



# Factors associated with clinical and radiological status on admission in patients with aneurysmal subarachnoid hemorrhage

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## Abstract

Grading scales yield objective measure of the severity of aneurysmal subarachnoid hemorrhage and serve as to guide treatment decisions and for prognostication. The purpose of this cohort study was to determine what factors govern a patient's disease-

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Daniel W. Zumofen and Michel Roethlisberger contributed equally to this work.

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On behalf of the Swiss SOS Study Group Members and collaborators of the Swiss SOS Study Group are listed in the appendix

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specific admission scores in a representative Central European cohort. The Swiss Study of Subarachnoid Hemorrhage includes anonymized data from all tertiary referral centers serving subarachnoid hemorrhage patients in Switzerland. The 2009–2014 dataset was used to evaluate the impact of patient and aneurysm characteristics on the patients' status at admission using descriptive and multivariate regression analysis. The primary/co-primary endpoints were the GCS and the WFNS grade. The secondary endpoints were the Fisher grade, the presence of a thick cisternal or ventricular clot, the presence of a new focal neurological deficit or cranial nerve palsy, and the patient's intubation status. In our cohort of 1787 consecutive patients, increasing patient age by 10 years and low pre-ictal functional status (mRS 3–5) were inversely correlated with "high" GCS score (GCS  $\geq$  13) (OR 0.91, 95% CI 0.84–0.97 and OR 0.67, 95% CI 0.31–1.46), "low" WFNS grade (grade VI–V) (OR 1.21, 95% CI 1.04–1.20 and OR 1.47, 95% CI 0.66–3.27), and high Fisher grade (grade III–IV) (OR 1.08, 95% CI 1.00–1.17 and OR 1.54, 95% CI 0.55–4.32). Other independent predictors for the patients' clinical and radiological condition at admission were the ruptured aneurysms' location and its size. In sum, chronological age and pre-ictal functional status, as well as the ruptured aneurysm's location and size, determine the patients' clinical and radiological condition at admission to the tertiary referral hospital.

**Keywords** Aneurysm · Subarachnoid hemorrhage · Age · Clinical presentation · Radiological presentation

## Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) accounts for about 5% of strokes but has a disproportionate mortality rate of 40 to 60% [1–3]. Aneurysm characteristics such as location, size, and morphology govern an intracranial aneurysm's tendency to bleed [4, 5], while outcome following aneurysm rupture is determined by factors that include patient age and severity of the bleed [6, 7]. The severity of aSAH is assessed by a series of grading scales that yield objective measure of a patient's clinical and radiological condition at admission. In routine clinical practice, these aSAH-specific indexes serve as to guide treatment decisions and for prognostication [8–10]. They include in particular the World Federation of Neurosurgical Societies (WFNS) classification [11] with the GCS score [12] as its main component [13]. In addition, radiological scores such as the Fisher grading scale [14] and the presence or absence of a thick cisternal or ventricular blood clot on CT scan serve as to predict the risk of developing hydrocephalus and/or vasospasm with or without delayed cerebral ischemia (DCI) [15–17]. Although used in everyday practice, aSAH-specific indexes were often based on poorly representative data from a today's point of view, which may lead to conflicting results as to the nature and the extent of associations in contemporary Western populations defined by increased health condition and life expectancy [6, 18–22].

The purpose of the present nationwide cohort study was to investigate what factors determine the patients' clinical and radiological status at the time point of initial admission to the tertiary referral hospital in a representative Central European cohort of aSAH patients. Only few registries offer the combination of a dedicated nationwide all including registration of aSAH patients with highly detailed data acquisition that is not part of more general stroke registries [23–28]. The Swiss Study of Subarachnoid Hemorrhage (SOS) database provides the exceptional property that all aSAH in Switzerland are treated

within one of the participating centers, hence to a certain extent representing the nations' true epidemiology [29]. In sum, we expect our finding to apply eventually to all Western countries with typical aging demographics and with a similar healthcare system, meaning with universal access and coverage.

## Materials and methods

### Patient registry

The SOS registry was implemented in 2009, and study details were previously published [29]. Internal Review Board and Ethical committee approval was obtained for all participating centers (under the supervision of the Geneva ethical committee board no. 11-233R, NAC 11-085R). Most local Ethic Committees waived the need for obtaining written informed consent (justification: disproportionality). Written informed consent was obtained however from all participating patients if the local Ethic Committee had requested it. As of 2014 (implementation of the new Swiss Human Research Act), written informed consent was obtained from all participating patients in all participating centers. This study was a retrospective analysis of a prospectively collected database and does not require clinical trial registration.

### Study centers and data collection

Patients with aSAH in Switzerland are cared for in one of the eight accredited neurovascular referral centers (university hospitals of Basel, Bern, Geneva, Lausanne, and Zurich and the cantonal hospitals of Aarau, Lugano, and St. Gallen). All eight centers contributed data to the Swiss SOS registry [29]. Clinical and radiological assessment at admission was performed at each individual center with the center-specific standard procedures for the management and treatment of aSAH

[30]. A predefined set of clinical and radiological variables were prospectively pooled in a secured, pseudonymized web-based registry for the present study (secuTrial®, InterActive Systems GmbH, Berlin, Germany) [29].

## Study population

Data was collected for all patients with aSAH from a documented ruptured intracranial aneurysm from 2009 to 2014 that were admitted to one of the participating centers. Patients were excluded if they had non-aneurysmal SAH, an angiographically negative SAH, SAH of another confirmed cause, or no available information regarding the source of SAH.

## Study variables

For the present study, the following variables were extracted and anonymized from the SOS database: *patient characteristics* (age, gender, and pre-aSAH mRankin scale score (mRS) [31]), *aneurysm characteristics* (location and maximal diameter of the ruptured index aneurysm, and any unruptured bystander aneurysm(s) aneurysm multiplicity), *admission scores* (GCS score, WFNS grade, Fisher grade), and *additional variables* (new neurological deficits (ND), new cranial nerve palsies (CNP), intubation status at admission, and presence of a thick cisternal or ventricular blood clot larger than  $5 \times 3$  mm in the axial plane on the admission CT scan).

## Endpoints

The *primary/co-primary endpoints* were defined as the GCS score and the WFNS grade at the time point of initial admission to the tertiary referral hospital. The *secondary endpoints* were defined as the Fisher grade, the presence or absence of a thick blood clot on admission CT scan, the presence or absence of a new neurological deficit or new cranial nerve palsy on admission exam, and the patient's intubation status at the time point of initial admission to the tertiary referral hospital.

## Statistical analysis

Statistical analysis was performed with R (R Foundation for Statistical Computing. Release date 2014. R for Windows. Version 3.0.3. Vienna, Austria). For the multivariate mixed effect logistic regression model, univariate models were calculated to test for associations between the variable of interest and independent variables (see study variables above). For this purpose, data was dichotomized into “high” GCS score (GCS  $\geq 13$ ) versus “low” GCS score (GCS  $\leq 12$ ), high WFNS grade (WFNS grade IV–V) versus low WFNS grade (WFNS grade I–III), and high Fisher grade (Fisher grade III–IV) versus low Fisher grade (Fisher grade I–II). Covariates with a  $p$

value  $\leq 0.2$  were included in an initial multivariate model and model selection based on likelihood ratio tests. The Akaike information criterion was performed to reduce the set of covariates. For confounder-adjusted analysis, sex, pre-aSAH mRS, anterior vs. posterior circulation aneurysm, and a “center” variable were entered into either a cumulative or a logistic linear mixed model depending on the type of the outcome. To account for non-independence of the measurements of the same center, a random center intercept was included in the statistical models. For multiple testing, post hoc testing was performed using Bonferroni-Holm [32] method. To account for missing values, all statistical models were computed for a dataset of complete cases, for each covariate univariate, and on an imputed dataset, for which it was assumed that the missing values were missing at random (MAR). Five imputed datasets were produced by generating a random forest for each, with a different value for the random forest number generator for each dataset (nonparametric missing value imputation using random forest, r: package missForest). Statistical models were then computed for each imputed dataset, and *Rubin's rule* was applied to combine the estimates. The complete correlation tables are provided in Suppl. Data Table 1. Forrest plots are provided in Suppl. Data Fig. 1. Statistical significance was defined as  $p \leq 0.05$ .

## Results

The locked SOS dataset 2009–2014 included 1787 patients. A detailed patient inclusion profile that specifies the number of patients assessed for each of the tested variables is provided in Fig. 1.

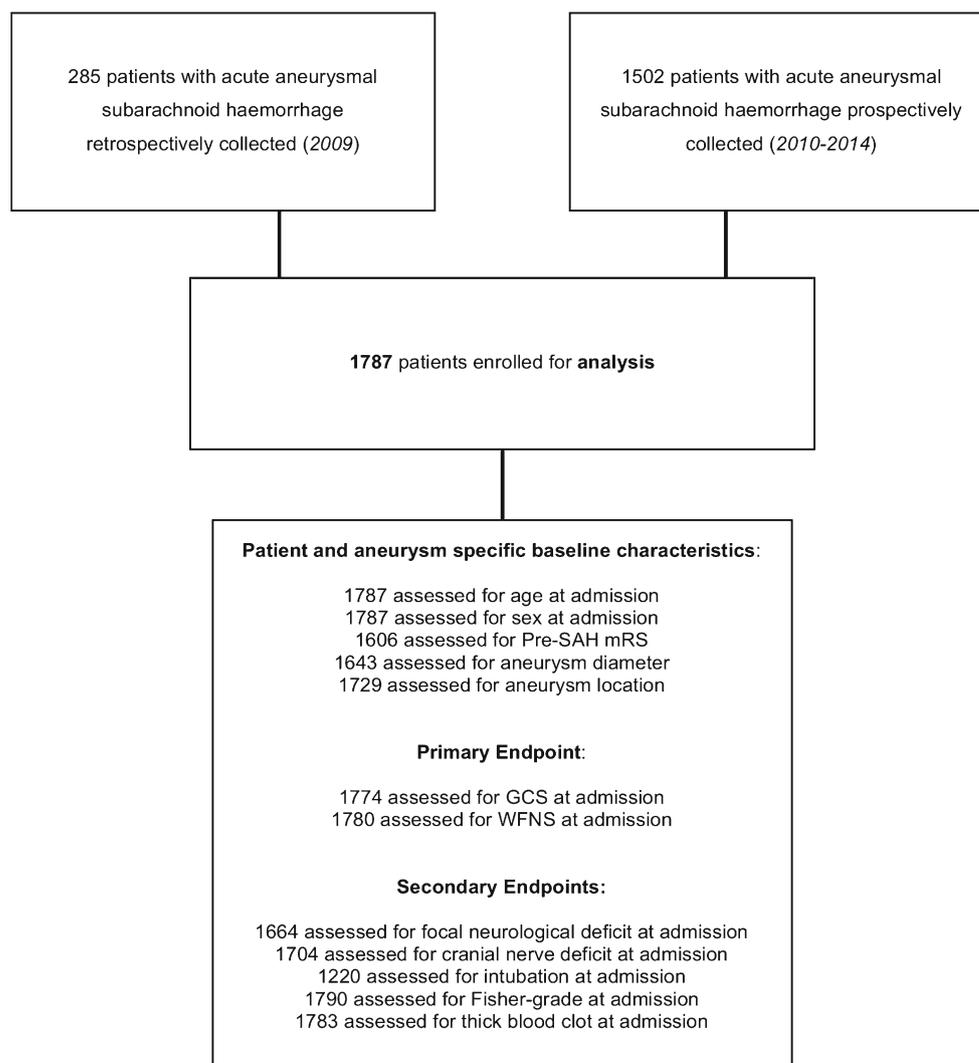
## Baseline characteristics

The mean age at ictus was 55.9 (SD  $\pm$  13.2) years. A majority of patients were in the age range 40 to 64 years. The sex ratio was 1.52 (F/M). Details are provided in Table 1.

**Table 1** Baseline characteristics

Study population			
<i>n</i>	1787		
Age at admission	Total	Females	Males
Mean	55.9 years (SD $\pm$ 13.2)	57 years	53.7 years
Age groups	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
0–39 years	202 (11.3)	108 (9.2)	94 (15.3)
40–64 years	1175 (65.5)	764 (64.9)	409 (66.7)
65–74 years	264 (14.7)	191 (16.2)	73 (11.9)
$\geq 75$ years	152 (8.5)	115 (9.8)	37 (6.0)

Fig. 1 Patient inclusion profile



## Cumulative empirical distributions

The number of patients in each severity level of the different admission scores, broken down for different age groups (if applicable), is provided in Table 2. Overall, the proportion of patients with no pre-existing disability (mRS = 0) decreased with increasing patient age, while the proportion of patients with “no significant” or “slight” disability (mRS = 1–2) simultaneously rose (Suppl. Data Fig. 2A). Similarly, the proportion of patients who presented with a high GCS score and with a high WFNS grade decreased with increasing patient age. Nonetheless, more than half of patients older than 75 years had favorable clinical admission scores if the latter were defined as GCS 13–15 and WNFS I–III (Suppl. Data Fig. 2B and C). With regard to the radiological scores, the proportional distribution of patients by Fisher grade remained about constant with increasing patient age (Suppl. Data Fig. 2D).

A summary breakdown of the aSAH causing aneurysms’ characteristics is provided in Table 3. Overall, more than three

quarters of the aSAH-causing aneurysms were located in the anterior (carotid) circulation with ruptured anterior communicating artery (ACommA) aneurysms being the most frequent ( $n = 546/1787$ ; 30.6%). The largest proportion of aneurysms was  $\geq 7$  mm in maximal diameter ( $n = 717/1787$ ; 40.1%). The proportion of patients who presented with a “high GCS score” and a “good WFNS grade” was lower in the posterior circulation aneurysm group (Fig. 2a, b) and in those patients whose aneurysm was larger than 7 mm in maximal diameter (Fig. 2c, d).

## Correlations

*Impact of patient characteristics:* increasing patient age by steps of 10 years was correlated with low GCS score. A patient’s risk for presenting with a low GCS increasing by 10.5% per each 10 years of additional age. Increasing patient age by 10 years was also correlated with low WFNS grade, with high Fisher grade, with presence of a large blood clot, and with

**Table 2** Admission scores

	Total n (%)	Age 0–40 years n (%)	Age 40–65 years n (%)	Age 65–75 years n (%)	Age ≥ 75 years n (%)
<b>Pre-SAH mRS</b>					
mRS 0	1392 (77.9)	171 (95)	935 (89)	195 (82.3)	91 (65.5)
mRS 1–2	193 (10.8)	8 (4.4)	105 (10)	39 (16.5)	41 (29.5)
mRS 3–5	21 (1.2)	1 (0.6)	10 (1)	3 (1.2)	7 (5)
Missing <sup>a</sup>	181 (10.1)				
Total	1787 (100)	180 (11.2)	1050 (65.4)	237 (14.8)	139 (8.7)
<b>GCS</b>					
GCS 3–6	485 (27.5)	45 (22.5)	304 (26.6)	95 (35.7)	41 (26.6)
GCS 7–12	190 (10.8)	15 (7.5)	121 (10.6)	31 (11.7)	23 (14.9)
GCS 13–15	1090 (61.8)	140 (70)	720 (62.9)	140 (52.6)	90 (58.4)
Missing <sup>a</sup>	22 (1.2)				
Total	1765 (100)	200 (11.3)	1145 (64.9)	266 (15.1)	154 (8.7)
<b>WFNS grade</b>					
I–III	1104 (62.3)	140 (70)	729 (63.4)	142 (53.2)	93 (60.4)
IV–V	667 (37.7)	60 (30)	421 (36.6)	125 (46.8)	61 (39.6)
Missing <sup>a</sup>	16 (0.9)				
Total	1771 (100)	200 (11.3)	1150 (64.9)	267 (15.1)	154 (8.7)
<b>Fisher grade</b>					
I	54 (3.0)				
II	163 (9.1)				
III	989 (55.3)				
IV	576 (32.5)				
Missing <sup>a</sup>	5 (0.3)				
	Neurological deficit n (%)	Cranial nerve palsy n (%)	Thick blood clot n (%)	Intubated n (%)	
Yes	453 (27.1)	345 (20.7)	1565 (87.6)	389 (31.9)	
Missing <sup>a</sup>	123 (6.9)	83 (4.6)	4 (0.2)	567 (31.7)	

Age group-related number of patients in each severity level of the different admission scores

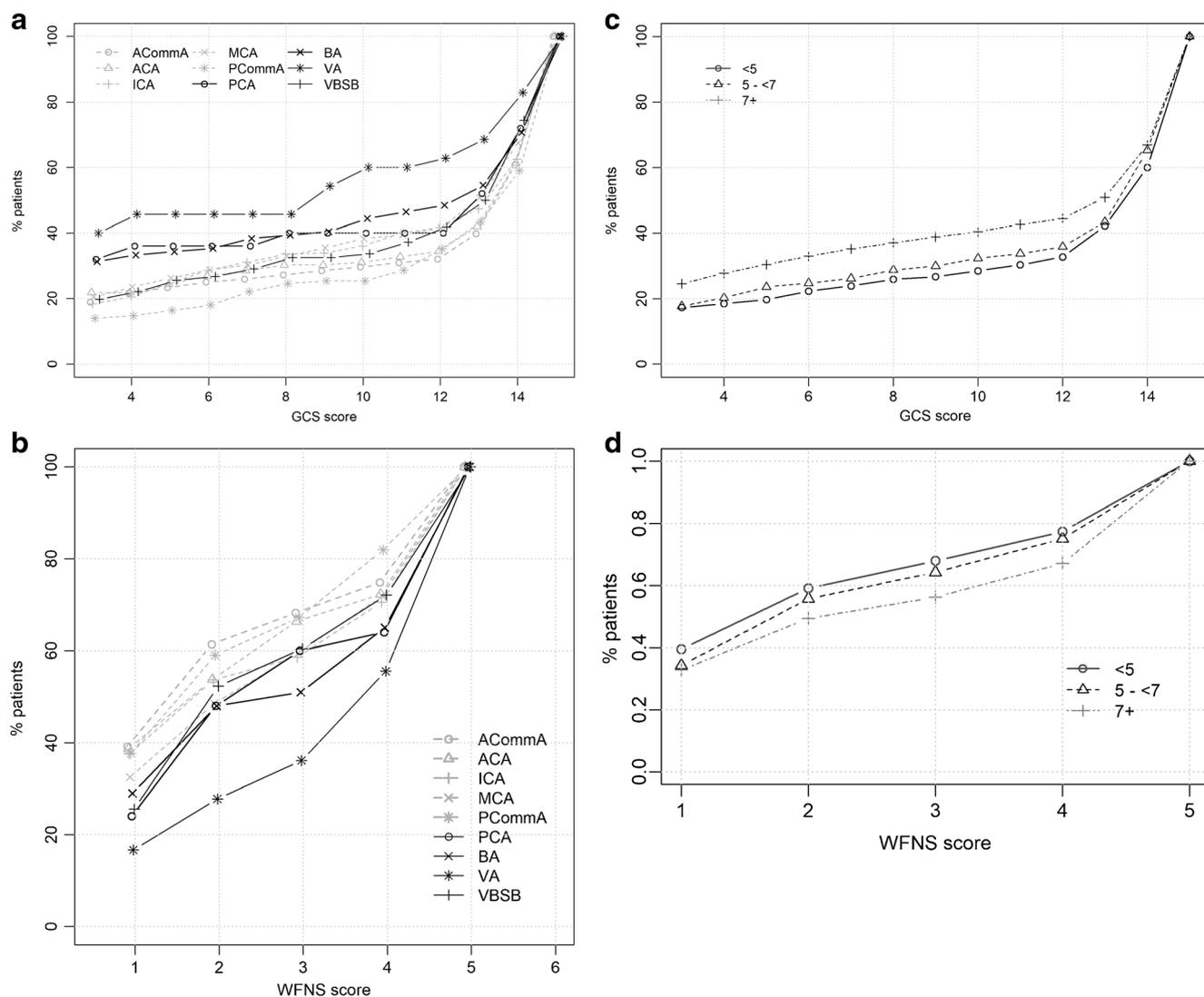
<sup>a</sup>No information available

presence of ND. These findings remained significant after accounting for multiple testing (Table 4, Suppl. Data Table 1, Suppl. Data Fig. 1). The impact of lower pre-ictal functional status largely paralleled the impact of increasing patient age. However, our study remained underpowered to estimate the effect (Suppl. Data Table 1).

*Impact of aneurysm characteristics:* vertebral artery (VA) and basilar artery (BA) location were correlated with low GCS score and low WFNS grade, as well as with the intubation status “intubated.” In contrast, middle cerebral artery (MCA) location was correlated with “good” WFNS grade and with high Fisher grade. In addition, MCA location was correlated with the presence of a ND and with the presence of a CNP. Aneurysm size ≥ 7 mm when compared to ≤ 5 mm was correlated with low GCS score, with low WFNS grade, and with the presence of a CNP. These findings remained significant after accounting for multiple testing (Table 4, Suppl. Data Table 1, Suppl. Data Figure 1).

## Discussion

While previous work focused on outcome analysis, the purpose of the present nationwide cohort study was to investigate what factors determine the patients’ clinical and radiological status at the time point of initial admission to the tertiary referral hospital [7, 33]. In line with a previous report, we found that patient age and lower pre-ictal functional status were both independent predictors for worse clinical and radiological status at the time of a patient’s initial admission to the tertiary neurovascular referral hospital [7]. In other words, they both independently predicted worse admission scores, which in turn foretells poor outcome following aSAH [8–10]. In contrast to previous work, we also modeled specific aneurysm-related prognostic factors including detailed aneurysm location and size [7]. We found that certain specific locations of the aSAH causing aneurysm particularly in the posterior circulation (e.g., VA and BA), as well as increasing



**Fig. 2** Empirical cumulative distribution. **a** Cumulative GCS distribution by index aneurysm location. **b** Cumulative WFNS grade distribution by index aneurysm location. **c** Cumulative GCS grade distribution by index aneurysm size (maximal diameter in millimeters). **d** Cumulative WFNS grade distribution by index aneurysm size (maximal diameter in millimeters). *ACommA* anterior communicating artery, *ACA* anterior

cerebral artery, *ICA* internal carotid artery, *MCA* middle cerebral artery, *PCommA* posterior communicating artery, *PCA* posterior cerebral artery, *BA* basilar artery, *VA* vertebral artery, *VBSB* vertebrobasilar side branches including the superior cerebellar artery (SCA), the anterior inferior cerebellar artery (AICA), and the posterior inferior cerebellar artery (PICA)

aneurysm size ( $\geq 7$  mm), were additional independent predictors for worse clinical and radiological status at admission to

the tertiary referral hospital (Table 4, Suppl. Data Table 1, Suppl. Data Fig. 1).

**Table 3** Frequency table

Aneurysm size distribution	Total <i>n</i> (%)	< 5 mm <i>n</i> (%)	5–< 7 mm <i>n</i> (%)	$\geq 7$ mm <i>n</i> (%)	Missing <sup>a</sup> <i>n</i> (%)
Anterior (carotid) circulation	1479 (82.8)	420 (28.4)	367 (24.8)	623 (42.1)	69 (4.7)
Posterior (vertebrobasilar) circulation	250 (14.0)	79 (31.6)	59 (23.6)	94 (37.6)	18 (7.2)
Missing <sup>a</sup>	58 (3.2)	1 (1.7)	0 (0)	0(0)	57 (98.3)
Total	1787 (100)	500 (28)	426 (23.8)	717 (40)	144 (8.1)

A detailed breakdown of aneurysms by size and by location will be published separately

<sup>a</sup>No information available

**Table 4** Correlation tables

	MV OR	<i>p</i> values	CI (95%)	UV OR	<i>p</i> values	CI (95%)	IMP OR	<i>p</i> values	CI (95%)
High GCS score									
Age	0.91	0.006	0.84–0.97	0.90	0.001	0.84–0.96	0.91	0.003	0.85–0.97
MCA	0.78	0.053	0.60–1.00	0.75	0.014	0.59–0.94	0.76	0.027	0.60–0.97
VA	0.32	0.002	0.15–0.65	0.34	0.001	0.19–0.63	0.36	0.001	0.20–0.66
BA	0.58	0.011	0.38–0.89	0.56	0.003	0.39–0.83	0.58	0.006	0.39–0.86
PICA/AICA/SCA	0.61	0.027	0.40–0.95	0.70	0.077	0.47–1.04	0.68	0.057	0.46–1.01
> 7 mm	0.66	< 0.001	0.52–0.82	0.69	0.001	0.56–0.85	0.69	0.001	0.55–0.86
High WFNS score									
Age	1.12	0.003	1.04–1.10	1.12	< 0.001	1.05–1.20	1.11	0.002	1.04–1.19
MCA	1.33	0.031	1.02–1.72	1.36	0.010	1.09–1.72	1.33	0.019	1.05–1.69
VA	3.09	0.002	1.50–6.35	2.89	0.001	1.57–5.32	2.64	0.002	1.44–4.83
BA	1.72	0.012	1.13–2.61	1.70	0.008	1.15–2.51	1.64	0.014	1.12–2.43
PICA/AICA/SCA	1.62	0.030	1.05–2.50	1.43	0.077	0.96–2.14	1.47	0.063	0.98–2.19
> 7 mm	1.54	< 0.001	1.23–1.93	1.45	< 0.001	1.18–1.79	1.47	0.001	1.18–1.83
High Fisher grade (grade III–IV)									
Age	1.09	0.044	1.00–1.17	1.09	0.018	1.01–1.17	1.08	0.042	1.00–1.16
MCA	1.39	0.025	1.04–1.85	1.25	0.091	0.97–1.62	1.22	0.139	0.94–1.60
New focal neurological deficit									
Age	1.12	0.016	1.02–1.24	1.10	0.033	1.01–1.19	1.11	0.024	1.02–1.20
MCA	2.17	< 0.001	1.56–3.03	2.11	< 0.001	1.56–2.86	2.02	< 0.001	1.49–2.73
PCA	2.53	0.049	1.00–6.40	2.13	0.098	0.87–5.19	2.25	0.072	0.92–5.49
New cranial nerve palsy									
ICA	1.62	0.026	1.06–2.47	1.73	0.005	1.18–2.52	1.56	0.019	1.08–2.26
MCA	1.92	0.001	1.31–2.81	2.08	< 0.001	1.48–2.92	1.84	0.001	1.30–2.58
> 7 mm	1.76	0.001	1.20–2.48	1.77	< 0.001	1.30–2.42	1.64	0.003	1.19–2.25
Thick clot present									
Age	1.21	0.002	1.07–1.36	1.16	0.009	1.04–1.29	1.18	0.003	1.06–1.32
Sedated at admission									
VA	3.17	0.020	1.20–8.39	3.40	0.003	1.52–7.61	3.21	0.002	1.53–6.74
> 7 mm	1.45	0.032	1.03–2.03	1.38	0.037	1.02–1.88	1.49	0.038	1.08–2.06
Intubed at admission									
BA	1.88	0.046	1.01–3.50	1.84	0.030	1.06–3.19	1.58	0.100	0.94–2.64
VA	3.04	0.025	1.15–8.02	3.27	0.004	1.46–7.32	2.85	0.003	1.43–5.67
> 7 mm	1.51	0.017	1.08–2.11	1.45	0.015	1.08–1.96	1.59	0.002	1.22–2.09

Correlation tables of multivariate analysis (MV), univariate analysis (UV), and analysis of imputed data of missing values (IMP) for correlations with *p* value < 0.5. Data was dichotomized into “high” GCS score (GCS ≥ 13) versus “low” GCS score (GCS ≤ 12), high WFNS grade (WFNS grade IV–V) versus low WFNS grade WFNS score (I–III), and high Fisher grade (III–IV) versus low Fisher grade (Fisher grade I–II). Details are provided in Suppl. Data Table 1. Forest plots are provided in Suppl. Data Fig. 1

Further strengths of the present study include its comparatively large-scale dataset that was prospectively provider-collected, nationwide, and hence relatively unselected. This obviates to some extent coding errors, patient selection, and center-specific bias. In addition, data quality was high, and statistical analysis was comprehensive and adjusted for relevant confounders, multiple testing, and missing values. Finally, reporting of data and results is in accordance to the principles of the STROBE statement to minimize the risk of unsaid bias.

We found that the aSAH causing aneurysm’s location and size independently predicted the patients’ clinical and radiological condition at time point of initial admission to the tertiary referral hospital (Table 4, Suppl. Data Table 1, Suppl. Data Fig. 1). Our results hence support the concept that aneurysm characteristics should be handled as key factors in any potential aSAH-specific outcome assessment tool [6, 18, 21]. That being said, increasing patient age and pre-existing medical conditions have alike been identified as independent predictors for worse outcome following aSAH [7, 21, 33–37].

Several attempts have been made over the year to integrate these elements into indexes so as to enhance the ability and the accuracy to predicting the course of the disease (e.g., Charlson comorbidity index [38, 39], SAH [40], FOUR score [41]). Accordingly, we found in our cohort that the older was a patient, the lower was his pre-ictal functional status, and the more likely he presented in poor condition following aSAH (Table 4, Suppl. Data Table 1, Suppl. Data Fig. 1). This being the case, the age at which patients develop a substantial decline in functional status has shifted from around age 50 a decade ago [42], to 60–65 years [7, 43–47], to 70–75 more recently [48] as well as in the present cohort (Table 1).

The question still remains whether there is an age beyond which prognosis become decisively worse [42, 43, 47–51], which means for instance that active aneurysm treatment might be withheld in all patients older than that cutoff age [52, 53]. We found in our cohort that for instance, about half of patients older than 75 years had favorable outcome-predicting WFNS scores (Suppl. Data Fig. 2B). We hence agree that active treatment should probably not be refused solely on the basis of advanced age [7], but instead suggest that chronological age be taken into consideration along with the patient's pre-ictal functional status when making management decisions and for prognostication [7, 19, 21, 33, 35, 36, 54–57].

## Limitations

Although there is a policy in Switzerland to transfer all aSAH patients to one of the accredited neurovascular centers that participate in the SOS registry, in practice, a fraction of patients may not end up in these centers (e.g., because they die at the admitting hospital from devastating brain hemorrhage of unclear etiology). However, the purpose of this study was not to assess outcome after aSAH, but to determine what factors influence a patient's clinical and radiological status once admitted to a tertiary referral hospital. Besides that, risk factors and co-morbidities such as cigarette smoking and arterial hypertension were not included into our analysis mainly because of missing values in our dataset. However, their influence has been studied elsewhere [58, 59]. Data quality was comparatively high. Still, there was missing data in our dataset. We compared the results of our regression models with pooled estimates obtained from imputed datasets to reduce the variability of the estimates in our multivariate analysis as well as to investigate whether missing values had introduced bias. We found that there was no relevant difference between coefficients estimated from imputed datasets and those estimated from the dataset restricted to complete cases. Finally, multivariate analyses concerning the impact of the pre-ictal mRS found associations, but ultimately lacked the necessary power to estimate the effect. This

indicates that more statistical power is eventually needed, and we suggest that in the future study, cohorts from countries with similar populations and similar treatment standards be merged to obtain valuable additional patients.

## Conclusions

Chronological age should be considered when managing aSAH patients along with multiple other aspects that include aneurysm location, aneurysm size, and pre-ictal functional status that all influence the patients' clinical and radiological condition at admission, and hence the likely course of the disease. However, further research and even larger datasets will be required to determine the extent of associations in representative contemporary aSAH populations.

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**Author contributions** DZ, MR, RA, HB, LM, and RG designed the study. DZ, MR, SB, MS, CF, DD, NM, AF, MC, DS, JG, DV, TR, RB, MS, JB, and SM carried out sample collection. DZ, MR, RA, and HB performed data analysis. DZ, MR, KB, HB, LM, and RG wrote the manuscript. DZ, MR, RA, HB, KB, and RG revised the manuscript. All authors read and approved the final manuscript.

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## Compliance with ethical standards

**Statement of human rights** Internal Review Board (IRB) and Ethical Committee approval were obtained for all participating centers (under the supervision of the Geneva ethical committee board no. 11-233R, NAC 11-085R). Most local Ethic Committees waived the need for obtaining written informed consent (justification: disproportionality). Written informed consent was obtained however from all participating patients for both the retrospective collection of data in 2009 and the prospective collection of data from 2010 onward if the local Ethic Committee had requested it. As of 2014 (implementation of the new Swiss Human Research Act), written informed consent was obtained from all participating patients in all participating centers. *Consent to publish:* No consent to publish from the participants to report individual patient data was obtained as no individual participant's data in any form will be published.

**Trial registration** This study was a retrospective analysis of a prospectively collected database and does not require clinical trial registration.

**Conflict of interest** The authors declare that they have no conflict of interest.

**Reporting** Our results are reported as recommended in the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement.

**Availability of data and materials** The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request. Previous presentation: Preliminary results of this study were presented in form of a poster and abstract at the Joint Annual Meeting of the Swiss Society of Neurosurgery and the Swiss Society of Neuroradiology, September 2015, Lucerne, Switzerland.

## Appendix: Swiss SOS Study Group

Members or collaborators of the Swiss SOS Study Group that were not listed as authors include Javier Fandino, Daniel Colluccia, Marta Arrighi, Alice Venier, Dominique E. Kuhlen, Michael Reinert, Astrid Weyerbrock, Martin Hlavica, Jean-Yves Fournier, Andreas Raabe, Juergen Beck, David Bervini, Karl Schaller, Roy T. Daniel, Daniele Stamoni, Mahmoud Messerer, Marc Levivier, Emanuela Keller, Luca Regli, Oliver Bozinov, Sina Finkenstaedt, Luca Remonda, Christoph Stippich, Jan Gralla, Zsolt Kulcsar, Vitor Mendes-Pereira, Alessandro Cianfoni, Peter Ahlborn, Nicolas R. Smoll, Veit Rohde, Sina Tok, Fabian Baumann, Karl Kothbauer, Hassen Kerkeni, Hiroki Dan-Ura, Hans Landolt, Khaled Mostaguir, Yvan Gasche, Asita Sarrafzadeh, Gerhard Hildebrandt, Kerstin Winkler, Christoph Woernle, and Rene Bernays.

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