Operative complications and differences in outcome after clipping and coiling of ruptured intracranial aneurysms

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OBJECT Aneurysmal subarachnoid hemorrhage (aSAH) is associated with substantial morbidity and mortality, with better outcomes reported following endovascular coiling compared with neurosurgical clipping of the aneurysm. The authors evaluated the contribution of perioperative complications and neurological decline to patient outcomes after both aneurysm-securing procedures.

METHODS A post hoc analysis of perioperative complications from the Clazosentan to Overcome Neurological iSchemia and Infarction Occurring after Subarachnoid hemorrhage (CONSCIOUS-1) study was performed. Glasgow Coma Scale (GCS) scores for patients who underwent neurosurgical clipping and endovascular coiling were analyzed preoperatively and each day following the procedure. Complications associated with a decline in postoperative GCS scores were identified for both cohorts. Because patients were not randomized to the aneurysm-securing procedures, propensity-score matching was performed to balance selected covariates between the 2 cohorts. Using a multivariate logistic regression, the authors evaluated whether a perioperative decline in GCS scores was associated with long-term outcomes on the extended Glasgow Outcome Scale (eGOS).

RESULTS Among all enrolled subjects, as well as the propensity-matched cohort, patients who underwent clipping had a significantly greater decline in their GCS scores postoperatively than patients who underwent coiling ($p = 0.0024$). Multivariate analysis revealed that intraoperative hypertension ($p = 0.011$) and intraoperative induction of hypotension ($p = 0.0044$) were associated with a decline in GCS scores for patients undergoing clipping. Perioperative thromboembolism was associated with postoperative GCS decline for patients undergoing coiling ($p = 0.03$). On multivariate logistic regression, postoperative neurological deterioration was strongly associated with a poor eGOS score at 3 months (OR 0.86, 95% CI 0.78–0.95, $p = 0.0032$).

CONCLUSIONS Neurosurgical clipping following aSAH is associated with a greater perioperative decline in GCS scores than endovascular coiling, which is in turn associated with poorer long-term outcomes. These findings provide novel insight into putative mechanisms of improved outcomes following coiling, highlighting the potential importance of perioperative factors when comparing outcomes between clipping and coiling and the need to mitigate the morbidity of surgical strategies following aSAH.

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KEY WORDS subarachnoid hemorrhage; complications; clipping; coiling; vascular disorders

ABBREVIATIONS aSAH = aneurysmal subarachnoid hemorrhage; CONSCIOUS-1 = Clazosentan to Overcome Neurological iSchemia and Infarction Occurring after Subarachnoid hemorrhage; DCI = delayed cerebral ischemia; DIND = delayed ischemic neurological deterioration; eGOS = extended Glasgow Outcome Scale; GCS = Glasgow Coma Scale; ISAT = International Subarachnoid Aneurysm Trial; WFNS = World Federation of Neurosurgical Societies.

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ANEURYSMAL subarachnoid hemorrhage (aSAH) occurs in 8–9 people per 100,000,^{21,23} leading to significant morbidity¹ and mortality.^{3,13,14,31} To reduce the risk of rehemorrhage, the ruptured aneurysm is treated either by neurosurgical clipping²⁹ or endovascular coiling.^{16,28,30} Since publication of the International Subarachnoid Aneurysm Trial (ISAT)³⁰ in 2002, endovascular coiling has gained wide acceptance and has become the preferred treatment modality at many centers.²⁰ The most appropriate treatment modality for specific patient subgroups and at particular treatment centers with varying levels of experience remains a subject of controversy.

To date, several prospective trials^{28,30} and meta-analyses^{17,19} comparing surgical clipping to endovascular coiling have suggested that clinical outcomes are better at 1 year for patients undergoing coil embolization after aSAH. The increasing acceptance of coiling is partly attributable to the perception that these improved outcomes are related to the lower periprocedural morbidity of endovascular treatment compared with open surgery.³⁶ The majority of studies, however, focus on long-term outcomes rather than periprocedural complications,^{28,30} and other factors may also mediate discrepancies in treatment outcomes. These include differences between the 2 cohorts in the incidence and severity of delayed cerebral ischemia (DCI) or problems encountered during the subsequent hospital course.^{5,14}

Recent evidence has suggested that patients undergoing surgical clipping after aSAH demonstrate substantial perioperative decline,²⁶ but these outcomes have not been compared with patients who have undergone endovascular coiling. Furthermore it is not known to what extent periprocedural complications contribute to overall patient outcomes relative to other predictors. Because perioperative morbidity is potentially modifiable, it is important to identify perioperative factors associated with outcomes and to take their relative influence under consideration when comparing outcomes between neurosurgical clipping and endovascular coiling.

In the present study we analyzed changes in Glasgow Coma Scale (GCS)³⁷ scores during the early postoperative period following neurosurgical clipping or endovascular coiling after aSAH, compared with baseline, in patients who were enrolled in the Clazosentan to Overcome Neurological iSChemia and Infarction Occurring after Subarachnoid hemorrhage (CONSCIOUS-1) study. This unique data set included patients who underwent clipping or coiling and were randomized to receive clazosentan for the prevention of angiographic vasospasm.^{24,25} Because patients were not randomized to clipping or coiling in that study, a propensity-score matching algorithm was used to balance selected covariates between the 2 cohorts of patients. Perioperative variables associated with a postoperative decline in GCS scores were identified for each cohort, and the contribution of postoperative neurological deterioration to long-term outcomes was determined.

Methods

Study Population

Data were obtained from the CONSCIOUS-1 study, a prospective, randomized, double-blinded Phase IIb

study assessing clazosentan in preventing angiographic vasospasm (clinical trial registration no.: NCT00111085 [clinicaltrials.gov]).²⁵ A post hoc analysis of subjects (n = 413) was undertaken to analyze GCS scores during the early postoperative period following lesion securing after aSAH. All patients enrolled in the study were recruited within 48 hours following aneurysm rupture. Therefore, approximations of postoperative neurological decline are unlikely to be biased by other causes of neurological deterioration, such as delayed ischemic neurological deterioration (DIND) due to angiographic vasospasm or other causes.

Clinical Assessment

Patients were admitted to the respective neurosurgical services if they had a CT-confirmed SAH. Information on clinical and demographic factors was obtained for all subjects. The World Federation of Neurosurgical Societies (WFNS) scale³⁸ was used to classify the severity of the subjects' presenting symptoms. The GCS was used to assess neurological status at baseline and each subsequent day after the aneurysm-securing procedure. When multiple GCS scores were present for a given day the lowest score was used for analysis, to identify the greatest neurological decline. Long-term clinical outcomes were evaluated using the extended Glasgow Outcome Scale (eGOS) at 12 weeks following aSAH.³⁹ A long-term outcome score indicating a disability worse than "moderate disability" (eGOS score < 5) was considered a poor neurological outcome.

Radiological Studies

All patients underwent CT scans on presentation. The Hijdra scale was used to quantify the subarachnoid clot burden and to evaluate the amount of clot in 10 fissures and cisterns of the brain (scoring system as follows: 0, no blood; 1, small amount of blood; 2, moderately filled with blood; or 3, completely filled with blood—for a range of scores from 0 to 30).¹⁰ The extent of intraventricular hemorrhage was quantified using the Graeb score: (0, no blood; 1, sedimentation [less than 25% filled]; 2, moderately filled; or 3, completely filled—and a score was given to each ventricle for a maximum possible score of 12).^{8,18} All patients underwent digital subtraction angiography within 48 hours of intracranial aneurysm rupture, and between 7 and 11 days post-aSAH. Angiographic vasospasm was quantified by calculating the percent change in the diameter of large proximal arteries between baseline and follow-up imaging.

Statistical Analysis

Data are presented as the mean $\pm$ SD. The primary outcomes of interest were the differences between preoperative and early postoperative GCS scores (within the first 24 hours after the procedure) between patients who underwent neurosurgical clipping and those treated with endovascular coiling. The distribution of GCS scores in the early postoperative period, before the DIND risk period, was analyzed. Change in GCS scores before and after surgery was defined as the greatest difference between pre- and postoperative GCS scores, and these values were analyzed using the Student t-test. The motor, verbal, and

eye components of the GCS as well as the aggregate score were analyzed separately.

Because patients were not randomized to undergo endovascular coiling and neurosurgical clipping, a propensity-score matching algorithm was used. The goal of this approach is to balance selected covariates between the 2 cohorts in observational data to decrease variability that may have arisen due to the lack of randomization.³⁴ In this algorithm, the dichotomous, dependent treatment variable was the aneurysm-securing procedure, and subjects were matched for age, sex, nicotine use, history of hypertension, preexisting heart conditions, WFNS scores, aneurysm location, presence of subdural hematoma, subarachnoid clot burden, presence of intracerebral hemorrhage, and the extent of angiographic vasospasm. Propensity score matching was performed on the basis of the logit of the propensity score by using calipers of width equal to 0.25 of the standard deviation of the logit of the propensity score.² The distribution of propensity scores before and after matching as well as the covariate balance are presented in the Supplemental Material, available as online-only content.

We also sought to identify specific complications associated with postoperative neurological decline in patients treated with clipping or coiling. Perioperative adverse events that occurred fewer than 5 times were excluded due to failure of model convergence, and thus complications with event rates greater than 5 were included as independent variables in a multivariate linear regression with perioperative difference in GCS as the dependent variable. Perioperative complications, if any, were collected for each patient in the study. Perioperative complications were coded for analysis from an existing database (see Table 2).

Finally, we evaluated the contribution of a perioperative decline in GCS scores to long-term outcomes based on the dichotomized eGOS by using a multivariate logistic regression. Independent variables included in this analysis were previously identified predictors of outcome from prior analyses based on the CONSCIOUS-1 study.^{12,40} These included subarachnoid clot burden, presence of subdural hematoma, presence of intracerebral hemorrhage, angiographic vasospasm, and poor WFNS scores on admission. Clazosentan treatment was also included as a covariate, as was the aneurysm-securing procedure. For all final models, statistical significance was set at $p < 0.05$. Analysis was performed using R statistical software and MATLAB, using custom scripts written in-house.

Results

Patient Demographic Data

The CONSCIOUS-1 study enrolled 413 patients with CT-confirmed aSAH. Twenty patients were excluded from analysis because they underwent both clipping and coiling. The mean age of subjects in the study was 51 ± 11 years, and 124 (30%) were male. Seventy-six percent ($n = 313$) of patients had WFNS Grades I–III on presentation, and 87% ($n = 361$) had a ruptured aneurysm in the anterior circulation. A summary of the clinical and radiographic information is presented in Table 1. Of the patients in this study, 45% ($n = 185$ before exclusion) had their ruptured aneurysm repaired by neurosurgical clipping.

TABLE 1. Demographic and radiological characteristics in 413 patients with aSAH*

Variable	Total
No. of patients	413
Age in yrs	51.0 ± 10.8
Male	124 (30.0)
WFNS score	
Grades I–III	313 (75.8)
Grades IV–V	100 (24.2)
Subarachnoid clot burden; Hijdra score	18.3 ± 5.9
Intraventricular clot burden; Graeb score	3.9 ± 2.4
Intracerebral hemorrhage	50 (12.1)
Aneurysm location	
Anterior circulation	361 (87.4)
Posterior circulation	45 (11.1)
Aneurysm size	
≤ 5 mm	167 (42.2)
> 5 mm	229 (57.8)

* Units in parentheses represent percentages; error is expressed as $\pm$ SD.

Postoperative Neurological Decline

The GCS scores were analyzed preoperatively as well as on each day postoperatively. Prior to the aneurysm-securing procedure there were no differences in GCS scores between groups (neurosurgical clipping [13.5 ± 2.5] vs endovascular coiling [13.1 ± 2.6], $p = 0.1$). A decline in GCS scores following the aneurysm-securing procedure was observed in 46% (80 of 174) of patients undergoing neurosurgical clipping and in 25% (53 of 208) of those undergoing endovascular coiling. The greatest difference in GCS scores was between the preoperative period and postoperative Day 1 (see Supplemental Material for longitudinal measures of GCS trends). Postoperative neurological decline was significantly greater in patients who underwent neurosurgical clipping compared with those who were treated with coils (Fig. 1; neurosurgical clipping [-1.2 ± 3.0] vs endovascular coiling [-0.3 ± 2.6], $p = 0.0028$). The GCS scores tended to improve over the first several postoperative days (Supplemental Fig. S4; Supplemental Material).

Individual components of the GCS were also analyzed (Supplemental Material). All components of the GCS showed a significantly greater decline after surgical clipping compared with endovascular coiling, except for the motor component (GCS motor, clipping [-0.3 ± 1.3] vs coiling [-0.1 ± 1.0], $p = 0.08$; GCS eye, clipping [-0.5 ± 1.0] vs coiling [-0.05 ± 0.9], $p < 0.0001$; and GCS verbal, clipping [-0.5 ± 1.4] vs coiling [-0.2 ± 1.2], $p = 0.014$).

In this study population the patients were not randomized to neurosurgical clipping or endovascular coiling. To account for this, a subgroup analysis was performed on subjects who were propensity-score matched to account for the influence of selected covariates. The propensity-score-matching algorithm matched 83 patients who underwent neurosurgical clipping to an equal number who underwent endovascular coiling. The distribution of pro-

FIG. 1. Perioperative changes in GCS. **A:** From left to right, matrices of GCS scores for all subjects, neurosurgical clipping cohort, and endovascular coiling cohort before and after procedure. Color bars represent the proportion of patients in each element. Whereas more patients treated with coiling improved postprocedure, a greater number of patients who underwent clipping deteriorated. **B:** Histogram displaying the distribution of GCS score differences between preprocedure and the 1st postprocedure day for clipping and coiling cohorts. Patients who underwent clipping were significantly more likely to deteriorate neurologically postprocedure than were patients who underwent coiling ($p = 0.0028$).

pensity scores was acceptable after matching (Supplemental Material). In this subgroup analysis, the postoperative GCS score decline remained significantly greater in this subset of patients undergoing neurosurgical clipping compared with endovascular coiling (neurosurgical clipping $[-1.2 \pm 2.8]$ vs endovascular coiling $[-0.2 \pm 2.7]$, $p = 0.033$) (Fig. 2).

Perioperative Factors Associated With Neurological Deterioration

We then sought to identify specific perioperative complications associated with postoperative decline in GCS score. Table 2 presents the perioperative complications that occurred during the respective aneurysm-securing procedures. Multivariate analysis for the surgical clipping cohort revealed that intraoperative induction of hypotension ($p = 0.0044$) and the presence of intraoperative hypertension ($p = 0.011$) during surgery were significantly associated with postoperative GCS score decline (Table 3). Thromboembolic complications during endovascular coiling were also significantly associated with postoperative neurological deterioration in patients who underwent that procedure ($p = 0.03$) (Table 4).

Perioperative Neurological Deterioration and Long-Term Outcome

Finally, we assessed whether postoperative decline in GCS score following the aneurysm-securing procedure was independently associated with long-term outcomes. On multivariate logistic regression, postoperative GCS score decline was independently associated with poor outcome on the eGOS (OR 0.86, 95% CI 0.78–0.95, $p = 0.0032$). Other variables related to aSAH that were significantly associated with poor neurological outcomes on multivariate logistic regression included male sex (OR 2.18, 95% CI 1.1–4.3, $p = 0.025$); greater subarachnoid clot burden (OR 1.09, 95% CI 1.03–1.15, $p = 0.0017$); intracerebral hemorrhage (OR 2.58, 95% CI 1.13–5.86, $p = 0.024$); and moderate or severe angiographic vasospasm (OR 0.51, 95% CI 0.28–0.93, $p = 0.027$) (Table 5). Interestingly, postprocedure GCS decline was a stronger predictor of overall neurological outcome than the aneurysm-securing procedure itself. Other components of the GCS (motor, verbal, and eye) related to aSAH and long-term outcome are presented in Supplemental Tables S1–S3; Supplemental Material. Analysis of the 83 subjects who were propensity-score matched indicated that there was a

FIG. 2. Propensity-score matched analysis. Histogram displaying the distribution of GCS score differences between preprocedure and the 1st postprocedure day for clipping (n = 83) and coiling (n = 83) cohorts in the subset of patients after propensity-score matching. Patients who underwent clipping were significantly more likely to deteriorate neurologically postprocedure than were patients who underwent coiling ($p = 0.033$).

nonsignificant trend for perioperative neurological decline as a predictor of outcome at 3 months on the eGOS ($p = 0.15$). It is possible that this trend can be explained by a relatively small sample size.

Discussion

In this exploratory, post hoc analysis of the CONSCIOUS-1 clinical study, we show that neurosurgical clipping was associated with a greater postoperative GCS score decline compared with endovascular coiling, and that this deterioration was significantly associated with poor long-term outcomes. We also identified perioperative variables that significantly contributed to procedure-related GCS deterioration. During surgical clipping the presence of hypertension or the need to induce hypotension significantly contributed to neurological decline, whereas thromboembolic complications were associated with neurological decline in patients who underwent coil treatment.

Previous and ongoing prospective trials^{28,30,36} comparing clipping to coiling typically focus on long-term outcomes and dismiss the contribution of procedure-related postoperative deterioration to the overall end point. Although it is assumed that differences in overall outcome may be related to periprocedural morbidity, the current study is the first to explicitly compare perioperative neurological decline between patients treated with clipping and coiling after rupture of intracranial aneurysms. We show that patients undergoing neurosurgical clipping are subject to greater neurological decline postoperatively than those undergoing endovascular coiling, which is in turn associated with outcomes. Our findings are supported by several early studies that have implicated adverse perioperative events following neurosurgical clipping as a contributing factor to long-term disability. Indeed, sur-

TABLE 2. Perioperative complications occurring during neurosurgical clipping and endovascular coiling in 393 patients with aSAH*

Periop Complications	Neurosurgical Clipping (n = 181)	Endovascular Coiling (n = 212)
Anesthetic-related (i.e., difficult intubation)	0	1
Angioplasty	0	25
Arterial injury	1	7
Asystole	1	0
Brain laceration	1	0
Brain protection administered (propofol/burst suppression)	28	0
Bypass	1	0
Coil migration	0	5
Thromboembolism	0	14
Hemorrhagic event	26	4
Hypotension	9	0
Increased ICP/brain edema	5	1
Induced hypotension	6	0
Infarction	8	1
Intraop bradycardia	1	1
Intraop hypertension	5	2
Local vasodilators	27	0
Mannitol administration	3	0
Multiple complications	51	12
Parent artery sacrifice	0	2
Stent-assisted coiling	0	2
Temporary artery occlusion	52	2
Other	4	4

ICP = intracranial pressure.

* Twenty patients were excluded because they had undergone both clipping and coiling.

TABLE 3. Multivariate analysis of complications associated with perioperative GCS score decline after neurosurgical clipping in patients with aSAH

Periop Complication	Coefficient (SE)	p Value
Brain protection administered	0.52 (0.91)	0.57
Hemorrhage	0.85 (0.77)	0.27
Hypotension	0.96 (1.15)	0.41
Increased ICP/brain edema	-2.18 (1.51)	0.15
Induced hypotension	-3.95 (1.36)	0.0044*
Infarction	1.34 (1.24)	0.28
Intraop hypertension	-3.52 (1.37)	0.011*
Local vasodilator application	1.20 (0.72)	0.10
Multiple complications	-0.048 (0.89)	0.96

SE = standard error.

* $p < 0.05$.

TABLE 4. Multivariate analysis of complications associated with perioperative GCS score decline after endovascular coiling in patients with aSAH

Periop Complication	Coefficient (SE)	p Value
Angioplasty	-1.11 (0.60)	0.065
Arterial injury	0.99 (1.00)	0.33
Coil migration	0.23 (1.14)	0.84
Multiple complications	-1.34 (0.96)	0.16
Thromboembolism	-1.74 (0.80)	0.0304*

* p < 0.05.

gical complications often explained more disability than vasospasm and rebleeding, and intraoperative blood pressure in particular has consistently been associated with postoperative outcomes in patients who survive the initial hemorrhagic event and receive early repair of the ruptured aneurysm.^{6,7,15,22,32,33} These early studies were not able to compare neurosurgical clipping to endovascular coiling.

Our results in the subgroup of patients who underwent neurosurgical clipping are concordant with a recent study by Mahaney and colleagues,²⁶ who also demonstrated an association between neurological deterioration and poor outcomes at 3 months after surgical clipping of ruptured intracranial aneurysms. However, those authors did not compare neurosurgical clipping to endovascular coiling. In the present study we extend their findings by directly comparing neurological deterioration between clip- and coil-treated cohorts. We showed comparable rates of postoperative neurological deterioration in patients treated with clipping (46% vs 43% in Mahaney et al.) and identified similar perioperative factors that were associated with neurological decline after clipping (presence of intraoperative hypertension and induction of intraoperative hypo-

tension).^{7,26} Although Mahaney and colleagues identified additional factors associated with postoperative neurological deterioration, it is important to highlight that the time to the aneurysm-securing procedure following aneurysm rupture was shorter in our study; therefore, it is unlikely that our results were biased by other causes of neurological deterioration not attributable to the procedure itself, such as DCI. All patients in the CONSCIOUS-1 study underwent treatment of the aneurysm prior to the DIND risk period.

A recent analysis of the ISAT data by Dorhout-Mees and colleagues⁵ revealed that patients undergoing neurosurgical clipping had higher rates of DCI compared with patients undergoing endovascular coiling of ruptured aneurysms, a finding that has been corroborated by other groups.^{4,9,11,14,16} Higher incidences of DCI after neurosurgical clipping can explain, at least in part, outcome differences between clipping and coiling. In the present study, however, we show that specific periprocedural complications play a critical role in mediating worse outcomes in patients who have undergone neurosurgical clipping.^{17,19,27,28,30,36} The results presented here highlight several important considerations in the management of ruptured intracranial aneurysms. First and foremost, perioperative complications must be taken into consideration when evaluating the long-term outcome differences between neurosurgical clipping and endovascular coiling. Second, these data highlight the importance of mitigating the morbidity associated with the surgical treatment of aSAH. Our results highlight several periprocedural factors that should be avoided to mitigate procedure-related neurological decline. First, thromboembolic events during coiling should be minimized, for instance via strict monitoring of periprocedural heparinization. Second, intraoperative induction of hypotension should be avoided during clipping. In the present study intraoperative aneurysm rupture was not a significant predictor of worse procedure-related neurological decline, which is probably due to the small number of these events in the data set, which precluded our ability to detect a statistically significant effect. Importantly, the influence of perioperative complications on the incidence of angiographic vasospasm and DCI was not assessed in the current study and could be further explored in future analyses.

There are also several limitations associated with the current study. First, the intent of the original CONSCIOUS-1 study was to assess the effect of clazosentan on angiographic vasospasm and outcome after aSAH, rather than perioperative complications. By performing propensity-score matching, however, we have demonstrated that the findings are robust in a subset of patients in whom selected covariates were balanced. Second, the relatively small data set analyzed in this study may have led to fewer perioperative factors being identified that could contribute to poor neurological outcomes after aneurysm repair. Despite the relatively small sample size the perioperative factors that significantly predict neurological decline in our study have been recently corroborated by others.²⁶ Third, early brain injury^{23,35} after aSAH, due to effects of the initial hemorrhage and unrelated to the procedure, cannot necessarily be excluded. Finally, outcome was assessed at 3 months; therefore, it is unknown if long-term differences persisted thereafter.

TABLE 5. Multivariate logistic regression of predictors of long-term neurological outcomes following aSAH

Variable	OR	95% CI	p Value
Age	1.02	0.99–1.05	0.30
Sex	2.18	1.1–4.30	0.025*
WFNS score (IV–V vs I–III)	25.87	0.87–769.22	0.06
Clazosentan (vs placebo)			
1 mg/hr	1.08	0.49–2.37	0.85
5 mg/hr	0.90	0.40–2.0	0.79
15 mg/hr	1.64	0.73–3.67	0.23
Nicotine use	0.94	0.54–1.67	0.85
Hypertension	1.65	0.92–2.93	0.09
SAH clot burden (Hijdra score)	1.09	1.03–1.15	0.0017*
Intracerebral hemorrhage	2.58	1.13–5.86	0.0238*
Coiling (vs clipping)	0.73	0.42–1.28	0.273
Vasospasm (none/mild vs moderate/severe)	0.51	0.28–0.93	0.0269*
Difference in total GCS score btwn preop & postop Day 1†	0.86	0.78–0.95	0.0032*

* p < 0.05.

† The GCS aggregate score.

Conclusions

Patients undergoing neurosurgical clipping exhibited a significantly worse decline in postoperative GCS score compared with those undergoing endovascular coiling. Postoperative GCS score decline is also independently associated with long-term outcomes. Our results suggest that adverse events occurring in the perioperative period, which disproportionately affected patients who underwent neurosurgical clipping, independently contributed to poor long-term outcomes, and this finding supports existing data on outcome differences between clipping and coiling after aSAH. The rates of perioperative complications must therefore be considered when comparing the efficacy and safety of the different aneurysm-securing procedures, as well as when forming institutional and personal policies toward the treatment of aSAH.

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Conception and design: Macdonald. Acquisition of data: Ayling, Ibrahim. Analysis and interpretation of data: Macdonald, Ayling, Ibrahim. Drafting the article: Macdonald, Ayling, Ibrahim. Critically revising the article: all authors. Reviewed submitted version of manuscript: Macdonald. Approved the final version of the manuscript on behalf of all authors: Macdonald. Statistical analysis: Ayling, Ibrahim. Study supervision: Macdonald.

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