Manipulation of intracranial arteries is associated with consistent vessel diameter reductions during microsurgical aneurysm clipping

Peer-reviewed author version

Kashtiara, A; RAYMAEKERS, Vincent; Thijs, D; Aboukais, R; Devalckeneer, A; Bourgeois, P; Boogaarts, HD & Menovsky, T (2025) Manipulation of intracranial arteries is associated with consistent vessel diameter reductions during microsurgical aneurysm clipping. In: Neurosurgical Review, 48 (1) (Art N° 532).

DOI: 10.1007/s10143-025-03573-3
Handle: http://hdl.handle.net/1942/49352

Title page

Title

Manipulation of intracranial arteries are associated with consistent vessel diameter reductions during microsurgical aneurysm clipping

Authors

Ardavan Kashtiara, M.D. [a, b, c]; Vincent Raymaekers, M.D. [a, b, d]; Dieter Thijs, M.D [a, b, c], Rabih Aboukais, M.D. PhD. [e]; Antoine Devalckeneer, M.D. [e]; Philippe Bourgeois, M.D. [e]; Hieronymus Damianus Boogaarts, M.D. PhD [f]; Tomas Menovsky, M.D. PhD [a, b, g]

Affiliations:

[a] Department of Neurosurgery, Antwerp University Hospital, Edegem, Belgium

[b] Faculty of Medicine and Health sciences, University of Antwerp, Antwerp, Belgium

[c] Department of Neurosurgery, VITAZ hospital, Sint-Niklaas, Belgium

[d] Faculty of Medicine and Life Science, Hasselt University, Hasselt, Belgium

[e] Department of Neurosurgery, Lille University hospital, Lille, France

[f] Department of Neurosurgery, Radboud University Medical Center, Nijmegen, The Netherlands

[g] Department of Translational Neurosciences, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium

Corresponding author

Ardavan Kashtiara

Department of Neurosurgery at university hospital Antwerp

ardavan.kashtiara@uza.be

Key words:

1. Intracranial arteries 2. Intracranial aneurysms 3. Aneurysm clipping 4. Ruptured aneurysms 5. Non-ruptured aneurysms 6. Symptomatic vasospasm

Word count

Abstract: 253

Text: 2094

Number of tables: 5

Number of figures: 1

Number of videos: 0

Previous presentations

None.

Funding

We declare that this study did not receive any funding.

Ethics declaration

Ethics declaration: not applicable since this is a retrospective study.

Abbreviation list:

A1 – A1 segment anterior cerebral artery

ACA – Anterior cerebral artery

Acom – Anterior communicating artery

aSAB – Aneurysmal subarachnoid hemorrhage

CHU Lille – Centre Hospitalier Universitaire de Lille

CT – Computed tomography

D – Diameter

DCI – Delayed cerebral ischemia

EVD – External ventricular drain

GCS – Glasgow coma scale

ICH – Intracerebral hemorrhage

IQR – Interquartile range

MCA – Middle cerebral artery

mRS – Modified Rankin Scale

OR – Odds ratio

Pcom – Posterior communicating artery

PICA – Posterior inferior cerebellar artery

RA – Ruptured aneurysm

SAH – Subarachnoid hemorrhage

SVS – Symptomatic vasospasm

UZA – Universitair Ziekenhuis Antwerpen

WFNS – World Federation of Neurosurgical Societies scale

Abstract:

OBJECTIVE: To report the rate of diameter reduction of intracranial arteries during aneurysm clipping. Also, in the subset of ruptured aneurysm (RA) the relationship between diameter reduction and symptomatic vasospasm (SVS) Is investigated.

METHODS: A retrospective dataset containing demographics, aneurysm characteristics, vessel dynamics and SVS in adults with surgically clipped intracranial aneurysms was analyzed. The vessel diameters were recorded intraoperatively, both pre- and post-clipping. SVS was assessed by transcranial doppler ultrasound or CT-angiogram in the presence of neurological deterioration. Backward multivariable logistic regression models were applied to define variables associated with SVS.

RESULTS: A total of 117 surgically clipped adults with intracranial aneurysms were included of which 49 (42%) presented with subarachnoid hemorrhage due to a RA. Intraoperatively measured vessel diameters were smaller in the RA group compared to the non-RA group. The vessel diameter changes before and after placement of the surgical clip are comparable in all groups, with a mean reduction of 15% (RA, non-RA, SVS and no-SVS). Incidence of SVS was 57.1% (in RA group), mean age 53 years and 73.5% were women. Female sex was independently associated with the occurrence of SVS ($p = .024$)

CONCLUSIONS: Surgical aneurysm manipulation leads to a consistent reduction of 15% in intracranial artery diameters. Although vessel diameters are smaller in patients with RA compared to non-RA, there is no difference in intraoperative vessel diameter dynamics for both groups. We found no association between the degree of vessel diameter reduction and the occurrence of symptomatic vasospasm in the RA group.

Manuscript:

INTRODUCTION

Vessel diameter reduction during surgical clipping of intracranial aneurysm is frequently encountered, presumably due to direct vessel manipulation. While surgical aneurysm clipping is widely practiced, the dynamic changes in the diameter of intracranial arteries during surgery have not been extensively investigated. The main focus of this study is to investigate the occurrence of diameter changes of intracranial arteries during aneurysm clipping for both RA and non-RA and to objectify these diameter changes. In the subgroup of ruptured aneurysm (RA) one could hypothesize that more reactive blood vessels (i.e., greater diameter reduction during the surgical procedure) could lead to a higher rate of symptomatic vasospasm (SVS). The pathogenesis of SVS is complex, and multiple risk factors such as age, aneurysm location, modified Fisher grade, the amount of blood in the Sylvian fissure, smoking and hypertension have been identified in previous studies. [1-4]. This study also aims to investigate the relationship between intraoperative changes in vessel diameters and the subsequent occurrence of SVS.

METHODS

Study design and participants

In this cohort study, data from two neurovascular referral hospitals were retrospectively collected. All surgically clipped RA and non-RA between July 2020 and December 2022 were eligible for inclusion. The aneurysm clipping procedures were performed by vascular neurosurgeons. Both neurosurgical departments routinely measured and documented vessel diameters pre- and post-clipping using a micro-ruler (see figure 1.) for all surgically treated aneurysms, as a standard of care. Only vessels that had been exposed for the aneurysm treatment, were analyzed. No additional dissection was done solely for the purpose of this study. Ethical board approval was unnecessary given the analysis of anonymized patient data and the standard of care treatment that was not altered for this study.

Data collection and outcome measures

Clinical data were obtained by reviewing electronic medical records. Treating hospital, age, gender, arterial hypertension, smoking, history of RA, polycystic kidney disease, familial history of intracranial aneurysms, multiple intracranial aneurysms, the indication for clipping, preoperative vasospasm, World Federation of Neurosurgical Societies scale (WFNS), GCS at admission, presence of subarachnoid hemorrhage (SAH), presence of intracerebral hemorrhage (ICH), modified Fisher grading scale, external ventricular drain placement (EVD), aneurysm size, localization of the primary treated aneurysm, laterality of the primary treated aneurysm, localization of a secondary aneurysm, SVS (after clipping), endovascular treatment for SVS, delayed cerebral ischemia (DCI), shunting for hydrocephalus, SVS with focal neurological deficit, modified Rankin score (mRS) at three months and presence of neuropsychological problems at last follow-up were analyzed. Data regarding the blood vessel diameters (parent artery, bifurcation and secondary bifurcation artery) before and after clipping, duration between measurements and relative reduction in diameter pre- and post-clipping (in percentage) were obtained from the surgical reports. The diagnosis of SVS was made following the criteria defined by the Japanese consensus of 2009 : 1. The presence of neurological worsening; 2. No other identifiable cause of neurological worsening (e.g. hydrocephalus, infection); and 3. Confirmation of vasospasm on medical imaging. [5] In this study both transcranial doppler ultrasound as well as CT-angiography were used as medical imaging modalities and the results were interpreted by either a vascular neurologist or neurovascular interventional radiologist.

Statistical analysis

Data are presented as mean +/- standard deviation, median (interquartile range / IQR), or frequencies (percentage), when appropriate. Groups were compared with the unpaired student's t-test for normally distributed variables, the Mann-Whitney U test for skewed variables and the chi-squared test for categorical variables. A correlation matrix was created to examine multicollinearity. Multivariable logistic regression analysis was performed to identify factors independently associated with SVS. Analyses were performed using SPSS software version 29.

RESULTS

RA versus no-RA group

A total of 117 adults were included, of which 68 had surgery for non-RA and 49 for RA. Baseline characteristics for both groups are listed in tables 1 and 2. Baseline characteristics such as sex, age, history of smoking and arterial hypertension did not differ between the groups. Also, the aneurysm related variables such as size, location and side of ruptured aneurysm did not differ between the groups. The non-RA group had zero cases of SVS compared to the 57.1% in the RA-group ($p < .001$). Patients with RA had a significantly higher intra-operative rupture rate (32.7% vs. 4.4%, $p < .001$). The initial diameter of the feeding artery in RA and the first post-bifurcation artery was smaller compared to the non-RA group (respectively 2.5 mm vs 3 mm, $p < .001$ and 1.7 mm vs. 2.0 mm, $p = .002$). There was no difference between the two groups regarding the relative vessel diameter reduction pre- and post-clipping.

Table 3 presents a comparison of the feeding artery diameters of the main arterial branches of the aneurysms in both the RA and non-RA group based on location of the aneurysm. Both MCA and the internal carotid artery were significantly smaller in the RA-group compared to the non-RA group, respectively 2 mm vs 3 mm ($p < .001$) and 3.5 mm vs 4 mm ($p = .04$).

SVS versus no-SVS group

Baseline characteristics are listed in table 4, grouped by SVS status within the RA-group since no SVS were observed in the non-RA group. 28 adults (57.1%) within the RA-group had SVS. In the SVS-group there was a higher rate of female sex ($p = .025$), history of smoking ($p = .017$) and right sided aneurysms ($p = 0.007$).

mRS at three months was worse in the SVS-group ($p < .001$). Age, arterial hypertension, aneurysm size, aneurysm location, GCS at admission, WFNS-grade, Fisher grading scale, presence of ICH, EVD placement and chronic hydrocephalus were comparable between the SVS and the no-SVS group. Finally, all the operative-related variables of measured vessel diameters were comparable between the two groups.

Variables independently related to SVS

Table 5 presents the variables associated with SVS in a multivariable logistic model. Gender, history of smoking, age, localization of aneurysm, history of arterial hypertension and modified fisher grading scale were entered in successive multiple regression models. According to this model female gender is associated with symptomatic vasospasm (OR 7.4, p value of 0.024).

DISCUSSION

To the best of our knowledge, this study is the first to investigate intraoperatively measured artery diameters during intracranial aneurysm clipping and its potential relationship with SVS. In the RA group the intraoperatively measured absolute diameters of the feeding artery and bifurcation artery were smaller compared to the non-RA group ($p < .001$). This held true for different aneurysm locations, such as the middle cerebral artery (median of 2 mm compared to 3 mm, $p < .001$) and the internal carotid artery (median of 3.5 mm compared to 4 mm, $p = .04$). In their meta-analysis regarding the diameters of the intracranial arteries, Mirza et al. reported a mean of 2.55 mm +/- 0.42 for the middle cerebral artery and 3.93 mm +/- 0.79 for the internal carotid artery. [6] A reduction in absolute vessel diameter of the large vessels has been observed in mice with induced subarachnoid hemorrhage. Neulen et al. reported this vessel diameter reduction and observed that hypoperfusion occurred independently of this diameter reduction. [7] Wang et al. reported that in patients with ruptured aneurysms (RA), both vessel diameter and flow velocity decreased, with lower values observed a few days after the rupture compared to the first day.

[8] However, there was no comparison between the RA and the non-RA group. The pathophysiology of this phenomenon is not well understood but is thought to be related to an inflammatory cascade leading to vascular wall irritation and subsequent vessel diameter and velocity reduction. [9] Therefore, the current study adds to the limited data of predominantly in vivo studies describing reduced vessel diameter in adults with RA. Next, diameter reduction was compared between RA and non-RA groups, something not previously reported in the literature. Interestingly, the relative diameter reduction pre- and post-clipping was comparable between the two groups with a mean of 15% +/- 12. A subgroup analysis of the SVS and no-SVS group within the RA group, did not show a difference regarding the relative diameter reduction or the absolute diameter values, even after correction for the location of the aneurysms. No correlation was found between the diameter dynamics during the surgical procedure and the occurrence of SVS both for RA and non-RA. These findings suggest that vessel diameter reduction is a direct effect of the surgical manipulation of the arteries, and not solely dependent on the presence or absence of rupture and blood in the subarachnoid space. The pathophysiology of symptomatic vasospasm and DCI is not only based on the reduction of vessel diameter, but other mechanisms are involved such as inflammation and immunologic factors. Even with the diameters of the vessels being reduced during surgery, it is apparent that the flow was maintained sufficiently since not all patients experience DCI. These findings may seem intuitive, however it still important to objectify the vessel diameter reduction with clinical studies to further understand intracranial aneurysms. Cerebral autoregulation and anesthetic parameters also play a role in maintaining good cerebral perfusion during aneurysmal clipping. These findings challenge a widely accepted assumption about the risk of SVS occurrence in microsurgical clipping of RA.

Several risk factors for SVS have been previously identified in the literature. Our study reveals female sex as an independent risk factor for SVS within the RA-group. The rate of smokers was higher in the SVS group but did not reach statistical significance in the multivariate analysis. Regarding the proportion of patients with ruptured aneurysm developing SVS, a recent meta-analysis by Donaldson et al.

made a pooled estimate of 42% (95% CI 0.39 – 0.46)[10], slightly below the present incidence of 57.1%. In contrast, a range of 30-70% has been reported earlier. [11] Both ruptured and non-ruptured aneurysms occur more often in women, with a meta-analysis by De Rooij et al. reporting that 65% of aneurysms occur in females . [12] In this study we report a similar incidence of 73.5%. A meta-analysis by Chandra et al. reported a mean age of 58.3 years +/- 7.1 for ruptured aneurysm. [13] In this study we report a similar mean age of 53 years +/- 13. 61.2% of adults in the RA-group had a mRS of 2 or less at three months, confirming earlier reports. [14]

Multiple studies have correlated the presence of subarachnoid hemorrhage, smoking, history of hypertension, younger age, female sex, modified Fisher grade and amount of blood in the Sylvian fissure with the occurrence of SVS [1-4,15,16] In this study, not all of these correlations were confirmed. In the univariate analysis, a correlation between female sex ($p = 0.025$) and smoking ($p = .017$) and the occurrence of SVS was found. Right-sided aneurysms are more prevalent in the SVS group ($p = .007$). However, a collinearity matrix showed that this finding is confounded, as most right-sided ruptured aneurysms in this study population were found in smokers ($p = .018$). Since no previous reports indicate a higher incidence of SVS in right-sided ruptured aneurysms, we omitted this finding from the multivariate analysis. The final multivariate model, containing female sex, smoking and other potential risk factors (age, localization of aneurysm, history of arterial hypertension, modified Fisher grade), confirmed female sex as an independent risk factor for the occurrence of SVS. Finally, there was no correlation between the occurrence of ruptured aneurysms and the development of SVS.

Some strengths of this study are as follows. The study includes a representative population containing both ruptured and non-ruptured aneurysms, making comparison to a control group possible. Second the data is diversified by including patients from two tertiary centers. A standardized definition of SVS was used, making future comparison with other studies easier. All aneurysms were operated in the first 24 hours, before the occurrence of symptomatic vasospasm (usually between day 4 and 10), making it possible to assess the arteries when cerebral autoregulation is still effective. Some limitations of this study are as follows. The vessel diameters were all grouped together regardless of the aneurysm location leading to confounding. However, the aneurysm locations are evenly distributed, mitigating this issue. The current study design does not allow to draw conclusions on causality. Furthermore, we do not report racial characteristics of the patients. Also, there was no assessment of the arterial blood flow during surgery. It can be argued that using a micro-ruler can potentially lead to inaccurate measurements due to microscope angle and ruler placement, however the relative diameter reduction measured via this method remains accurate. Also the arteries themselves are barely touched by the ruler, reducing potential bias by artery manipulation due to the pressure of the micro-ruler.

CONCLUSIONS

In conclusion, surgical manipulation leads to consistent vessel diameter reduction of 15% during surgical clipping of intracranial aneurysms. Intraoperatively measured arterial diameters were smaller in the RA group compared to the non-RA group. The diameter changes before and after placement of a surgical clip are comparable in all groups (RA, no-RA, SVS and no-SVS). There is no association between vessel diameter changes and the occurrence of SVS. Multivariable logistic regression analysis showed that female sex was independently associated with SVS.

Disclosures-conflict of interest:

The authors declare to have no conflicts of interest to disclose.

Funding

We declare that this study did not receive any funding.

References

1. Zhou Y, Qian D, Zhou Z, Li B, Ma Y, Chai E. A nomogram for predicting the risk of cerebral vasospasm after neurosurgical clipping in patients with aneurysmal subarachnoid hemorrhage. *Frontiers in Neurology.* 2024;15.
2. Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. *Neurosurgery.* 1980;6(1):1-9.
3. Nomura Y, Kawaguchi M, Yoshitani K, et al. Retrospective analysis of predictors of cerebral vasospasm after ruptured cerebral aneurysm surgery: influence of the location of subarachnoid blood. *J Anesth.* 2010;24(1):1-6.
4. Inagawa T, Yahara K, Ohbayashi N. Risk factors associated with cerebral vasospasm following aneurysmal subarachnoid hemorrhage. *Neurol Med Chir (Tokyo).* 2014;54(6):465-473.
5. Shirao S, Yoneda H, Ishihara H, Kajiwara K, Suzuki M. A proposed definition of symptomatic vasospasm based on treatment of cerebral vasospasm after subarachnoid hemorrhage in Japan: Consensus 2009, a project of the 25 Spasm Symposium. *Surg Neurol Int.* 2011;2:74.
6. Mirza M, Kummer K, Touchette J, et al. Variability in Intracranial Vessel Diameters and Considerations for Neurovascular Models: A Systematic Review and Meta-Analysis. *Stroke: Vascular and Interventional Neurology.* 2024;4(4):e001177.
7. Neulen A, Meyer S, Kramer A, et al. Large Vessel Vasospasm Is Not Associated with Cerebral Cortical Hypoperfusion in a Murine Model of Subarachnoid Hemorrhage. *Translational Stroke Research.* 2019;10(3):319-326.
8. Wang RL, Gingrich KJ, Vance A, Johnson MD, Welch BG, McDonagh DL. The effects of aneurysmal subarachnoid hemorrhage on cerebral vessel diameter and flow velocity. *Journal of Stroke and Cerebrovascular Diseases.* 2023;32(5):107056.
9. Lucke-Wold BP, Logsdon AF, Manoranjan B, et al. Aneurysmal Subarachnoid Hemorrhage and Neuroinflammation: A Comprehensive Review. *International Journal of Molecular Sciences.* 2016;17(4). doi:10.3390/ijms17040497.
10. Donaldson L, Edington A, Vlok R, et al. The incidence of cerebral arterial vasospasm following aneurysmal subarachnoid haemorrhage: a systematic review and meta-analysis. *Neuroradiology.* 2022;64(12):2381-2389.
11. Imamura H, Tani S, Adachi H, et al. Comparison of Symptomatic Vasospasm after Surgical Clipping and Endovascular Coiling. *Neurol Med Chir (Tokyo).* 2022;62(5):223-230.
12. de Rooij NK, Linn FH, van der Plas JA, Algra A, Rinkel GJ. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. *J Neurol Neurosurg Psychiatry.* 2007;78(12):1365-1372.
13. Chandra RV, Maingard J, Slater L-A, et al. A Meta-Analysis of Rupture Risk for Intracranial Aneurysms 10 mm or Less in Size Selected for Conservative Management Without Repair. *Frontiers in Neurology.* 2022;12.
14. Natarajan SK, Sekhar LN, Ghodke B, Britz GW, Bhagawati D, Temkin N. Outcomes of ruptured intracranial aneurysms treated by microsurgical clipping and endovascular coiling in a high-volume center. *AJNR Am J Neuroradiol.* 2008;29(4):753-759.
15. Khan MM, Shaikh N, Yousaf Z, et al. Risk Factors for Cerebral Vasospasm in Patients with Aneurysmal Subarachnoid Hemorrhage: A Tertiary Care Center Experience. *Asian J Neurosurg.* 2022;17(2):242-247.
16. Rumalla K, Lin M, Ding L, et al. Risk Factors for Cerebral Vasospasm in Aneurysmal Subarachnoid Hemorrhage: A Population-Based Study of 8346 Patients. *World Neurosurgery.* 2021;145:e233-e241.

Figure legend

Figure 1. Intraoperative measurement of the C7 segment of the internal carotid artery during microsurgical aneurysm clipping using a 0.1-mm ruler.