patients with prior statin use. Vasospasm was not significantly affected by discontinuation of the statin suggesting long-acting mechanisms of this drug conferring protection following the SAH. Further studies should be designed to explore the mechanisms underlying vasospasm and the protection of both acute and historic statin use.

Acknowledgments

We would like to thank Michael Lieber, Department of Quantitative Health Sciences, Cleveland Clinic Foundation, for his assistance with the statistical analysis, and Christine Moore, Department of Neurosurgery, Cleveland Clinic Foundation, for her editorial support.

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Table 1
Demographic characteristics and univariate analysis with vasospasm

Characteristics of all study patients and univariate analysis of each variable in relation to vasospasm.

Variable	n (% of total)	Vasospasm (%)	p-value ^α
Age (mean)			
With vasospasm		50 years	<0.0001 ^{*β}
without vasospasm		57 years	
Gender			
Male	101 (33%)	30	0.96
Female	207 (67%)	30	
Smoking			
Yes	200 (65%)	32	0.27
No	108 (35%)	26	
Hypertension			
Yes	152 (49%)	27	0.27
No	156 (51%)	33	
Nimodipine			
Yes	301 (98%)	31	0.08
No	7 (2%)	0	
Hydrocephalus			
Yes	153 (50%)	35	0.03 [*]
No	155 (50%)	24	
Microsurgical repair			
Yes	175 (57%)	25	0.02 [*]
No	133 (43%)	37	
Endovascular coiling			
Yes	147 (48%)	37	0.006 [*]
No	161 (52%)	23	
Fisher score			
1	19 (6%)	16	<0.05 [*]
2	65 (21%)	19	
3	160 (53%)	33	
4	61 (20%)	36	
Hunt and Hess grade			
1	68 (22%)	13	0.0004 [*]
2	88 (29%)	31	
3	97 (32%)	34	
4	44 (14%)	50	
5	11 (4%)	9	
Statin use			
Yes	26 (8%)	23	0.43
No	282 (92%)	31	

Variable	n (% of total)	Vasospasm (%)	p-value α
Vasospasm			
Yes	92 (30%)	N/A	N/A
No	216 (70%)	N/A	
Intervention for vasospasm			
Yes	53 (17%)	100	<0.0001 *
No	255 (83%)	15	

* -statistical significance for p strictly < 0.05,

α Chi-square test,

β Student's two-tailed t-test.

Table 2**Statin drugs prescribed**

Distribution of statin drugs and dosages of patients in group 1 with number of patients

Drug	Dose (mg)	N
Atorvastatin (n=11)	10	1
	20	1
	40	2
	Unknown	7
Lovastatin (n=3)	20	2
	40	1
Pravastatin (n=4)	10	3
	40	1
Simvastatin (n=8)	20	2
	40	1
	Unknown	5

Table 3
Comparison between statin and non-statin users

Characteristics of patients and comparison between those taking a statin and those not taking a statin prior to SAH.

Variable	Statin (n=26)	Non-Statin(n=282)	p-value ^{α}
Age (yrs; mean $\pm$ SD)	64 $\pm$ 12	54 $\pm$ 12	<0.0001 * ^{β}
Male	10 (38%)	91 (32%)	0.52
Smoking	14 (54%)	186 (66%)	0.22
Hypertension	18 (69%)	134 (48%)	0.03 *
Nimodipine	25 (96%)	276 (98%)	0.57
Hydrocephalus	11 (42%)	142 (51%)	0.42
Endovascular	18 (69%)	129 (46%)	0.02 *
Microsurgical repair	10 (38%)	165 (59%)	0.048 *
Fisher score			0.52
1	0 (0%)	19 (7%)	
2	5 (19%)	60 (22%)	
3	16 (62%)	144 (52%)	
4	5 (19%)	56 (20%)	
Hunt and Hess grade			0.48
1	7 (27%)	61 (22%)	
2	9 (35%)	79 (28%)	
3	6 (23%)	91 (32%)	
4	2 (8%)	42 (15%)	
5	2 (8%)	9 (3%)	
Vasospasm	6 (23%)	86 (31%)	0.43
Intervention	4 (15%)	49 (17%)	0.8

* -statistical significance for p strictly < 0.05,

^{α} -Chi-square test,

^{β} -Student's two-tailed t-test.

Table 4
Logistics regression model predicting vasospasm as outcome

Variable	p-value	Odds Ratio
Age	<0.0001*	0.947/year (CI 0.93-0.97)
Hydrocephalus	0.38	
Microsurgical repair	0.038*	1.80 (CI 1.03 – 3.13)
Hunt and Hess grade	0.044*	1.33 (CI 1.01 – 1.76)
Fisher score **	0.045*	1.44 (CI 1.01 – 2.05)
Statin use	0.78	

** Modeling performed for Fisher score separately from Hunt and Hess grade.

Table 5
Comparison of patients with and without surgery

Characteristics of patients and comparison between those with a surgical repair and those not repaired surgically.

Variable	No surgery	Surgery	p-value ^{<i>α</i>}
Age (years)	56.4	53.3	0.0375 ^{<i>β</i>}
Male	48 (36%)	53 (30%)	0.283
Smoking	86 (65%)	114 (65%)	0.930
Hypertension	75 (56%)	77 (44%)	0.031 [*]
Hunt and Hess grade			0.035 [*]
1	22 (17%)	46 (26%)	
2	33 (25%)	55 (31%)	
3	46 (35%)	51 (29%)	
4	25 (19%)	19 (11%)	
5	7 (5%)	4 (2%)	
Hydrocephalus	84 (63%)	69 (39%)	<0.0001 [*]
Vasospasm	49 (37%)	43 (25%)	0.020 [*]
Intervention for vasospasm	26 (20%)	27 (15%)	0.343
Statin	16 (12%)	10 (6%)	0.048 [*]

^{*}-statistical significance for p strictly < 0.05,

^{*α*}-Chi-square test,

^{*β*}-Student's two-tailed t-test.

Table 6
Comparison of patients with the statin continued and discontinued

No statistical significance ($p < 0.05$) is achieved for any variable.

Variable	Discontinued	Continued
n	19	7
Age (years)	63	67
Male	7 (37%)	3 (43%)
Smoking	10 (53%)	4 (56%)
Hypertension	12 (63%)	6 (86%)
Hunt and Hess grade	2.5	2
Fisher score	3.1	2.9
Surgery	7 (37%)	3 (43%)
Vasospasm	4 (21%)	2 (29%)