Michel Roethlisberger, MD[*]
Rita Achermann, MSc[‡]
Schatlo Bawarjan, MD[§]
Martin N. Stienen, MD[¶]
Christian Fung, MD[‖]
Donato D'Alonzo, MD[#]
Nicolai Maldaner, MD[#]
Andrea Ferrari, MD[**]
Marco V. Corniola, MD[‡‡]
Daniel Schöni, MD[‖]
Johannes Goldberg, MD[‖]
Daniele Valsecchi, MD[§§]
Thomas Robert, MD[§§]
Rodolfo Maduri, MD[¶¶]
Martin A. Seule, MD[**]
Jan-Karl Burkhardt, MD[‖‖]
Serge Marbacher, MD[#]
Philippe Bijlenga, MD[‡‡]
Kristine A. Blackham, MD[##]
Heiner C. Bucher, MD[‡]
Luigi Mariani, MD[*]
Raphael Guzman, MD[*]
Daniel W. Zumofen, MD[*,##]
on behalf of the Swiss SOS group

[*]Department of Neurosurgery, University Hospital Basel and University of Basel, Basel, Switzerland; [‡]Basel Institute for Clinical Epidemiology and Biostatistics, University Hospital Basel and University of Basel, Basel, Switzerland; [§]Department of Neurosurgery, University Hospital Göttingen, Göttingen, Germany; [¶]Department of Neurosurgery, University Hospital Zurich, Zurich, Switzerland; [‖]Department of Neurosurgery, Inselspital, University of Bern, Bern, Switzerland; [#]Department of Neurosurgery, Kantonsspital Aarau, Aarau, Switzerland; [**]Department of Neurosurgery, Kantonsspital St. Gallen, St. Gallen, Switzerland; [‡‡]Department of Neurosurgery, Hopitaux Universitaires Genève, Geneva, Switzerland; [§§]Department of Neurosurgery, Ospedale Civico di Lugano, Lugano, Switzerland; [¶¶]Service of Neurosurgery, Department of Clinical Neurosciences, University Hospital of Lausanne, Lausanne, Switzerland; [‖‖]Department of Neurological Surgery, NYU School of Medicine, NYU Langone Medical Center, New York, New York; [##]Department of Radiology, Division of Diagnostic and Interventional Neuroradiology, University Hospital Basel, Basel, Switzerland

Preliminary results of this study were presented in form of a short oral communication at the Joint Annual Meeting of the Swiss Society of Neurosurgery and the Society of Neuroradiology, June 8-9, 2017, Bern, Switzerland.

Correspondence:
Daniel W. Zumofen, MD,
Department of Neurosurgery and Department of Radiology,
University Hospital Basel and University of Basel,
Spitalstrasse 21,
CH/4031 Basel, Switzerland.
E-mail: daniel.zumofen@gmail.com

Received, November 7, 2017.
Accepted, June 21, 2018.
Published Online, August 3, 2018.

Impact of Aneurysm Multiplicity on Treatment and Outcome After Aneurysmal Subarachnoid Hemorrhage

BACKGROUND: One-third of patients with aneurysmal subarachnoid hemorrhage (aSAH) have multiple intracranial aneurysms (MIA).

OBJECTIVE: To determine the predictors of outcome in aSAH patients with MIA compared to aSAH patients with a single intracranial aneurysm (SIA).

METHODS: The Swiss Study of Subarachnoid Hemorrhage dataset 2009-2014 was used to evaluate outcome in aSAH patients with MIA compared to patients with SIA with the aid of descriptive and multivariate regression analysis. The primary endpoints of this cohort study were presence of new stroke on computed tomography (CT) after aneurysm treatment, and presence of stroke on CT prior to discharge. The secondary endpoints were the clinical and the functional status, and the overall mortality at discharge and at 1 yr.

RESULTS: Among 1689 consecutive patients, 467 had MIA (prevalence: 26.4%). The incidence of stroke was higher in the MIA than in the SIA group, both after aneurysm treatment (19.3% vs 15.1%) and at discharge (24% vs 21.4%). However, the 95% confidence interval (CI) for the corresponding odds ratio (OR) in our multivariate model included 1, indicating that the detected trends did not reach statistical significance. As for the secondary endpoints, aneurysm multiplicity was found to be an independent, statistically significant predictor for occurrence of a new focal neurological deficit between admission and discharge (OR 1.40, 95% CI 1.08-1.81). Yet, the MIA and SIA groups did not differ in terms of either functional outcome or overall survival.

CONCLUSION: aSAH patients with MIA have a higher short-term morbidity than patients with SIA. This excess morbidity does not worsen the functional outcome or lower overall survival.

KEY WORDS: Aneurysm, Bystander aneurysms, Multiple aneurysms, Stroke, Subarachnoid hemorrhage

Neurosurgery 84:E334–E344, 2019 DOI:10.1093/neuros/nyy331 www.neurosurgery-online.com

Multiple intracranial aneurysms (MIA) are reportedly present in 20% to 33% of patients with aSAH.[1,2] There has been extensive research on potential risk factors for aneurysm multiplicity,[3-6] yet there have been no more than a few publications concerned with the treatment and outcome of aSAH patients with MIA.[7-11] Also, the available literature consists largely of small retrospective cohort studies, or else studies conducted outside Europe and North America.[3,4,12] On the whole, the available evidence on whether aSAH patients with MIA have a worse outcome than those with a ruptured single intracranial aneurysm (SIA) is equivocal,[7-11] and there is likewise uncertainty about the optimal treatment modality and

ABBREVIATIONS: aSAH, aneurysmal subarachnoid hemorrhage; **BA,** basilar artery; **CI,** confidence interval; **CND,** cranial nerve deficit ; **CT,** computed tomography; **FND,** focal neurological deficit; **GCS,** Glasgow Coma Scale; **ICA,** internal carotid artery; **MCA,** middle cerebral artery; **MIA,** multiple intracranial aneurysm; **mRS,** mRankin scale score; **OR,** odds ratio; **SIA,** single intracranial aneurysm; **SOS,** Swiss Study of Subarachnoid Hemorrhage; **VA,** vertebral artery; **WFNS,** World Federation of Neurosurgical Societies

Supplemental digital content is available for this article at www.neurosurgery-online.com.

the best timing of aneurysm treatment in SAH patients with MIA.[8,10,11,13]

The Swiss Study of Subarachnoid Hemorrhage (SOS) database contains data from all of the 8 accredited neurovascular centers in Switzerland to which aSAH patients are referred for treatment.[14] Few of the existing registries offer this combination of a dedicated, nationwide, all-inclusive registration of aSAH patients with highly detailed data acquisition beyond what is found in more general stroke registries.[15-20] We therefore expect our data to provide a more solid basis for epidemiologic conclusions than earlier studies, and our findings are most likely applicable in all Western countries with comparable age demographics and with a similar health care system, ie, with universal or near-universal access and coverage. In sum, the purpose of this cohort study was to investigate the predictors of outcome in aSAH patients with MIA compared to aSAH patients with SIA in a nationwide cohort of unselected aSAH patients.

METHODS

The SOS registry is a multicenter cohort database containing core data that is collected in a standardized manner. The assessment, treatment, and follow-up, however, are performed at each individual center's discretion, meaning according to center-specific standard procedures for patients with aSAH. Study details have been published elsewhere.[14] Institutional Review Board (IRB) and ethics committee approval was obtained from all participating centers (under the supervision of the Geneva ethics committee, board no. 11–233R, NAC 11–085R). Most local ethics committees waived the requirement for written informed consent (justification: disproportionality). Written informed consent was obtained, however, from all participating patients if the local ethics committee 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.

Study Design

This is a cohort study with retrospective analysis of a retrospectively (year 2009) and prospectively (years 2010-2014) collected nationwide dataset. No clinical trial registration is therefore required.

Study Centers

All patients with acute aSAH in Switzerland are cared for in 1 of 8 accredited neurovascular centers: the university hospitals of Basel, Bern, Geneva, Lausanne, and Zurich, and the cantonal hospitals of Aarau, Lugano, and St. Gallen. All of these centers contributed to the SOS registry.

Study Population

Data were collected from all patients admitted to one of the participating centers with aSAH from a documented ruptured intracranial aneurysm. We excluded patients with nonaneurysmal SAH and those who had no available information regarding the source of SAH. We also excluded patients who died on the day of admission and those with missing information about the site of the ruptured aneurysm (index aneurysm), as we suspected that the diagnostic evaluation for any additional unruptured aneurysms (bystander aneurysms) might be incomplete in these cases.

Data Collection

A set of variables of interest was predefined as previously described.[14] These variables were extracted from the hospitals' charts by the local teams, anonymized, and pooled in the SOS database, which is a secured, web-based registry (secuTrial®, InterActive Systems GmbH, Berlin, Germany).[14]

Study Variables

For the present study, the following variables were extracted from the SOS database: patient characteristics (age, sex, pre-aSAH mRankin scale score[21] [mRS], intubation and sedation status at admission); aneurysm characteristics (aneurysm multiplicity, rupture state, location of the index aneurysm, location of any bystander aneurysm(s), and maximal aneurysm diameter); admission scores (Glasgow Coma Scale score [GCS],[22] World Federation of Neurosurgical Societies score [WFNS] and Fisher grade[23]; treatment modality (surgery, endovascular, hybrid, or conservative); duration of hospitalization in the accredited neurovascular center.

Note: The identity of the ruptured aneurysm was confirmed by surgical inspection where applicable, or presumed for nonsurgically treated cases on the basis of the blood distribution on admission computed tomography (CT) and the aneurysm's angioarchitectural features on CT angiography or digital subtraction angiography, in consensus by at least one board-certified vascular neurosurgeon and at least one board-certified neurointerventionalist in each center.

Primary and Secondary Endpoints

The primary/coprimary endpoints were the occurrence of new stroke on the first CT obtained after treatment of the ruptured aneurysm, and presence of stroke on the last CT obtained before hospital discharge. *The secondary endpoints* were the duration of hospitalization, the presence or absence of a new focal neurological deficit (FND) or cranial nerve deficit (CND), and the GCS score at discharge, as well as the mRS score and the overall mortality at discharge and at 1 yr.

Follow-up

The modality and the time point of the first clinical follow-up varied considerably across the 8 participating centers. To assure availability and consistency of data for statistical analysis, we collected standardized data only at uniform time points, eg, first CT after aneurysm treatment (new stroke), patient discharge (stroke, FND, CND, and in-hospital death), and 1-yr follow-up (overall survival; mRS). A detailed patient inclusion profile including the number of participants with available data at each time point is provided in Figure 1. Reasons for nonparticipation include, in particular, patient death.

Statistical Analysis, Efforts to Address Potential Sources of Bias, and Sensitivity Analysis

We provide descriptive statistics for a set of predefined variables of interest (see study variables). Associations between variables were assessed with a multivariate mixed effects logistic regression model. First, univariate models were calculated to test for associations between the variable of interest and independent variables. For this purpose, the data were dichotomized into "high GCS score" (GCS $\geq$ 13) and "low GCS score" (GCS $\leq$ 12), "good WFNS grade" (grade I-III) and "bad

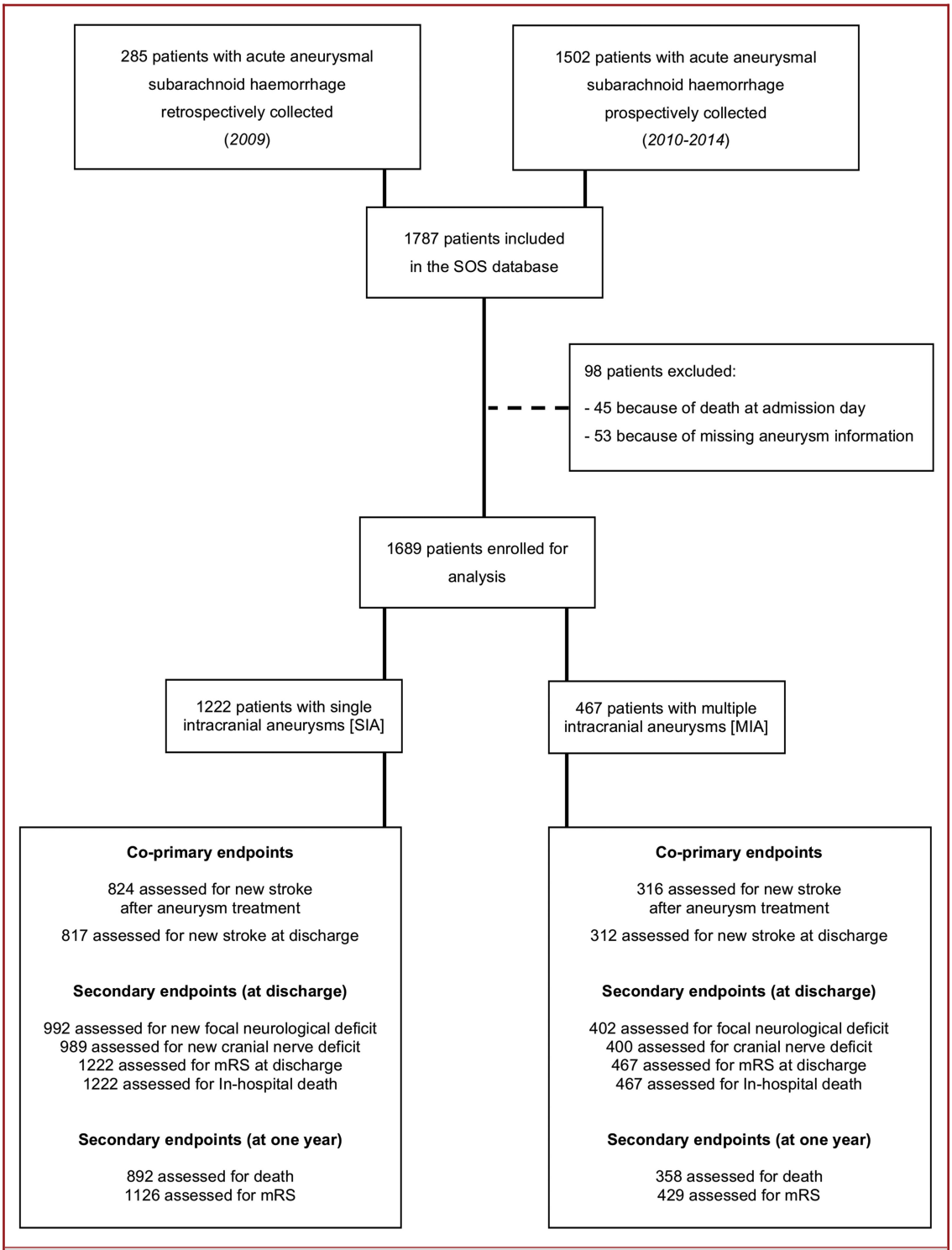

FIGURE 1. *Patient inclusion profile.*

WFNS grade" (grade IV-V), and "low Fisher grade" (grade I-II) and "high Fisher grade" (grade III-IV). Covariates with $P \leq .2$ were then included in an initial multivariable model. A stepwise model selection using the Akaike Information Criterion (AIC) was performed to reduce the set of covariates. Confidence intervals were calculated with the profile likelihood method based on Wald test statistic. The Bonferroni method was used to adjust for multiple testing. The center effect was modeled as a random intercept. A cumulative incidence and a Cox proportional hazard regression model were used to investigate the in-house mortality. As the exact date of death for discharged patients was unknown, a mixed effects logistic regression analysis was used to investigate the overall mortality at 1 yr. Statistical significance was set at $P \leq .05$.

Missing Values

To investigate whether missing values introduced biases, estimates were compared with pooled estimates obtained from 5 imputed datasets. The imputation was based on the random forest method (r package Miss Forest)[24] and was performed separately within the subsets of patients who had died, or who were alive at 1-yr follow-up. For the mixed effects logistic regression model for the secondary outcomes, the analysis was repeated on 2 further datasets, 1 with all missing values set to "yes" for the variables "FND" and "CND," and 1 with all values set to "no." The number of patients included at each stage of the analysis is provided in Figure 1. Statistical analyses were performed in R (R Foundation for Statistical Computing. R for Windows Version 3.3.3. Vienna, Austria).

RESULTS

Patient and Aneurysm Characteristics

The locked SOS dataset 2009 to 2014 comprises data on 1787 patients, of whom 1689 were included in the present analysis. Of these, 1313 patients had SIA (73.5%) and 474 patients had MIA (26.5%). The percentage of women was higher in the MIA group than in the SIA group (72.2% vs 63.7%). The mean diameter of the index aneurysm was larger in patients with MIA than in patients with SIA (7.7 mm vs 6.9 mm). Patients with MIA had a mean of 1.4 bystander aneurysms (range 1-6; Table 1). Ruptured anterior communicating artery (ACommA) aneurysms were the most common aneurysms in patients with SIA (n = 258; 34.7%). Ruptured middle cerebral artery (MCA) aneurysms were the most common aneurysms in patients with MIA (n = 136; 29.1%). Female predominance was seen in all aneurysm locations except the ACommA and vertebral artery (VA). For aneurysms at these 2 locations, the male-to-female ratio was approximately even (Table S1 of **Appendix, Supplemental Digital Content**).

Factors Favoring Aneurysm Multiplicity

The location of the index aneurysm was correlated with the probability of finding aneurysm multiplicity. In patients with MIA, the site of the index aneurysm predicted the likely anatomical distribution of bystander aneurysm(s) (Table 2; Table S2 and Figure S1 of **Appendix, Supplemental Digital Content**). Further independent predictors for aneurysm multiplicity included Fisher grade 3 compared to Fisher grade 1–2 (odds ratio [OR] 1.67, 95% confidence interval [CI] 1.12-2.47),

TABLE 1. Baseline Characteristics

	Total	Patients with SIA n % 1222 (72.4)	Patients with MIA n % 467 (27.6)
Number of bystander aneurysm(s)			
	0	1222 (72.4)	
	1	–	336 (71.9)
	2	–	83 (17.8)
	3	–	32 (6.9)
	4	–	11 (2.4)
	5	–	4 (0.9)
	6	–	1 (0.2)
Baseline characteristics			
Sex		n %	n %
	Female	778 (63.7)	337 (72.2)
Age		Years (SD)	Years (SD)
	Mean	55.7 (13.5)	55.9 (12.1)
Diameter		mm (SD)	mm (SD)
	Mean	6.9 (4.4)	7.7 (4.8)
		n %	n %
	≤5 mm	380 (31.1)	114 (24.4)
	>5 mm and ≤7 mm	299 (24.5)	124 (26.6)
	>7 mm	480 (39.3)	208 (44.5)
	Missing	63 (5.2)	21 (4.5)
Admission characteristics			
GCS score		n %	n %
	≤6	320 (26.2)	111 (23.8)
	7-12	133 (10.9)	54 (11.6)
	13,14	309 (25.3)	134 (28.7)
	15	444 (36.3)	164 (35.1)
	Missing	16 (1.3)	4 (0.9)
WFNS grade		n %	n %
	1	437 (35.8)	167 (35.8)
	2	221 (18.1)	104 (22.3)
	3	103 (8.4)	33 (7.1)
	4	124 (10.1)	51 (10.9)
	5	324 (26.5)	110 (23.6)
	Missing	13 (1.1)	2 (0.4)
Fisher grade		n %	n %
	1	36 (2.9)	15 (3.2)
	2	129 (10.6)	31 (6.6)
	3	652 (53.4)	279 (59.7)
	4	404 (33.1)	139 (29.8)
	Missing	1 (0.1)	3 (0.6)
Baseline (pre-aSAH) mRS		n %	n %
	0	951 (77.8)	369 (79)
	1	107 (8.8)	46 (9.9)
	≥2	32 (2.6)	17 (3.6)
	Missing	132 (10.8)	35 (7.5)
Focal neurological deficit (FND)		n %	n %
	No	843 (69)	320 (68.5)
	Yes	307 (25.1)	114 (24.4)
	Missing	72 (5.9)	33 (7.1)
Cranial nerve deficit (CND)		n %	n %
	No	947 (77.5)	362 (77.5)
	Yes	229 (18.7)	81 (17.3)
	Missing	46 (3.8)	24 (5.1)

TABLE 2. Mixed Effects Logistic Regression Model for Aneurysm Multiplicity

	OR	CI 95%		*P*-value
Male sex*	0.76	0.59	0.98	.034
Age by 10 yr	1	0.92	1.01	.909
Diameter per 1 mm**	1.03	1.01	1.06	.007
Artery location				
ACA*	1.61	1.01	2.57	.044
ICA*	1.50	1.05	2.14	.027
MCA****	1.87	1.36	2.57	.0001
PCommA*	1.67	1.06	2.62	.026
PCA	1.22	0.46	3.20	.709
BA**	2.11	1.30	3.30	.003
VA	0.94	0.37	2.38	.896
VBSB	0.73	0.38	1.38	.331
aSAH characteristics				
WFNS 2	1.25	0.91	1.72	.169
WFNS 3	0.85	0.54	1.35	.492
WNFS 4	0.93	0.62	1.39	.707
WFNS 5	0.81	0.57	1.11	.189
Fisher grade 3*	1.67	1.12	2.47	.011
Fisher grade 4	1.31	0.85	2.04	.216

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 branch.

Patients included into the analysis were n = 1689 respectively. Significance is indicated as follows: ns ($P > .05$), * ($P \leq .05$), ** ($P \leq .01$), *** ($P \leq .001$), **** ($P \leq .0001$).

The model includes the following variables: sex (reference level: female), age (by age-group of 10 yr), aneurysm diameter (per 1 mm), location of the index aneurysm (reference level: ACommA), WFNS grade at admission (reference level: WFNS grade 1) and higher blood clot burden defined as Fisher grade 3 or 4 (reference level: Fisher grade 1-2).

and larger size of the index aneurysm (OR per mm 1.03, 95% CI 1.01-1.06). In contrast, male sex was correlated with a lower probability of aneurysm multiplicity (OR 0.76, 95% CI 0.59-0.98). Details have been published separately.[25]

Characteristics of Index Aneurysms Treatment

Endovascular treatment was the most frequently selected treatment modality for index aneurysms overall (n = 856; 50.7%), for index aneurysms in patients with MIA (n = 227, 48.6%), and for index aneurysms in patients with SIA (n = 629, 51.5%). Surgery was the second most frequently selected treatment modality overall (n = 637, 37.7%). Index aneurysms were more frequently treated surgically in patients with MIA than in patients with SIA (40.0% vs. 36.9%).

Endovascular treatment was the preferred treatment modality in particular for ACommA, basilar artery, and internal carotid artery aneurysms in patients with either SIA or MIA. In contrast, surgical treatment was the most frequently chosen treatment modality for MCA aneurysms in patients with either SIA or MIA. Details are provided in Table 3.

In patients with a ruptured posterior communicating artery (PCommA) aneurysm, the percentage of patients undergoing surgical rather than endovascular treatment was higher in patients suffering from an acute CND (eg, oculomotor nerve palsy), in both the MIA and the SIA groups. Nonetheless, clipping was less frequently selected in terms of absolute numbers for PCommA aneurysms in all subgroups (Table S3 of **Appendix, Supplemental Digital Content**).

Characteristics of Bystander Aneurysms Treatment

Bystander aneurysms were most often managed conservatively (meaning that no surgical, endovascular, or hybrid procedure was performed within the observation period; n = 230; 31.6%). In contrast to the treatment of index aneurysms, surgery was the most frequent active (meaning non-conservative) treatment modality for bystander aneurysms (n = 176; 24.2%). In MIA patients in whom the index aneurysm was treated surgically, bystander aneurysms were most often managed surgically (n = 110; 41.5%). In contrast, bystander aneurysms were most often managed conservatively in MIA patients whose index aneurysm was treated endovascularly (n = 109; 36.7%). Details are provided in Table 3.

Primary Outcome

The percentage of patients with evidence of new stroke on the first CT after aneurysm treatment was higher in the MIA group than in the SIA group (19.3% vs 15.1%). This difference reached significance in univariate analysis ($P = .036$). However, the 95% confidence interval of OR in our multivariate model included 1, which implies either that the effect is truly nonexistent or that this study lacked the power to demonstrate it (OR 1.30; 95% CI 0.95-1.78; Figure 2A; Table S4 and Figure S2 of **Appendix, Supplemental Digital Content**). The percentage of patients with evidence of stroke on the last CT prior to hospital discharge was also higher in the MIA group than in the SIA group (24% vs 21.4%). This difference remained insignificant however in univariate ($P = .25$) and multivariate analysis (OR 1.14; 95% CI 0.86-1.53; Figure 2B; Table S4 and Figure S3 of **Appendix, Supplemental Digital Content**).

Endovascular treatment, compared to surgery, was the only variable that was independently correlated with a lower risk for stroke on CT after aneurysm treatment (OR 0.49, 95% CI 0.35-0.68), as well as on CT at discharge (OR 0.55, 95% CI 0.40-0.74). With regard to patient age and location of the index aneurysm, we found no significant correlation with the risk for stroke on CT after aneurysm treatment. However, older age (OR 1.14 per 10 yr; 95% CI 1.03-1.27) and posterior cerebral artery location (OR 3.38; 95% CI 1.19-9.64, reference level: ACommA) were correlated with a higher risk for stroke on CT at discharge (Figure 2A and 2B; Table S4, Figures S2 and S3 of **Appendix, Supplemental Digital Content**).

TABLE 3. Frequency Table for Treatment of Index and Bystander Aneurysms in Patients With SIA and Patients With MIA

Treatment of index aneurysms (ruptured)	Total n (%)	SIA n (%)	MIA n (%)
Total	1689 (100)	1222 (72.4)	467 (27.6)
Surgery	637 (37.7)	450 (36.9)	187 (40)
Endovascular	856 (50.7)	629 (51.5)	227 (48.6)
Hybrid[a]	47 (2.8)	20 (1.6)	27 (5.8)
Conservative	148 (8.7)	122 (10)	26 (5.6)
Missing information	1 (0.1)	1 (0.1)	0 (0)

Treatment of bystander aneurysms (unruptured)	Total n (%)	Surgery n (%)	Endovascular (n %)	Hybrid[b] n (%)	Conservative n (%)
Total	727 (100)	176 (27.6)	100 (15.7)	131 (20.6)	230 (36.1)
Surgical treatment of index aneurysm	265 (36.5)	110 (41.5)	21 (7.9)	40 (15.1)	94 (35.5)
Endovascular treatment of index aneurysm	297 (40.9)	45 (15.2)	70 (23.6)	73 (24.6)	109 (36.7)
Hybrid treatment of index aneurysm[a]	42 (5.8)	17 (40.5)	8 (19)	8 (19)	9 (21.4)
Conservatively treated index aneurysm	33 (4.5)	4 (12.1)	1 (3)	10 (30.3)	18 (54.5)
Missing information	90 (12.3)				

Treatment of index aneurysm (ruptured) with intracranial aneurysms (SIA)	Total n (%)	Surgery n (%)	Endovascular n (%)	Hybrid[b] n (%)	Conservative n (%)
Anterior circulation					
Total	1044 (100)	426 (40.8)	515 (49.3)	86 (8.2)	17 (1.6)
ACommA	424 (40.6)	150 (35.4)	240 (56.6)	23 (5.4)	11 (2.6)
ACA	83 (7.6)	24 (28.9)	46 (55.4)	12 (14.5)	1 (1.2)
ICA	197 (18.9)	57 (28.9)	120 (60.9)	19 (9.6)	1 (0.5)
MCA	258 (24.7)	183 (70.9)	47 (18.2)	26 (10.1)	2 (0.8)
PCommA	82 (7.6)	12 (14.6)	62 (75.6)	6 (7.3)	2 (2.4)
Posterior circulation					
Total	177 (100)	44 (24.9)	93 (52.5)	36 (20.3)	4 (2.3)
PCA	17 (9.6)	3 (17.6)	11 (64.7)	1 (5.9)	2 (11.8)
BA	58 (23.8)	1 (1.7)	44 (75.9)	13 (22.4)	0 (0)
VBSB	71 (40.1)	19 (26.8)	38 (53.5)	13 (18.3)	1 (1.4)
VA	31 (17.5)	21 (67.7)	0 (0)	9 (29.3)	1 (3.2)

Treatment of index aneurysms (ruptured) with multiple intracranial aneurysms (MIA)	Total n (%)	Surgery n (%)	Endovascular n (%)	Hybrid[b] n (%)	Conservative n (%)
Anterior circulation					
Total	403 (100)	181 (44.9)	179 (44.4)	21 (5.2)	22 (5.5)
ACommA	109 (27.1)	38 (34.9)	63 (57.8)	4 (3.7)	4 (3.7)
ACA	34 (8.4)	14 (41.2)	20 (58.8)	0 (0)	0 (0)
ICA	82 (20.3)	21 (25.6)	44 (53.7)	11 (13.4)	6 (7.3)
MCA	136 (33.7)	103 (75.7)	20 (14.7)	6 (4.4)	7 (5.1)
PCommA	42 (10.4)	5 (11.9)	32 (76.2)	0 (0)	5 (11.9)
Posterior circulation					
Total	64 (100)	11 (17.1)	44 (68.8)	5 (7.8)	4 (6.3)
PCA	6 (9.4)	2 (33.3)	3 (50)	0 (0)	1 (16.7)
BA	38 (59.4)	0 (0)	32 (84.2)	3 (7.9)	3 (7.9)
VBSB	13 (20.3)	4 (30.8)	8 (61.5)	1 (7.7)	0 (0)
VA	7 (10.9)	5 (71.43)	1 (14.29)	1 (14.29)	0 (0)

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-branch.

[a]In this context meaning any combination of surgical and endovascular treatment of the index aneurysm in a same session.

[b]In this context meaning any combination of surgical and endovascular treatment of the same aneurysm in one or in consecutive sessions.

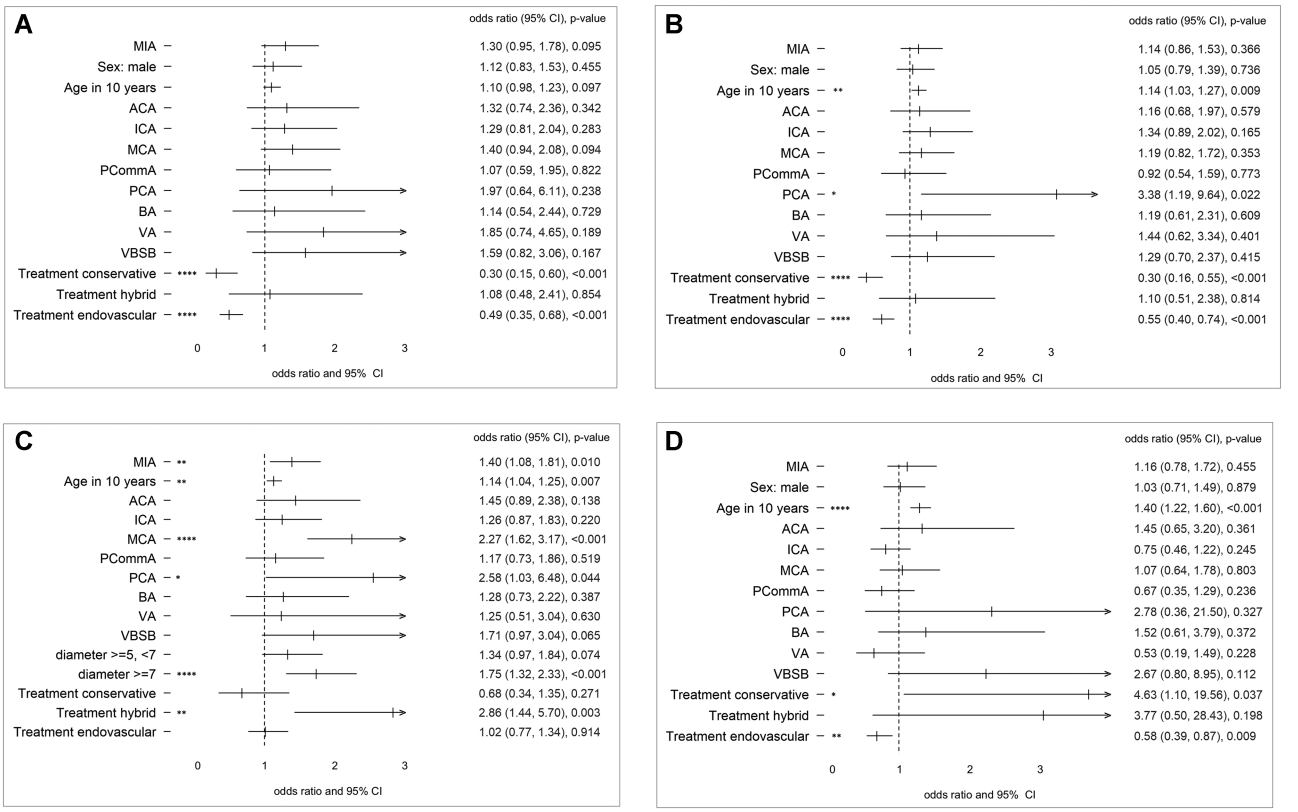

FIGURE 2. *Mixed effects logistic regression model.* **A**, *OR for the presence of a new stroke documented by CT scan after aneurysm treatment.* **B**, *OR for the presence of a new stroke documented by CT scan at hospital discharge.* **C**, *OR for the presence of a new focal neurological deficit (FND) at hospital discharge.* **D**, *OR for unfavorable functional outcome (mRS 3-6) at hospital discharge. The model includes the following variables: aneurysm multiplicity (MIA), sex (reference level: female), age (by decades), location of the index aneurysm (reference level: ACommA), and treatment modality (reference level: surgery). 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. n = 1139 and n = 1128 patients were included in the analysis, respectively. Significance is indicated as follows: ns (P > .05), * (P ≤ .05), ** (P ≤ .01), *** (P ≤ .001), **** (P ≤ .0001).*

Secondary Outcome

Patients with MIA, compared to patients with SIA, had longer hospital stays (mean, 22.7 vs 21.6 d; median, 21 vs 19 d), and a higher percentage of patients with MIA than with SIA suffered from a new FND at discharge (36.5% vs 24.3%). In multivariate analysis, aneurysm multiplicity was correlated with the presence of a new FND at discharge, meaning that the FND was not present on admission exam (OR 1.40; 95% CI 1.08-1.81; Figure 2C; Table S4 and Figure S4 of **Appendix, Supplemental Digital Content**).

There was no significant difference in terms of mRS between the MIA and the SIA groups on discharge or a year later (Figure 2D; Table S4 and Figures S5 and S6 of **Appendix, Supplemental Digital Content**). Likewise, the hazard ratio for in-hospital mortality and the estimate for overall mortality at 1 yr did not significantly differ between the 2 groups (hazard ratio for in-hospital mortality: 0.79 [95% CI 0.58-1.07]; estimate for overall mortality at 1 yr: 0.84 [95% CI 0.63-1.13]; Figures 3A and 3B; Table S4 of **Appendix, Supplemental Digital Content**).

Finally, older age at the time of aneurysm rupture was correlated with the presence of stroke on CT at hospital discharge (OR 1.14 per 10 yr; 95% CI 1.03-1.27), with the presence of a new FND at hospital discharge (OR 1.41 per 10 yr, 95% CI 1.04-1.25), with unfavorable functional outcome (mRS 3-6) at hospital discharge (OR 1.40 per 10 yr, 95% CI 1.22-1.60), and with death (mRS 6) at 1 yr (OR 1.47 per 10 yr, 95% CI 1.33-1.62; Figures 2A and 2B; Table S4, Figures S2 and S3 of **Appendix, Supplemental Digital Content**).

DISCUSSION

In this large nationwide cohort study, the prevalence of MIA was 27.6%. This accords well with previous reports.[4,26] The

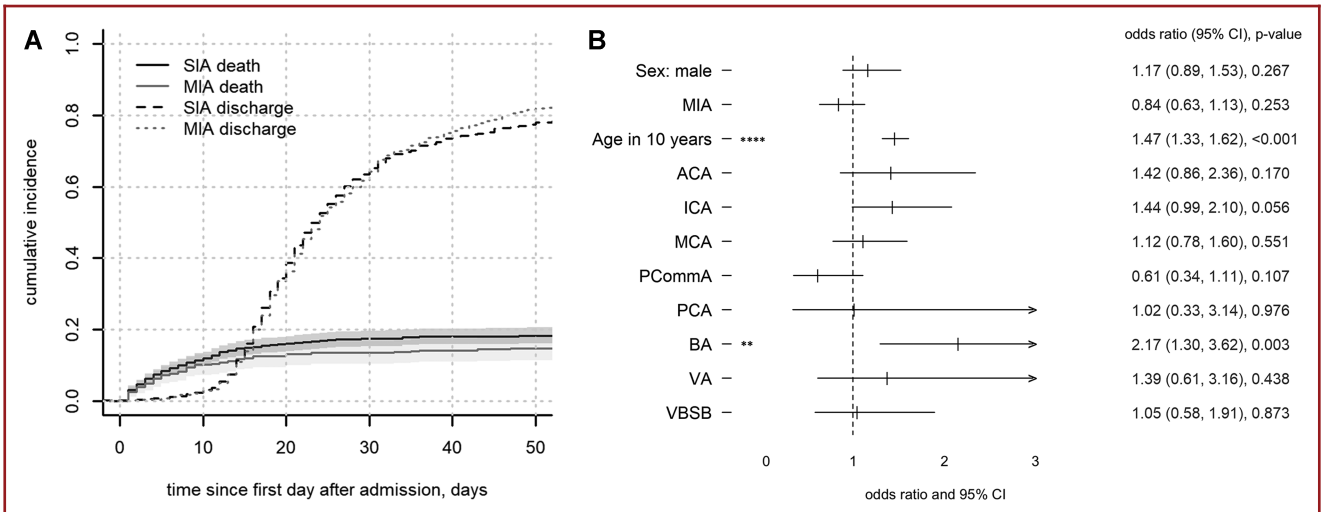

FIGURE 3. *Overall survival analysis.* **A**, *Cumulative incidence curve for mortality at hospital discharge for patients with an SIA and for patients with MIAs who survived beyond the day of admission. The hazard ratio for in-hospital mortality for patients with MIA compared to patients with SIA adjusted for age, sex, and location of the index aneurysm was 0.79 (95% CI 0.58-1.07).* **B**, *Mixed effects logistic regression for overall mortality at 1 yr. The estimate for overall mortality in patients with MIA compared to patients with SIA at 1 yr was 0.84 (95% CI 0.63-1.13). The model includes the following variables: sex (reference level: female), age (by age-group of 10 years), aneurysm diameter (per 1mm), and location of the index aneurysm (reference level: ACommA). 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. Patients included in the analysis were n = 1139 and n = 1128, respectively. Significance is indicated as follows: ns (P > .05), * (P ≤ .05), ** (P ≤ .01), *** (P ≤ .001), **** (P ≤ .0001).*

likelihood of MIA was higher in women, in patients with an index aneurysm at certain locations, and in patients with a ruptured aneurysm of larger size (Table 2; Table S2 and Figure S1 of **Appendix, Supplemental Digital Content**). The percentage of patients with evidence of a new stroke on the first CT after aneurysm treatment was higher in the MIA group than in the SIA group (Table S4 of **Appendix, Supplemental Digital Content**). However, the 95% confidence intervals for OR in our multivariate model included 1, implying either a nonexistent association or insufficient power to demonstrate one (Figure 2A; Figure S2 of **Appendix, Supplemental Digital Content**). As for the secondary endpoints, a higher percentage of patients in the MIA than in the SIA group suffered from a new FND at discharge, and aneurysm multiplicity was indeed found to independently predict the occurrence of FND between admission and discharge (Figure 2C; Figure S4 of **Appendix, Supplemental Digital Content**). Still, this excess short-term morbidity did not portend lower overall survival or lower functional outcome at hospital discharge or at 1 year (Figures 2D, 3A, and 3B; Table S4, Figures S5 and S6 of **Appendix, Supplemental Digital Content**).

Endovascular treatment was overall the most frequently selected treatment modality in patients with MIA and in patients with SIA. Endovascular therapy was also the most frequently selected treatment for aneurysms at all sites except the MCA and the VA. In contrast, surgical treatment was the most frequently selected treatment modality for MCA aneurysms in all subgroups. Index aneurysms were more frequently treated surgically in patients with MIA than in patients with SIA, which we presume reflects the higher percentage of MCA aneurysms in the MIA group compared to the SIA group (29.1% vs 21.1%). In multivariate analysis, endovascular compared to surgical treatment was associated with a significantly lower OR for stroke on CT after aneurysm treatment, independently of the patient's MIA or SIA status (Figures 2A and 2B; Figures S2 and S3 of **Appendix, Supplemental Digital Content**). We think, however, that selection bias may have skewed this result. Our model was built to reflect the fact that the size and location of aneurysms are the main considerations entering into the choice of treatment once a decision to intervene has been made. Further adjustment for patient severity on presentation under this model assumption would have led to a biased estimate of the intervention effect. For this reason, we decided not to adjust for additional patient factors on presentation when modeling the impact of aneurysm multiplicity on outcome. Moreover, among the MIA patients, bystander aneurysms were more often managed conservatively in patients whose index aneurysm was managed conservatively rather than surgically. But again, our model did not conclusively differentiate morbidity related to the treatment of the index aneurysm from morbidity associated with the treatment of (a) bystander aneurysm(s) or treatment-unrelated morbidity (see limitations). Finally, the time to full recovery from aSAH, especially after surgery, is often measured in months, and many patients suffering from a FND at discharge would probably have recovered, especially in the surgical arm, if longer follow-up for

this variable had been taken into account (Table 3; Table S1 of **Appendix, Supplemental Digital Content**).

Regarding the primary and co-primary outcomes of our study, we found that a higher proportion of patients with MIA than patients with SIA suffered from a new stroke after aneurysm treatment (Table S4 of **Appendix, Supplemental Digital Content**). This difference reached significance in univariate analysis ($P = .036$), but the association was not statistically significant in our multivariate model (Figure 2A; Figure S2 of **Appendix, Supplemental Digital Content**). Similarly, there was a higher percentage of MIA compared to SIA patients with evidence of stroke on the predischarge CT (Table S4 of **Appendix, Supplemental Digital Content**), but once again our multivariate model did not reveal a significant association between aneurysm multiplicity and the risk of stroke on the predischarge CT (Figure 2B; Figure S3 of **Appendix, Supplemental Digital Content**). We presume that our multivariate model was either insufficiently powered, or did not quantify these associations reliably because of the confounding effect of treatment-related and treatment-unrelated causes of stroke and the relatively rarity of stroke (see limitations below).

As for the secondary outcomes, we found that aneurysm multiplicity was an independent predictor of more FND at discharge (Figure 2C; Figure S4 of **Appendix, Supplemental Digital Content**). We speculate that this finding may relate to a cumulative effect of differences in the aneurysms' anatomical distribution (eg, more MCA aneurysms in patients with MIA), as well as a larger number of treated aneurysms and a higher proportion of aneurysms treated surgically in the MIA group (Table 3; Table S1 of **Appendix, Supplemental Digital Content**). Although we found in our cohort slightly longer hospitalization times for patients with MIA, functional outcome, and overall survival at hospital discharge and at 1 yr did not differ significantly between the MIA and SIA groups (Figures 3A and 3B; Figures S5 and S6, and Table S4 of **Appendix, Supplemental Digital Content**). More and better follow-up data will be needed, however, to rule out bias towing to differential follow-up or unmeasured confounding.

Limitations

This study's potential weaknesses and limitations include the broad definition of the primary stroke endpoint as "ischemia not seen on the admission CT." This definition potentially includes both treatment-related and treatment-unrelated morbidity. Similarly, our study did not conclusively differentiate between morbidity related to the treatment of the index aneurysm, morbidity related to the treatment of (a) bystander aneurysm(s), and treatment-unrelated morbidity. However, stroke and neurological deficits are, in practice, often hard to attribute to a precise cause (eg, the treatment of 1 aneurysm rather than another). Moreover, we relied on the written radiological interpretation by center-based radiologists, and the clinical assessment was obtained by the local teams, meaning that there was no blinded radiological or clinical assessment.

The influence of constitutional and modifiable risk factors for MIA has been investigated in detail in a previous study.[4-6] In the present study, risk factors were too inconsistently recorded for inclusion in our multivariate model. For instance, our dataset did not differentiate among patients who were active smokers, former smokers, ever smoked, or never smoked. That being said, patients were strongly advised not to smoke and arterial pressure was tightly controlled in all patients during interval from ictus until discharge. The question remains whether these factors had different impacts on the endpoints of our study after aneurysm treatment, at discharge, and during the extended follow-up period. Unfortunately, this cannot conclusively be assessed from our data, but we think that their impact was small.

For the sake of data consistency, we assessed outcomes only at the time of patient discharge, with the exception of functional outcome (mRS) and overall survival, for which we included 1-yr follow-up. Nonetheless, there were missing data for both the primary/coprimary and the secondary endpoints. Yet, we compared the estimates with pooled estimates obtained from 5 imputed datasets to investigate whether missing values introduced bias, and we found that there was no relevant difference between coefficients estimated from imputed datasets and those estimated from the dataset restricted to complete cases.

As already mentioned, our analysis found associations, but ultimately lacked the necessary statistical power to reliable estimate the effect, as reflected by broad confidence intervals that included the value 1 for most of the ORs studied. Further research on larger cohorts would be required to confirm and quantify these associations.

Finally, we cannot fully explain the relatively high percentage of patients with SIA who were treated conservatively. We presume this may be at least partly due to an intentionally incomplete imaging work-up, potentially missing the identification of bystander aneurysms, in patients who were not given any active treatment because of a neurologically devastating aSAH.[11]

CONCLUSION

aSAH patients with MIA fare worse in the short term than those with SIA. This excess morbidity is associated with longer hospital stays but not with lower survival or worse long-term clinical outcome. Further research on larger cohorts should be performed to clarify the nature of this excess morbidity, with the purpose of defining the optimal treatment of aneurysms in aSAH patients with MIA.

Disclosures

This research was supported by departmental funds of the Department of Surgery, Basel University Hospital, Basel, Switzerland. The Basel Institute for Clinical Epidemiology & Biostatistics receives funding from Stiftung Institut für klinische Epidemiologie.

REFERENCES

1. Juvela S. Risk factors for multiple intracranial aneurysms. *Stroke*. 2000;31(2):392-397.
2. Baumann F, Khan N, Yonekawa Y. Patient and aneurysm characteristics in multiple intracranial aneurysms. *Acta Neurochir Suppl*. 2008;103:19-28.
3. Ellamushi HE, Grieve JP, Jager HR, Kitchen ND. Risk factors for the formation of multiple intracranial aneurysms. *J Neurosurg*. 2001;94(5):728-732.
4. Qureshi AI, Suarez JI, Parekh PD, et al. Risk factors for multiple intracranial aneurysms. *Neurosurgery*. 1998;43(1):22-26.
5. Qureshi AI, Sung GY, Suri MF, Straw RN, Guterman LR, Hopkins LN. Factors associated with aneurysm size in patients with subarachnoid hemorrhage: effect of smoking and aneurysm location. *Neurosurgery*. 2000;46(1):44-50.
6. McDowell MM, Zhao Y, Kellner CP, et al. Demographic and clinical predictors of multiple intracranial aneurysms in patients with subarachnoid hemorrhage. *J Neurosurg*. 2018;128(4):961-968.
7. Jeon P, Kim BM, Kim DJ, Kim DI, Suh SH. Treatment of multiple intracranial aneurysms with 1-stage coiling. *Am J Neuroradiol*. 2014;35(6):1170-1173.
8. Mizoi K, Suzuki J, Yoshimoto T. Surgical treatment of multiple aneurysms. *Acta Neurochir*. 1989;96(1-2):8-14.
9. Shen X, Xu T, Ding X, Wang W, Liu Z, Qin H. Multiple intracranial aneurysms: endovascular treatment and complications. *Interv Neuroradiol*. 2014;20(4):442-447.
10. Rinne J, Hernesniemi J, Niskanen M, Vapalahti M. Management outcome for multiple intracranial aneurysms. *Neurosurgery*. 1995;36(1):31-38.
11. Kaminogo M, Yonekura M, Shibata S. Incidence and outcome of multiple intracranial aneurysms in a defined population. *Stroke*. 2003;34(1):16-21.
12. Pleizier CM, Ruigrok YM, Rinkel GJ. Relation between age and number of aneurysms in patients with subarachnoid haemorrhage. *Cerebrovasc Dis*. 2002;14(1):51-53.
13. Vajda J. Multiple intracranial aneurysms: a high risk condition. *Acta Neurochir*. 1992;118(1-2):59-75.
14. Schatlo B, Fung C, Fathi AR, et al. Introducing a nationwide registry: the Swiss study on aneurysmal subarachnoid haemorrhage (Swiss SOS). *Acta Neurochir*. 2012;154(12):2173-2178.
15. Ruiz-Sandoval JL, Cantu C, Chiquete E, et al. Aneurysmal subarachnoid hemorrhage in a Mexican multicenter registry of cerebrovascular disease: the RENAMEVASC study. *J Stroke Cerebrovasc Dis*. 2009;18(1):48-55.
16. Lagares A, de Toledo P, Fernandez-Alen JA, et al. Spontaneous subarachnoid haemorrhage multicenter database from the group for the study of vascular pathology of the Spanish Society for Neurosurgery: presentation, inclusion criteria and development of an internet-based registry. *Neurocirugía*. 2008;19(5):405-415.
17. Jaja BN, Attalla D, Macdonald RL, et al. The Subarachnoid Hemorrhage International Trialists (SAHIT) Repository: advancing clinical research in subarachnoid hemorrhage. *Neurocrit Care*. 2014;21(3):551-559.
18. Macdonald RL, Cusimano MD, Etminan N, et al. Subarachnoid Hemorrhage International Trialists data repository (SAHIT). *World Neurosurg*. 2013;79(3-4):418-422.
19. Ikawa F, Ohbayashi N, Imada Y, et al. Analysis of analysis of subarachnoid hemorrhage according to the Japanese Standard Stroke Registry Study–incidence, outcome, and comparison with the International Subarachnoid Aneurysm Trial. *Neurol Med Chir (Tokyo)*. 2004;44(5):275-276.
20. Fischer T, Johnsen SP, Pedersen L, Gaist D, Sorensen HT, Rothman KJ. Seasonal variation in hospitalization and case fatality of subarachnoid hemorrhage - a nationwide Danish study on 9,367 patients. *Neuroepidemiology*. 2005;24(1-2):32-37.
21. Farrell B, Godwin J, Richards S, Warlow C. The United Kingdom transient ischaemic attack (UK-TIA) aspirin trial: final results. *J Neurol Neurosurg Psychiatry*. 1991;54(12):1044-1054.
22. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet North Am Ed*. 1974;2(7872):81-84.
23. Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. *Neurosurgery*. 1980;6(1):1-9.
24. Stekhoven DJ, Buhlmann P. MissForest–non-parametric missing value imputation for mixed-type data. *Bioinformatics*. 2012;28(1):112-118.
25. Roethlisberger M, Achermann R, Bawarjan S, et al. Predictors of occurrence and anatomic distribution of multiple aneurysms in patients with aneurysmal subarachnoid hemorrhage. *World Neurosurg*. 2018;111:e199-e205.
26. Ostergaard JR, Hog E. Incidence of multiple intracranial aneurysms. Influence of arterial hypertension and gender. *J Neurosurg*. 1985;63(1):49-55.

Acknowledgments

The authors would like to thank Ethan Taub, MD, for reviewing the manuscript, Selina Ackermann for editorial assistance, and the members and contributors of the Swiss SOS group: Javier Fandino, Daniel Colluccia, Marta Arrighi, Alice Venier, Dominique E. Kuhlen, Michael, Reinert, Astrid Weyerbrock, Martin Hlavica, Jean-Yves Fournier, Andreas Raabe, Jürgen Beck, David Bervini, Karl Schaller, Roy Thomas Daniel, Daniele Starnoni, Mahmoud Messerer, Marc Levivier, Emanuela Keller, Luca Regli, Oliver Bozinov, Sina Finkenstaedt, Luca Remonda, Christoph Stippich, Jan Gralla, Zsolt Kulcsar, Vitor Mendes-Pereira, Guillaume Saliou, Johannes Weber, Alessandro Cianfoni, Peter Ahlborn, Nicolas Roydon Smoll, Veit Rohde, Sina Tok, Fabian Baumann, Karl Kothbauer, Hassen Kerkeni, Hiroki Dan-Ura, Ali Reza Fathi, Hans Landolt, Khaled Mostaguir, Yvan Gasche, Asita Sarrafzadeh, Gerhard Hildebrandt, Kerstin Winkler, Christoph Woernle, and René Bernays.

Supplemental digital content *is available for this article at www.neurosurgery-online.com.*

Supplemental Digital Content. Appendix.

Table S1. Frequency table of aneurysms by location. This table shows the anatomic distribution of ruptured (index) aneurysms and unruptured (bystander) aneurysms. The index aneurysms [r] are listed by location on the x-axis. The bystander aneurysms [nr] are listed by location on the y-axis. [r]SIA: n = 1222; [r]MIA: n = 467; [nr]MIA: n = 668. 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. Table S2. Factors favoring aneurysm multiplicity. This table provides the logistic regression analysis (multivariate model on the left, and univariate model on the right) for aneurysm multiplicity. The reference variable for sex was "female." The reference level for location was "ACommA." The reference level for WFNS grade was "WFNS grade 1." The reference level for thick clot: "no," meaning absence of a thick clot. The reference level for GCS score was "GCS score 3-6." The reference level for Fisher scale grade was "Fisher scale grade 1." The reference level for mRS was "mRS 6." The reference level for new FND was "no," meaning absence of FND. The reference level for new CND was "no," meaning absence of CND. Table S3. Frequency table of ruptured posterior communicating aneurysms (PCommA) by presentation with or without acute cranial nerve deficit. This table provides the subgroup analysis of ruptured PCommA aneurysms for patients with MIA and patients with an SIA. The modality of aneurysm treatment is provided for each subgroup, meaning for the group of patients that presented with acute cranial nerve deficit (eg, oculomotor nerve palsy), and for the group of patients that presented without acute cranial nerve deficit. Table S4. Outcome table. This table provides the univariate analysis for outcome in aSAH patients with multiple intracranial aneurysms (MIA) and in patients with a single intracranial aneurysm (SIA). *P* values were calculated with a chi-square test for categorical variables and *t*-test for continuous variables. Figure S1. Effect plots and forest plot for the mixed effects logistic regression model for aneurysm multiplicity. This figure illustrates the effect of the following variables: sex (reference level: female), age (by decade), aneurysm diameter (per 1mm), location of the index aneurysm (reference level: ACommA), WFNS-grade at admission (reference level: WFNS-grade 1), and Fisher scale grade 3 or 4 (reference level: Fisher scale grade 1 and 2). 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. Patients included into the analysis were n = 1689. Significance is indicated as follows: ns ($P > .05$), * ($P \leq .05$), ** ($P \leq .01$), *** ($P \leq .001$), **** ($P \leq .0001$). Figure S2. Effect plots and forest plot for the mixed effects logistic regression

models for the primary endpoint "new stroke on the post-treatment CT scan." This figure illustrates the effect of the following variables: aneurysm multiplicity (reference level: SIA), sex (reference level: female), increasing patient age (by steps of ten years), aneurysms location (reference level: ACommA), modality of aneurysms treatment (reference level: surgery). SIA: aSAH patients with a single intracranial aneurysms, 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. Figure S3. Effect plots and forest plot for the mixed effects logistic regression models for coprimary endpoint "new stroke on the last CT scan prior to hospital discharge." This figure illustrates the effect of the following variables: aneurysm multiplicity (reference level: SIA), sex (reference level: female), increasing patient age (by steps of 10 yr), aneurysms location (reference level: ACommA), modality of aneurysms treatment (reference level: surgery). SIA: aSAH patients with a single intracranial aneurysms, 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. Figure S4. Effect plots and forest plot for the mixed effects logistic regression models for the secondary endpoint "new focal neurological deficit at hospital discharge." This figure illustrates the effect of the following variables: aneurysm multiplicity (reference level: SIA), sex (reference level: female), increasing patient age (by steps of 10 yr), aneurysms location (reference level: ACommA), modality of aneurysms treatment (reference level: surgery). SIA: aSAH patients with a single intracranial aneurysms, 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. Figure S5. Effect plots and forest plot for the mixed effects logistic regression models for the secondary endpoint "unfavorable functional outcome (defined as mRS 3-6) at hospital discharge." This figure illustrates the effect of the following variables: aneurysm multiplicity (reference level: SIA), sex (reference level: female), increasing patient age (by steps of 10 yr), aneurysms location (reference level: ACommA), modality of aneurysms treatment (reference level: surgery). SIA: aSAH patients with a single intracranial aneurysms, 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: vertebro basilar side branches. Figure S6. Effect plots and forest plot for the mixed effects logistic regression models for the secondary outcome "dearth (mRS 6) at 1 yr." This figure illustrates the effect of the following variables: aneurysm multiplicity (reference level: SIA), sex (reference level: female), increasing patient age (by steps of ten years), aneurysms location (reference level: ACommA), modality of aneurysms treatment (reference level: surgery). SIA: aSAH patients with a single intracranial aneurysms, 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.

COMMENT

The authors present an interesting paper with the intention of determining the impact of multiple intracranial aneurysms (MIA cohort) on short-term outcomes for patients with aSAH. The authors culled patients from the Swiss Study of Subarachnoid Hemorrhage Registry (Swiss SOS) between 2009 and 2014. The authors utilized robust and appropriate statistical techniques for retrospective analysis. The authors found that the incidence of stroke was common in the MIA group as compared to the single intracranial aneurysm (SIA) group both after initial treatment and at discharge. No difference in functional status or survival was discovered between the study groups at 1-year. Not surprisingly, surgical treatment was associated with a higher stroke rate than endovascular treatment.

C. Michael Cawley
Atlanta, Georgia