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ORIGINAL ARTICLE - VASCULAR NEUROSURGERY - ANEURYSM

Ruptured PICA aneurysms: presentation and treatment outcomes compared to other posterior circulation aneurysms. A Swiss SOS study

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Abstract

Background and purpose Aneurysms of the posterior inferior cerebellar artery (PICA) are relatively uncommon and evidence is sparse about patients presenting with ruptured PICA aneurysms. We performed an analysis of the Swiss SOS national registry to describe clinical presentation, treatment pattern, and neurological outcome of patients with ruptured PICA aneurysms compared with other ruptured posterior circulation (PC) aneurysms.

Methods This was a retrospective analysis of anonymized data from the Swiss SOS registry (Swiss Study on Aneurysmal Subarachnoid Hemorrhage; 2009–2014). Patients with ruptured PC aneurysms were subdivided into a PICA and non-PICA group. Clinical, radiological, and treatment-related variables were identified, and their impact on the neurological outcome was determined in terms of modified Rankin score at discharge and at 1 year of follow-up for the two groups.

Results Data from 1864 aneurysmal subarachnoid hemorrhage patients were reviewed. There were 264 patients with a ruptured PC aneurysm. Seventy-four PICA aneurysms represented 28% of the series; clinical and radiological characteristics at admission were comparable between the PICA and non-PICA group. Surgical treatment was accomplished in 28% of patients in the PICA group and in the 4.8% of patients in the non-PICA group. No statistically significant difference was found between the two groups in terms of complications after treatment. Hydrocephalus requiring definitive shunt was needed in 21.6% of PICA patients ($p = 0.6$); cranial nerve deficit was present in average a quarter of the patients in both PICA and non-PICA group with no statistical difference ($p = 0.3$). A more favorable outcome (66.2%) was reported in the PICA group at discharge ($p < 0.05$) but this difference faded over time with a similar neurological outcome at 1-year follow-up ($p = 0.09$) between both PICA and non-PICA group. The Kaplan-Meyer estimation showed no significant difference in the mortality rate between both groups ($p = 0.08$).

Conclusions In the present study, patients with ruptured PICA aneurysms had a favorable neurological outcome in more than two thirds of cases, similar to patients with other ruptured PC aneurysms. Surgical treatment remains a valid option in a third of cases with ruptured PICA aneurysms.

Keywords Aneurysmal subarachnoid hemorrhage · Posterior circulation · Posterior inferior cerebellar artery · Intracranial aneurysms · Endovascular procedures · Intracranial vasospasm · Hydrocephalus

Introduction

Aneurysms of the posterior inferior cerebellar artery (PICA) are relatively uncommon, representing approximately 0.5 up to 3% of all intracranial aneurysm. [10, 14, 31]

Despite recent advancements in endovascular and microsurgical techniques, treatment of ruptured PICA aneurysms remains challenging due to the rarity of these aneurysms and

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their location in the proximity to the brainstem and lower cranial nerves. [14]

Evidence about clinical presentation, treatment modalities, and complications is sparse for patients with ruptured PICA aneurysms [14, 24, 31] and published data about neurological outcome are controversial [3, 5–7, 9, 24, 31]. Furthermore, the available literature shows that patients with ruptured PICA aneurysms may present a more unfavorable clinical outcome when compared with patients with other ruptured PC aneurysms. This difference is attributed to the particular anatomical characteristics of ruptured PICA aneurysms with more severe neurological compromise at presentation. [31] In the BRAT study, [31] 91% of patients with ruptured PICA aneurysms presented an unfavorable neurological outcome due to a higher rate of persistent lower cranial nerve deficit compared to patients with ruptured aneurysm in other locations. Additionally, PICA aneurysms have been associated with a higher rate of intraventricular hemorrhage and secondary hydrocephalus, due to their localization near the Luschka and Magendie foramen. Nevertheless, more recent large series contradicted the results of the BRAT series, showing a favorable neurotological outcome for patients with ruptured PICA aneurysms in up to 80% of patients.

In an attempt to characterize clinical presentation, treatment patterns, and neurological outcome of patients with ruptured PICA aneurysms in Switzerland, we reviewed the data from the nationwide Swiss SOS database on aneurysmal subarachnoid hemorrhage (Swiss SOS study; http://www.swiss-sos.ch). [23]

Methods

We performed a retrospective analysis of anonymized data of patients suffering from a posterior circulation ruptured aneurysm from the Swiss SOS registry, a nationwide cohort study for aSAH (https://clinicaltrials.gov/ct2/show/NCT03245866).

Ethics committee approval was obtained from all seven participating centers (under the supervision of the Geneva Ethics Committee Board no. 11-233R, NAC 11-085R). Prespecified uniform definitions were used for recorded variables, and data were entered into a Secutrial™ platform (InterActive Systems GmbH, Berlin, Germany), at the time of patient discharge and follow-up. Swiss SOS study registry and methods of collection of data and analysis have been published previously. [4, 16, 21, 26, 32]

Collected data included patient characteristics in terms of age, sex, World Federation of neurosurgical Society (WFNS) grading scale [17] and Fisher grade [8] at admission, presence of cranial nerve deficit (at admission, discharge, and 1-year follow-up), epilepsy, aneurysm morphology (fusiform vs. saccular), treatment modalities, and modified Rankin Scale (mRS) score at discharge and at 1 year.

The complications considered in our analysis were the following:

- Rebleeding before aneurysm occlusion: a sudden clinical deterioration with signs of increased hemorrhage on consecutive computed tomography (CT) scans, or if no CT scan was obtained, sudden clinical deterioration suspected to be the cause of rebleeding with fresh blood in the ventricular drain. In addition, acute clinical deterioration (e.g., acute neurological deterioration, bradycardia, or sudden blood hypertension) at the emergency department or before imaging was considered as rebleeding. Acute clinical deterioration before admission was not taken into account. [29]
- Hydrocephalus defined as the dilatation of the cerebral ventricles requiring cerebrospinal fluid (CSF) diversion (EVD or VP shunt placement);
- Symptomatic vasospasm requiring endovascular treatment (chemical and/or mechanical dilatation);
- Clinical deterioration attributable to delayed cerebral ischemia (DCI) defined as the development of new focal neurological signs and/or deterioration in level of consciousness, lasting for more than 1 h without other reasons explaining the condition. [30]
- Cerebral infarction attributable to DCI and not related to the primary bleed or treatment [30];

The performance status at discharge and 1 year was assessed according to the mRS scale [28] and dichotomized in favorable (mRS 0–3) and unfavorable (mRS 4–5); in order to better compare our outcome to that of previously published series, the dichotomization into mRS 0–2 and 4–5 is also reported in Table 4.

Statistical analysis

Patient characteristic, treatment modalities, and complication data both from patients with ruptured PICA and non-PICA aneurysms were compared using Fisher's exact test and Chi-square test.

For correlation analysis between clinical, radiological, treatment variables, and mRS at discharge, the Fisher's, the Chi-square, and Mann-Whitney tests were used.

Survival time (months) was estimated by means of the Kaplan-Meier function, whereby data were censored for patients alive at the last known follow-up date. A log-rank test was applied to compare the survival curves of the three groups. The Kaplan-Meier function was also used to estimate median length of follow-up, with data censored in case of death. We analyzed the data on the statistical Stata®, version 14 (StataCorp LP, Lakeway Drive, Texas - USA). A p value < 0.05 was considered significant.

Results

From January 1st 2009 to December 31st 2014, among 1864 eligible aSAH patients, 264 (14.2%) patients presented with a ruptured posterior circulation aneurysm. The mean age was 55.8 years (range 16–88). A female preponderance was observed with 180 women (68.2%). PICA aneurysms (74 patients) represented 28% of the overall series; clinical and radiological characteristics at admission were comparable between patients of PICA and non-PICA group (Table 1).

No difference was found within the two groups in terms of Fisher grade, with the majority of patients (> 90%) presenting with large extent of blood in the subarachnoid space and within the ventricles (Fisher III and IV). There was no difference among PICA and non-PICA patients regarding the presence of cranial nerve deficit at admission.

Endovascular occlusion was the treatment modality in more than 70% of non-PICA aneurysms and 55% of PICA aneurysms. Surgical treatment represented the treatment modality in 28% in the PICA group compared to 4.8% in the non-PICA group (Table 2).

No significant difference was found between the PICA and non-PICA groups in terms of complications (Table 2).

Aneurysm rebleeding before treatment occurred in 1.8% of PICA patients and 6.8% of non-PICA patients. A total of 21.6% of PICA patients presented hydrocephalus requiring definitive shunt placement compared with 24.1% of non-PICA patients ($p = 0.6$). Cranial nerve deficit and clinical deterioration attributable to DCI occurred in average a quarter of both PICA and non-PICA patients.

At discharge, 49 patients (66.2%) with ruptured PICA aneurysms presented a favorable outcome (mRS score 0–3) compared to 52.1% in the non-PICA group ($p < 0.05$) but this difference faded over time with a comparable outcome at 1 year (mRS 0–3) in 73.9% of PICA patients vs. 62.4% of non-PICA patients, respectively; $p = 0.09$) (Table 4).

The aneurysm shape (fusiform or saccular) did not influence the neurological outcome in the PICA group ($p = 0.23$).

In the overall series, age > 65 years, high WFNS (3–5) and Fisher grade (3–4) at presentation, hydrocephalus and aneurysm rebleeding before treatment were correlated with unfavorable neurological outcome death and at discharge and at 1-year follow-up.

The mortality rate during the overall period of observation was 5%. The mortality rate was 3.4% in the PICA group and 5.8% in the non-PICA group. Despite the fact that the Kaplan-Meyer estimation showed no significant difference in the mortality rate between both PICA and non-PICA group, there was a tendency of favorable outcome in the PICA group ($p = 0.087$) (Fig. 1).

Discussion

Ruptured PICA aneurysms are less frequent than other ruptured posterior circulation aneurysms and treatment remains challenging despite advances both in endovascular and microsurgical techniques. [31]

In the BRAT series reported by Williamson and coworkers, among 22 patients with ruptured PICA aneurysm, unfavorable outcome was reported in 91% of patients at discharge and 63% at 3 years [31]. The high rate of unfavorable neurological outcome for PICA patients in the BRAT cohort was apparently related to the higher rate of lower cranial nerve deficit in the PICA group compared to patients with ruptured aneurysms in other locations. Furthermore, the extent of blood in the

Table 1 Clinical and radiological characteristics at presentation: correlation with aneurysm location

	Aneurysm location		Total no. (% of the overall series)	*P* value
	PICA (%)	Non-PICA (%)		
Number of patient	74 (28)	190 (72)	264	–
Mean age (years)	54 (25–82)	56 (16–88)	55 (16–88)	0.3[b]
Female	49/74 (66.2)	131/190 (68.9)	180/264 (68.2)	0.7[b]
WFNS at admission				
Low (1 or 2)	37/74 (50)	82/187 (43.9)	119/261 (45.6)	0.4[a]
High (3–5)	37/74 (50)	105/187 (56.1)	142/261 (54.4)	
Cranial nerve deficit at admission	11/64 (17.2)	38/175 (21.7)	49/239 (20.5)	0.4[b]
Epilepsy	8/49 (16.3)	18/106 (17)	26/155 (16.8)	0.9[b]
Fisher grade				
Low (1–2)	6/74 (8.1)	19/190 (10)	25/264 (9.5)	0.6[b]
High (3–4)	68/74 (91.9)	171/190 (90)	239/264 (90.5)	
Intraventricular hemorrhage	36/45 (80)	77/109 (70.6)	113/154 (73.4)	0.2[b]

[a] Fisher exact test

[b] Pearson Chi^2

Table 2 Treatment and complications

Treatment	Aneurysm location		Total no. (% of the overall series)	*P* value
	PICA (%)	Non-PICA (%)		
Endovascular	41/74 (55.4)	133/189 (70.4)	174/263 (66.2)	*< 0.00001*[a]
Surgery	21/74 (28.4)	9/189 (4.8)	30/263 (11.4)	
Combined	0/74	8/189 (4.2)	8/263 (3)	
None	12/74 (16.2)	39/189 (20.6)	51/263 (19.4)	
Complications				
Hydrocephalus with temporary CSF diversion (EVD placement)	50/70 (71.4)	122/178 (68.6)	172/248 (69.4)	0.66[b]
Hydrocephalus with definitive CSF diversion (VP shunt)	16/74 (21.6)	45/187 (24.1)	61/261 (23.4)	0.67[b]
Vasospasm requiring EVT (chemical or mechanical dilatation)	11/73 (15.1)	24/178 (13.5)	35/251 (13.9)	0.74[b]
Clinical deterioration secondary to DCI	16/64 (25)	45/164 (27.4)	61/228 (26.8)	0.7[b]
Cerebral infarction related to DCI	7/48 (14.6)	19/108 (17.6)	26/156 (16.7)	0.64[b]
Rebleeding before aneurysm treatment	1/56 (1.8)	8/126 (6.4)	9/182 (5)	0.28[a]
Cranial nerve deficit at discharge	12/61 (19.7)	38/146 (26)	50/207 (24.2)	0.33[b]
Cranial nerve deficit at 12 months	10/69	35/173	45/242	0.3[b]

[a] Fisher exact test

[b] Pearson Chi^2

Italics: probability as calculated with the Fisher exact test for the different treatment modalities. There was a significant statistical difference with a prevalence of endovascular occlusion ($p < 0.00001$)

CSF cerebrospinal fluid, *DCI* delayed cerebral ischemia (see text for details), *EVD* external ventricular drainage, *EVT* endovascular treatment, *VP shunt* ventriculo-peritoneal shunt

subarachnoid compartment with mass effect on the brainstem and the aneurysm shape (fusiform) was also considered responsible for the higher rate of unfavorable neurological outcome in the PICA group [31].

Our data, however, show a pattern that is different from the BRAT series where the outcome of patients with ruptured PICA aneurysms was not inferior to the non-PICA group.

The rate of cranial nerve deficit was also similar in both PICA and non-PICA group with no effect on neurological outcome. This was also evidenced from the multicenter study from Sejkorová and Lanzino [24] that analyzed patients with 83 PICA aneurysms (65 ruptured). The authors showed that despite a higher rate of lower cranial nerve deficit (50%) in the PICA group, a large number of these patients (> 76%) recovered from the cranial nerve deficit within 6 months from the aneurysm treatment [24]. In our series, PICA patients presented a more favorable outcome at discharge when compared with other non-PICA patients, but this difference faded out with a comparable neurological outcome at follow-up among both groups.

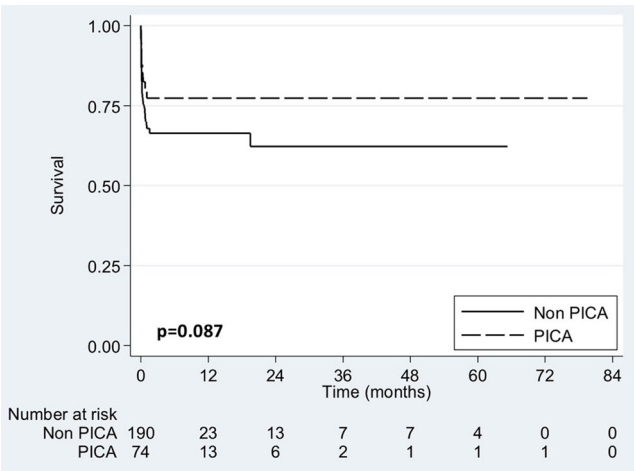

Fig. 1 Kaplan-Meier survival estimate of patients with ruptured PICA aneurysms compared to other PC ruptured aneurysms from the Swiss SOS cohort. *P* value was determined by using the log-rank test.

In our series, converse to the BRAT cohort, the aneurysm shape did not influence the neurological outcome in both PICA and non-PICA patients. This could be due to the fact that the BRAT cohort for ruptured PICA aneurysms had confounded data due to a skewed randomization with 86.4% of patients with PICA aneurysms assigned to clipping. As known from literature, the surgical occlusion of fusiform PICA aneurysms is more challenging than the treatment of their saccular counterpart (mortality rate between 40 and 61%), [11, 13] while the mortality rate of endovascular treatment of fusiform PICA aneurysms is lower when compared to surgery in the current era of flow diversion. [2]

As in the BRAT series, our data showed that a large amount of blood in the subarachnoid compartment and/or intraventricular bleeding (Fisher grade 3–4) correlated with unfavorable outcome (Table 3). In our series, 80% of patients in the PICA group presented with intraventricular hemorrhage, with no difference with the non-PICA group (70.6%, $p = 0.2$).

Table 3 Correlation analysis between clinical, radiological, treatment variables and mRS at discharge

Variables	mRS at discharge			*P* value
	Favorable outcome *N* (%)	Unfavorable outcome *N* (%)	Dead *N* (%)	
PICA/nonPICA				
PICA	49 (66.2)	11 (14.9)	14 (18.9)	0.047[a]
Non-PICA	99 (52.1)	40 (21.1)	51 (26.8)	
PICA fusiform	7 (87.5)	0	1 (12.5)	0.23[a]
PICA sacciform	42 (63.6)	11 (16.7)	13 (19.7)	
Whole series				
Age ≥ 65 years	22 (36.1)	17 (27.8)	22 (36.1)	0.002[b]
Female	105 (58.3)	36 (20)	39 (21.7)	0.26[b]
High WFNS (3 + 4 + 5)	49 (34.5)	40 (28.2)	53 (37.3)	*< 0.001*[b]
High Fisher grade (3 + 4)	125 (52.3)	50 (20.9)	64 (26.8)	*0.001*[c]
Aneurysm shape (fusiform)	17 (63)	3 (11.1)	7 (25.9)	0.612[a]
Craniectomy	8 (42.1)	7 (36.8)	4 (21.1)	0.14[c]
Hydrocephalus	81 (47.1)	44 (25.6)	47 (27.3)	0.03[b]
Epilepsy	11 (42.3)	8 (30.8)	7 (26.9)	0.23[b]
Vasospasm requiring EVT	20 (57.1)	11 (31.4)	4 (11.4)	0.08[c]
Rebleeding before aneurysm treatment	1 (11.1)	1 (11.1)	7 (77.8)	*0.001*[c]
	mRS at 12 Mo			
PICA/non-PICA				
PICA	51 (73.9)	3 (4.4)	15 (21.7)	0.09[a]
Non-PICA	108 (62.4)	9 (5.2)	56 (32.4)	
PICA fusiform	6 (85.7)	0	1 (14.3)	0.48[a]
PICA saccular	45 (72.6)	3 (4.8)	14 (22.6)	
Whole series				
Age ≥ 65 years	29 (50.9)	4 (7)	24 (42.1)	0.023[c]
Female	112 (67.9)	9 (5.4)	44 (26.7)	0.42[c]
High WFNS (3 + 4 + 5)	65 (49.6)	10 (7.6)	56 (42.8)	*< 0.001*[c]
High Fisher grade (3 + 4)	137 (62.6)	12 (5.5)	70 (31.9)	*0.005*[c]
Aneurysm shape (fusiform)	16 (64)	2 (8)	7 (28)	0.94[a]
Hydrocephalus	93 (60.4)	9 (5.8)	52 (33.8)	0.004[c]
Epilepsy	13 (56.5)	2 (8.7)	8 (34.8)	0.32[c]
Vasospasm requiring EVT	23 (71.9)	3 (9.4)	6 (18.7)	0.26[c]
Rebleeding before aneurysm treatment	2 (22.2)	0	7 (77.8)	*0.007*[c]

[a] Mann-Whitney test

[b] Pearson Chi^2

[c] Fisher exact test

EVT endovascular treatment, *Mo* months, *mRS* modified Rankin score

Despite in literature, PICA aneurysms have been associated with a higher rate of intraventricular hemorrhage and hydrocephalus [3, 12, 24, 25], our data failed to show a significant difference in the rate of hydrocephalus requiring treatment between the PICA and non-PICA group.

($p = 0.66$ and $p = 0.67$, respectively).

The reported rate of favorable neurological outcome in literature for patient with ruptured PICA aneurysms ranges from 37 up to 90% depending on the series and our findings are in line with the results reported in literature (Table 4) [15, 20, 24, 19, 3, 5–7, 9, 14, 15, 24, 27, 31].

Sejkorová and Lanzino showed a favorable neurological outcome for patients with ruptured PICA in up 58% of patients, ranging from 37% in patients with distal PICA aneurysms to 58% of patients with proximal PICA aneurysms. Rodriguez-Hernandez et al. reported a 80% favorable outcome in patients treated with microsurgical clipping; however, they did not specify how many of them were ruptured. [20] In

Table 4 Neurological outcome reported in literature for ruptured posterior inferior cerebellar artery aneurysms in recent series with ≥20 patients

Series (year)	No. of patients	EVT %	Surgery %	Combined approach	Mean follow-up months (range)	Definition of favorable outcome	% of favorable outcome at discharge	% of favorable outcome at last follow-up
Present study (2018)	74	55.4	28.4	0	NA (1–60)	mRS 0–3 mRS 0–2	66.2 41.9	73.9 66.7
Sejkorova et al.[24] (2017)	65	52.3	47.7	0	36 (1–120)	mRS 0–2	52.3%	NR
Williamson et al.[31] (2015)	22	9.1	86.4	0	36 (NA)	mRS 0–2	9%	37%
Bohnstedt et.[3] (2015)	79	39.2	60.8	0	NA	GOS 4–5	NA	NA
Lehto et al.[14] (2014)	68	1.5	91.2	0	105 (0–42)	NR	NA	69%
Chalouhi et al.[5] (2013)	61	100	0	0	21 (1–96)	GOS 4–5	NA	78.7%
Tokimura et al.[27] (2010)	25	12	76	0	NA	GOS 4–5	NA	76%
Mericle et al.[15] (2006)	31	100	0	0	10 (0.5–48)	GOS 4–5	NA	68%
Horiuchi et al.[9] (2003)	23	3.7	96.3	0	NA	GOS 4–5	NA	82.6%

Favorable outcome defined as mRS = 0–2 or GOS = 4–5

EVT endovascular treatment, *mRS* modified Rankin score, *GOS* Glasgow outcome scale, *NA* not available

the series of Mericle et al. [15], 61.5% of patients with ruptured PICA aneurysms presented a favorable outcome after endovascular treatment. Peluso et al. [19] reported a more than 90% rate of favorable outcome in their series with 80% of ruptured aneurysms. Other large series reported a favorable outcome in 60 and 80% of patients with ruptured PICA aneurysms . [3, 5–7, 9, 14, 15, 24, 27, 31]

In our cohort, the endovascular occlusion was the principal treatment modality in more than 70% of non-PICA patients versus 55% of PICA patients; in this last group, surgery represented the first-line treatment in more than 28% of cases compared to less than 5% in the non-PICA group. These results support the importance of a multidisciplinary treatment discussion with the possibility of surgical occlusion as alternative treatment for patients with particular subgroups of ruptured PICA aneurysm which are not suitable for endovascular treatment. For example, surgical treatment may be preferred to endovascular occlusion in ruptured PICA aneurysms with wide-collar and/or fusiform shape as well as in presence of hypoplastic, dissected, or stenosed vertebral artery which may yield to a challenging endovascular treatment. [22] Furthermore, surgery could be preferred for the treatment of ruptured PICA aneurysms in the proximal (medullary) segment of the artery, where the endovascular treatment seldomly leads to the sacrifice of the parent artery with possible ischemia of the brainstem and/or cerebellum. [1, 18]

However, clipping for PICA aneurysms is technically demanding and harbors a non-negligible rate of morbidity: the close anatomical relationship with lower cranial nerves and the aneurysms location on the anterior medullary segment of PICA yield to a challenging surgical procedure, requiring an advanced experience. [20]

Due to the available published evidence showing no difference in terms of neurological outcome between treatment modality (endovascular vs microsurgery) for ruptured PICA aneurysms [24], our analysis has not been enhanced to investigate the clinical outcome according to the treatment modality, which variates for every aneurysm location according to the local treatment policy.

Due to the retrospective and multicentric nature of our series, some data could not be investigated or analyzed, such as the localization of the aneurysm along the course of PICA (proximal vs distal).

Conclusion

In this Swiss series, ruptured PICA aneurysms present a favorable outcome in more than 2/3 of cases at 1 year after treatment, with no significant difference with other posterior circulation locations. This is in line with other recent published series of patients with ruptured posterior circulation aneurysm.

Surgical occlusion was the first treatment option in 28% of patients with ruptured PICA aneurysms, thus suggesting that, in the actual endovascular era, surgery still represents a valid treatment alternative to endovascular occlusion.

Our findings support the need of maintaining knowledge in microsurgical occlusion of ruptured PICA aneurysms in high-volume neurovascular centers.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the local Ethical Committee (Geneva Ethics Committee Board no. 11-233R, NAC 11-085R) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this retrospective type of study, formal consent is not required.

Appendix: List of contributors to the Swiss SOS study group

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Previous presentations

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