Patterns of care for ruptured aneurysms of the middle cerebral artery: analysis of a Swiss national database (Swiss SOS)

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OBJECTIVE The objective of this study was to determine patterns of care and outcomes in ruptured intracranial aneurysms (IAs) of the middle cerebral artery (MCA) in a contemporary national cohort.

METHODS The authors conducted a retrospective analysis of prospective data from a nationwide multicenter registry of all aneurysmal subarachnoid hemorrhage (aSAH) cases admitted to a tertiary care neurosurgical department in Switzerland in the years 2009–2015 (Swiss Study on Aneurysmal Subarachnoid Hemorrhage [Swiss SOS]). Patterns of care and outcomes at discharge and the 1-year follow-up in MCA aneurysm (MCAA) patients were analyzed and compared with those in a control group of patients with IAs in locations other than the MCA (non-MCAA patients). Independent predictors of a favorable outcome (modified Rankin Scale score ≤ 3) were identified, and their effect size was determined.

RESULTS Among 1866 consecutive aSAH patients, 413 (22.1%) harbored an MCAA. These MCAA patients presented with higher World Federation of Neurosurgical Societies grades (p = 0.007), showed a higher rate of concomitant intracerebral hemorrhage (ICH; 41.9% vs 16.7%, p < 0.001), and experienced delayed cerebral ischemia (DCI) more frequently (38.9% vs 29.4%, p = 0.001) than non-MCAA patients. After adjustment for confounders, patients with MCAA were as likely as non-MCAA patients to experience DCI (aOR 1.04, 95% CI 0.74–1.45, p = 0.830). Surgical treatment was the dominant treatment modality in MCAA patients and at a significantly higher rate than in non-MCAA patients (81.7% vs 36.7%, p < 0.001). An MCAA location was a strong independent predictor of surgical treatment (aOR 8.49, 95% CI 5.89–12.25, p < 0.001), despite statistical adjustment for variables traditionally associated with surgical treatment, such as (space-occupying) ICH (aOR 1.73, 95% CI 1.23–2.45, p = 0.002). Even though MCAA patients were less likely to die during the acute hospitalization (aOR 0.52, 0.30–0.91, p = 0.022), their rate of a favorable outcome was lower at discharge than that in non-MCAA patients (55.7% vs 63.7%, p = 0.003). At the 1-year follow-up, 68.5% and 69.6% of MCAA and non-MCAA patients, respectively, had a favorable outcome (p = 0.676).

ABBREVIATIONS aOR = adjusted odds ratio; aSAH = aneurysmal subarachnoid hemorrhage; BRAT = Barrow Ruptured Aneurysm Trial; DCI = delayed cerebral ischemia; IA = intracranial aneurysm; ICH = intracerebral hemorrhage; ISAT = International Subarachnoid Aneurysm Trial; MCA = middle cerebral artery; MCAA = MCA aneurysm; mRS = modified Rankin Scale; RCT = randomized controlled trial; WFNS = World Federation of Neurosurgical Societies.

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CONCLUSIONS Microsurgical occlusion remains the predominant treatment choice for about 80% of ruptured MCAAs in a European industrialized country. Although patients with MCAAs presented with worse admission grades and greater rates of concomitant ICH, in-hospital mortality was lower and long-term disability was comparable to those in patients with non-MCAA.

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KEYWORDS aneurysmal subarachnoid hemorrhage; ruptured middle cerebral artery aneurysms; MCA; pattern of care; outcome; surgical treatment; vascular disorders

Since the results of the International Subarachnoid Aneurysm Trial (ISAT) were published in 2002, most neurovascular centers have shifted from microsurgical clipping toward the endovascular embolization (coiling) of ruptured intracranial aneurysms (IAs) that are amenable to both treatment modalities.[10,27] This is especially true for patients with aneurysmal subarachnoid hemorrhage (aSAH) and an IA location in either the posterior circulation or the deep locations of the anterior circle of Willis. However, ruptured IAs of the middle cerebral artery (MCA) seem to be exempt from a general preference for coiling. Apart from carrying a great risk (around 40%–50%) of concomitant intracerebral hemorrhage (ICH) that can require surgical evacuation, MCA aneurysms (MCAAs) also tend to present with wide-necked bases and/or branching arteries arising from either the neck or the dome, making their endovascular treatment particularly challenging.[6,29] In contrast, microsurgical treatment has been successfully conducted for decades with low morbidity despite occlusion rates close to 100%.[30]

The fact that a 1-year subgroup analysis of MCAA patients in the ISAT showed no difference in outcome between patients who had undergone coiling and those who had undergone clipping further fueled discussion over the best treatment modality in this particular population.[21] With MCAAs composing only 14.1% of all cases, one can speculate that the lack of clinical equipoise, a prerequisite for patient inclusion into the ISAT, was the central reason for MCAA underrepresentation in the trial.[12,20] A similar trend can be observed in the latest prospective, single-center randomized controlled trial (RCT)—the Barrow Ruptured Aneurysm Trial (BRAT)—in which MCAAs showed a 68% cross-over rate from coiling to clipping compared with only 38% in the overall cohort.[22,33]

It remains unclear how this controversy influences clinical decision-making outside of randomized trials, and there is a lack of knowledge regarding current patient management and outcomes in contemporary series of MCAA patients. Therefore, we aimed to analyze the MCAA population of the Swiss Study on Aneurysmal Subarachnoid Hemorrhage (Swiss SOS) with special emphasis on the patterns of care and outcomes.

Methods

The Swiss SOS (http://www.swiss-sos.ch) is a nationwide prospective registry of patients with ruptured IAs who are admitted to an acute neurovascular center in Switzerland.[31] Given the governmental healthcare regulation in Switzerland, aSAH management is centralized and all aSAH patients are referred to one of the eight participating neurovascular centers: Cantonal Hospital Aarau, University Hospital Basel, University Hospital (Inselspital) Bern, University Hospital Geneva, University Hospital Lausanne, Cantonal Hospital Lugano, Cantonal Hospital Sankt Gallen, and University Hospital Zurich. If a previously unknown aSAH is initially diagnosed at a peripheral hospital, the patient is transferred, even in cases of a poor clinical status, for clinical evaluation by a neurosurgeon. Exceptions are made in rare individual cases (e.g., denial of transfer by patient or next of kin).[35]

A set of pre-specified variables were uniformly defined, collected prospectively by the local teams, and pooled into a secured, anonymized Web-based registry (secuTrial), as described previously.[35] Study variables including patient characteristics and outcome were assessed by treating physicians and the local study team. Responsibility for accurate and complete data collection lies with a principal investigator (PI) at each site, and central data reviews are performed. This PI is either specialized in cerebrovascular surgery or closely supervised by the department's senior cerebrovascular surgeon. Incomplete data for the most important variables are only accepted with substantial justification.

Study Design

This is a retrospective cohort study of the anonymized 2009–2015 data set within the framework of a nationwide multicenter registry (Swiss SOS).[31] Patients with non-aSAH were not registered.

Study Variables and Definitions

The following variables were extracted from the Swiss SOS database and used for further analysis: patient characteristics (age, sex, historical premorbid modified Rankin Scale [mRS] score before admission); aneurysm and aSAH characteristics (aneurysm location, aneurysm side, maximal aneurysm diameter in mm grouped according to the stratification used by the International Study of Unruptured Intracranial Aneurysms [ISUIA], Fisher grade); ICH (intraparenchymal hemorrhage of any size due to the aneurysm rupture with or without subarachnoid extension; solely intraventricular hemorrhage or extraaxial hemorrhages were not considered as ICH); treatment modality (microsurgical [clipping, clipping+revascularization], endovascular [coiling, stenting, flow diversion], hybrid [microsurgical+endovascular], or conservative [no aneurysm occlusion attempted]); admission and outcome scores (World Federation of Neurosurgical Societies [WFNS] grade, mRS score at discharge and the 1-year follow-up); and delayed cerebral ischemia (DCI). Favorable outcome at discharge and follow-up was defined as mRS score ≤ 3, whereas unfavorable outcome was defined as mRS score 4–6.[36]

Complications were defined as follows: rebleeding, including in-hospital sudden clinical deterioration with signs of increased hemorrhage on consecutive CT scans, or if no CT scan was obtained, sudden clinical deterioration with evidence of fresh blood in the ventricular drain, as well as acute clinical deterioration suggestive of rebleeding (e.g., acute neurological decline associated with bradycardia or sudden hypertensive blood pressure) at the emergency department and before imaging was obtained;[35,39] DCI, that is, clinical deterioration or new cerebral infarction on imaging attributable to DCI, per the definition of Vergouwen et al.[38,40]

Statistical Analysis

The study cohort consisted of all patients who presented with ruptured IAs originating from the MCA, including its M_1–M_4 segments. The control cohort comprised the remaining patients with ruptured IAs in any non-MCA location. Sensitivity analyses excluding the 264 patients with posterior circulation aneurysms were performed.

Comparisons of baseline characteristics between the patient groups were made using Pearson chi-square tests or Student t-tests for variables on an interval, and data are presented as count (percent) and mean (standard deviation). The same applies to the comparisons of treatment modalities and outcome measures. For the latter, analyses usually focused on patients in whom treatment was initially pursued (i.e., aneurysm occlusion therapy was conducted), as the Swiss SOS registry also contains information on patients with a dismal clinical status and a particularly bad prognosis for which comfort therapy was administered.

In order to minimize potential type I errors due to multiple testing, the absolute number of analyzed variables was kept to a minimum. Univariate and multivariate logistic regression analyses were used to calculate direct and adjusted odds ratios (aORs) and 95% confidence intervals (CIs) to determine the effect size of clinical and radiological predictors of an unfavorable outcome in patients with MCAAs at discharge and the 1-year follow-up. Univariate and multivariate logistic regressions were also used to determine the influence of MCAAs on the decision for surgical treatment, the likelihood of complications (DCI or aneurysm rebleeding), and in-hospital mortality.

Statistical analysis was performed using Stata version 14.2 (StataCorp). Statistical significance was set at $p \leq 0.05$.

Ethical Considerations and Data Collection

The study was approved by the ethics committee at each participating center (under the supervision of the Geneva University Institutional Review Board).[31] All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Results

Patient and Aneurysm Characteristics

The registry comprised data on 1866 consecutive aSAH patients, 413 (22.1%) of whom had presented with MCAAs. The IAs in a non-MCA location were most commonly found at the anterior cerebral artery or anterior communicating artery (48.2%), followed by the internal carotid artery or posterior communicating artery (29.5%) and the posterior circulation (18.2%); the location was unspecified in 4.1% of cases. The MCAA cohort was slightly younger (mean age 54.4 ± 12.0 vs 56.2 ± 13.8 years, $p = 0.014$) and predominantly female (71% vs 64%, $p = 0.006$). Table 1 lists patient and radiological characteristics of the MCAA and non-MCAA cohorts. While mRS scores before aSAH and Fisher grades were similar between the groups, patients with MCAAs presented with a substantially higher rate of ICH (41.9% vs 16.7%, $p < 0.001$) as well as slightly higher admission WFNS grades ($p = 0.007$) and larger aneurysm sizes ($p = 0.043$).

Treatment of Aneurysms in MCA Versus Non-MCA Locations

Aneurysm occlusion therapy differed between patients with MCAAs and those with IAs in non-MCA locations ($p < 0.001$; Table 2). After the exclusion of patients in whom no occlusion had been performed or treatment type was unspecified, microsurgical aneurysm occlusion was the predominant treatment modality in the MCAA group (81.7%) and at a rate significantly higher than that in the non-MCAA group (36.7%; $p < 0.001$).

An MCAA location was a strong and significant predictor of microsurgical occlusion (OR 7.69, 95% CI 5.77–10.25, $p < 0.001$). After adjusting for potential confounding covariables (age, sex, WFNS grade, aneurysm size, and presence of ICH), an MCAA location remained a strong independent predictor of microsurgical aneurysm occlusion (aOR 8.49, 95% CI 5.89–12.25, $p < 0.001$; Table 3). Additional positive or negative independent predictors were the presence of ICH (aOR 1.73, 95% CI 1.23–2.45, $p = 0.002$) and every 1-step increase in the WFNS grade (aOR 0.86, 95% CI 0.79–0.94, $p = 0.001$).

Complications in MCA Versus Non-MCA IA Locations

The rates of aneurysm rebleeding were 4.8% for MCAA patients and 5.2% for non-MCAA patients ($p = 0.738$). In a multivariate analysis, the likelihood for re-rupture was similar between the two patient groups (aOR 0.82, $p = 0.562$; Table 4 and Supplementary Table 1). Patients with MCAAs experienced DCI significantly more frequently than those with IAs in non-MCA locations (38.9% vs 29.4%, $p = 0.001$). However, after adjusting for confounders, patients with MCAAs were as likely as patients with IAs in non-MCA locations to experience DCI (aOR 1.04, $p = 0.830$).

In-Hospital Mortality in MCA Versus Non-MCA IA Locations

In-hospital mortality was 17.4% for patients with MCAAs and 20.7% for those with IAs in non-MCA locations ($p = 0.141$). After the exclusion of 197 patients in

TABLE 1. Basic characteristics of 1866 aSAH patients from the Swiss SOS database

Variable	MCAA	Non-MCAA	p Value
No. of patients	413 (22.1)	1453 (77.9)	
Age in yrs	54.4 ± 12.0	56.2 ± 13.8	0.014
Sex			
F	294 (71.2)	928 (63.9)	0.006
M	119 (28.8)	525 (36.1)	
Aneurysm location			—
MCA	413 (100)	0 (0)	
ACA/ACoA	0 (0)	700 (48.2)	
ICA/PCoA	0 (0)	429 (29.5)	
Posterior	0 (0)	264 (18.2)	
Other/unspecified	0 (0)	60 (4.1)	
Aneurysm side			
Lt	178 (43.1)	380 (26.2)	<0.001
Rt	234 (56.7)	391 (26.9)	
Middle	0 (0)	589 (40.5)	
Unspecified	1 (0.2)	93 (6.4)	
Premorbid mRS score			0.974
0	324 (78.5)	1131 (77.8)	
1	35 (8.5)	133 (9.2)	
≥2	13 (3.1)	48 (3.3)	
Unspecified	41 (9.9)	141 (9.7)	
WFNS grade			
I	136 (32.9)	528 (36.3)	
II	64 (15.5)	284 (19.5)	0.007
III	44 (10.7)	94 (6.5)	
IV	53 (12.8)	132 (9.1)	
V	113 (27.4)	403 (27.7)	
Unspecified	3 (0.7)	12 (0.8)	
Fisher grade			
1	8 (1.9)	46 (3.2)	
2	35 (8.5)	134 (9.2)	0.206
3	221 (53.5)	816 (56.2)	
4	147 (35.6)	455 (31.3)	
Unspecified	2 (0.5)	2 (0.1)	
ICH			<0.001
No	168 (58.1)	835 (83.3)	
Yes	121 (41.9)	167 (16.7)	
Aneurysm size in mm			0.043
2–5	153 (37.0)	602 (41.4)	
6–9	134 (32.4)	471 (32.4)	
10–14	75 (18.2)	178 (12.3)	
15–24	18 (4.4)	62 (4.3)	
≥25	7 (1.7)	21 (1.4)	
Unspecified	26 (6.3)	119 (8.2)	

ACA = anterior cerebral artery; ACoA = anterior communicating artery; ICA = internal carotid artery; PCoA = posterior communicating artery.
Data are presented as count (percent) or mean ± standard deviation, unless indicated otherwise.
* Data were missing for 124 MCAA patients and 451 non-MCAA patients.

TABLE 2. Treatment choices for the two patient cohorts

Variable	MCAA	Non-MCAA	p Value
No. of patients	413 (22.1)	1453 (77.9)	
Aneurysm occlusion therapy			<0.001
Surgical	281 (68.0)	348 (24.0)	
Endovascular	68 (16.5)	790 (54.4)	
Combined	23 (5.6)	111 (7.6)	
None	36 (8.7)	161 (11.1)	
Unspecified	5 (1.2)	43 (3.0)	
Surgical treatment*			
No	68 (18.3)	790 (63.3)	<0.001
Yes	304 (81.7)	459 (36.7)	

Data are expressed as the count (percent), unless indicated otherwise.
* Analysis of 1621 patients, excluding patients in whom no aneurysm occlusion was performed (n = 197) or treatment was unspecified (n = 48).

TABLE 3. Effect size of the relationship between clinical and radiological predictors of surgical treatment, estimated using logistic regression analysis

	Univariate Model			Multivariate Model		
Variable	OR	95% CI	p Value	aOR	95% CI	p Value
MCAA	7.69	5.77–10.25	<0.001	8.49	5.89–12.25	<0.001
Age	0.89	0.73–1.08	0.234	0.98	0.76–1.28	0.897
Sex	0.95	0.77–1.16	0.603	0.98	0.75–1.29	0.886
WFNS grade	0.94	0.86–1.00	0.051	0.86	0.79–0.94	0.001
Aneurysm size	1.10	1.01–1.19	0.018	1.04	0.92–1.17	0.528
ICH	2.17	1.63–2.90	<0.001	1.73	1.23–2.45	0.002

whom no aneurysm occlusion therapy had been attempted, the MCAA patients had a lower in-hospital mortality rate than the non-MCAA patients (10.3% vs 14.9%, p = 0.023).

Among patients in whom active treatment was initially pursued, those with MCAAs were 66% as likely as patients with IAs in non-MCA locations to die during the acute hospitalization (OR 0.66, 95% CI 0.46–0.95, p = 0.024; Supplementary Table 1). After adjusting for potential confounding covariables (age, sex, WFNS grade, aneurysm size, DCI, microsurgical aneurysm occlusion, and presence of ICH), patients with MCAAs remained less likely to die during the acute hospitalization (OR 0.52, 95% CI 0.30–0.91, p = 0.022; Table 4).

Disability Outcome in MCAA Patients and Predictors of Unfavorable Outcome

The distribution of mRS scores across patients with MCAAs and IAs at non-MCA locations is illustrated for outcomes at discharge (Fig. 1A; 1866 patients) and the 1-year follow-up (Fig. 1B; 1644 patients). Patients with MCAAs showed a lower rate of a favorable outcome at discharge than those with IAs in non-MCA locations (55.7% vs 63.7%, p = 0.003). At the 1-year follow-up, patients with MCAAs and those with IAs in non-MCA locations had similar rates of a favorable outcome (68.5% vs 69.6%, p = 0. 676).

In the multivariate analysis, significant predictors of

TABLE 4. MCAA location–specific likelihood for complications

Variable	aOR	95% CI	p Value
DCI	1.04	0.74–1.45	0.830
Re-rupture	0.82	0.42–1.59	0.562
In-hospital mortality*	0.52	0.30–0.91	0.022

MCAA versus non-MCAA patients. Analyses are adjusted for age, sex, WFNS grade, aneurysm size, ICH, surgical treatment, and DCI, as appropriate. See Supplementary Table 1 for detailed analyses.
* In 1621 patients in whom treatment was initially pursued (i.e., aneurysm occlusion was attempted).

an unfavorable outcome at discharge for patients with MCAAs were ICH (aOR 4.80), DCI (aOR 3.19), age > 55 years (aOR 2.63), and each 1-step increase in the WFNS grade (aOR 1.55; Table 5). At the 1-year follow-up, DCI and ICH lost their predictive capacity. Significant predictive variables for an unfavorable outcome at the 1-year follow-up for patients with MCAAs included age > 55 years (aOR 2.08) and each 1-step increase in the WFNS grade (aOR 1.75). Surgical treatment was not associated with outcome at discharge or the 1-year follow-up.

Subgroup Analyses of MCAAs Versus Non-MCA Anterior Circulation Aneurysms

After the exclusion of 264 patients with IAs in the posterior circulation from the control group, similar results were obtained with regard to the preference for aneurysm occlusion therapy (aOR 8.26, 95% CI 5.69–11.98, p < 0.001), the likelihood of DCI (aOR 1.22, 95% CI 0.90–1.66, p = 0.198), aneurysm re-rupture (aOR 0.77, 95% CI 0.40–1.51, p = 0.453), and in-hospital mortality (aOR 0.50, 95% CI 0.28–0.88, p = 0.017; Supplementary Table 2).

The distribution of mRS scores across patients with MCAAs versus those with non-MCA anterior circulation IAs is illustrated in Supplementary Fig. 1A for the outcome at discharge and in Supplementary Fig. 1B for the 1-year follow-up outcome. Patients with MCAAs showed a lower rate of a favorable outcome at discharge than those with anterior circulation IAs in non-MCA locations (55.7% vs 65.4%, p < 0.001). At the 1-year follow-up, patients with MCAAs and those with anterior circulation IAs in non-MCA locations had similar rates of a favorable outcome (70.5% vs 69.6%, p = 0.460).

Discussion

In this study we set out to analyze patterns of care and clinical outcomes in patients presenting with ruptured MCAAs in a contemporary consecutive series of patients treated in the post-ISAT/post-BRAT era. This is important since previous studies have indicated ruptured MCAA as a pathology with a distinct set of characteristics as compared to aSAH of other locations.[6,29] In retrospectively

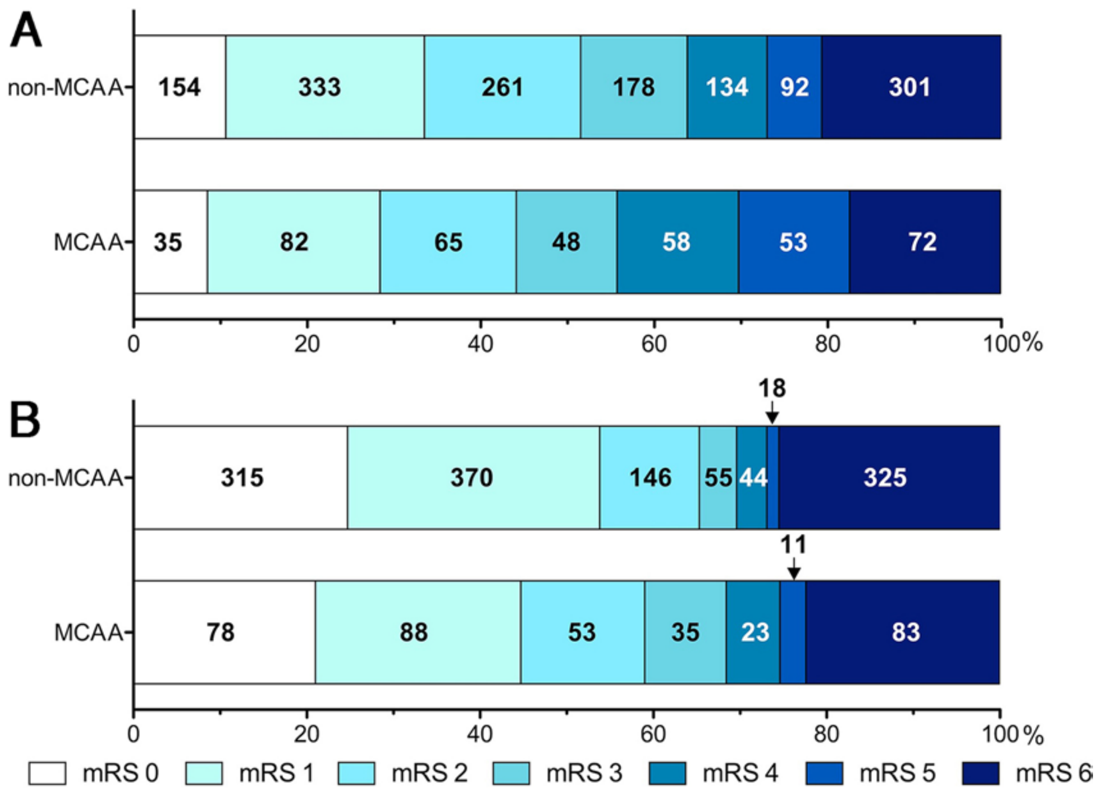

FIG. 1. A: Distribution of mRS scores at discharge in patients with MCAAs and IAs at non-MCA locations (n = 1866 patients). **B:** Distribution of mRS scores at the 1-year follow-up in patients with MCAAs and IAs at non-MCA locations (n = 1644 patients). Data are presented as counts and percents. Figure is available in color online only.

TABLE 5. Effect size of the relationship between clinical and radiological predictors of an unfavorable outcome in MCAA patients, estimated using logistic regression analysis

	Unfavorable Outcome at Discharge						Unfavorable Outcome at 1-Year FU					
	Univariate Model			Multivariate Model			Univariate Model			Multivariate Model		
Variable	OR	95% CI	p Value	aOR	95% CI	p Value	OR	95% CI	p Value	aOR	95% CI	p Value
Age	2.25	1.51–3.35	<0.001	2.63	1.40–4.94	0.003	2.36	1.51–3.69	<0.001	2.08	1.05–4.13	0.036
Sex	1.01	0.66–1.56	0.953	1.42	0.69–2.92	0.338	1.10	0.68–1.78	0.705	1.36	0.62–3.03	0.439
WFNS grade	2.02	1.75–2.34	<0.001	1.55	1.25–1.92	<0.001	2.05	1.73–2.43	<0.001	1.75	1.36–2.26	<0.001
Aneurysm size	1.12	0.97–1.30	0.107	0.85	0.65–1.11	0.229	1.07	0.92–1.26	0.384	0.75	0.54–1.05	0.091
DCI	2.02	1.32–3.08	<0.001	3.19	1.69–6.01	<0.001	1.14	0.71–1.84	0.588	1.41	0.71–2.80	0.331
Surgical treatment	1.02	0.60–1.76	0.929	0.62	0.26–1.49	0.287	0.88	0.46–1.68	0.695	1.14	0.45–2.92	0.778
ICH	5.44	3.27–9.07	<0.001	4.80	2.43–9.47	<0.001	2.38	1.38–4.10	0.002	1.20	0.57–2.54	0.637

FU = follow-up.
Unfavorable outcome was defined as mRS score 4–6.

analyzing a large nationwide sample from the prospective Swiss SOS registry, we found that surgical aneurysm occlusion continues to be the predominant treatment choice for patients with MCAA. Although MCAA patients presented with worse admission grades and higher rates of concomitant ICH, more than two-thirds showed a favorable outcome at the 1-year follow-up. In contrast to the highly selected patient population in RCTs, here we demonstrated complication rates and outcomes for a large, unselected, consecutive nationwide cohort of patients with ruptured MCAAs, which can serve as a reference for benchmarking purposes. Additional interesting findings that emerged are discussed in the following paragraphs.

Clinical Status at Admission and Complications

Given our data, one could argue that presenting with a ruptured MCAA is less favorable for the patient than presenting with an aSAH resulting from an IA at a non-MCA location. Clinical status on admission with a ruptured MCAA was shown to be significantly worse. These patients presented with higher WFNS grades and a considerably higher rate of brain injury associated with ICH (42% vs 17%).

ICH associated with MCAA can be temporal (intracerebral), sylvian (subarachnoidal), or combined.[32] Depending on the dominance of the affected hemisphere, patients with temporal ICH may suffer from direct injury of eloquent brain areas, and affected sylvian arterial and venous branches may predispose patients to subsequent ischemic complications. For the latter, early surgical evacuation has been suggested to increase the chance of a favorable outcome.[32]

The high frequency of ICH in our cohort of MCAA patients is in line with previous reports in the literature and is of particular interest since it naturally influences clinical status at admission (WFNS grade), subsequent treatment options, as well as patient outcome.[2,34]

Studies reporting on the frequency of DCI related to the location of the ruptured IAs and MCAAs in particular are scarce. Previous studies have demonstrated that vasospasm and DCI are reliably associated with the amount of subarachnoid blood, the presence of ICH or intraventricular hemorrhage, and a higher WFNS grade.[8,16,24] While patients with MCAA showed a significantly higher likelihood of DCI than those with IAs in non-MCA locations in the univariate analysis (OR 1.52, $p = 0.001$; Supplementary Table 1), the effect was diminished after adjusting for potential confounders (aOR 1.04, $p = 0.830$; Table 4). Factors that emerged as independent risk factors for DCI were each 1-step increase in WFNS grade and surgical treatment, whereas age > 55 years and male sex predicted a reduced risk of DCI (Supplementary Table 1). Our personal experience and hints from the literature suggest that brain vessel manipulation, e.g., during surgical dissection, may increase the likelihood of local vasospasm, which may explain the association of surgical treatment with a higher DCI rate.[9,11,41] However, the nature of our data does not allow for a more detailed analysis of this relationship, and no causal relationships can be proven. Further research is needed to substantiate this hypothesis, as there are also data contradicting an increase in vasospasm or DCI after vessel manipulation.[7,13,19]

Management and Pattern of Care

Besides the distinct clinical characteristics at admission, the existing literature and clinical experience from expert centers in the US have suggested a uniqueness of ruptured MCAAs in terms of management and aneurysm occlusion strategies with a considerable preference toward clipping.[33] Our nationwide cohort of patients treated between 2009 and 2015 provides the unique opportunity to compare this US treatment paradigm with that described in our contemporary European multicenter registry.

In our study, surgical aneurysm occlusion was the therapeutic choice in 82% of all treated MCAA patients, exceeding by far the surgical treatment rate of aneurysms in other locations (36.7%) and of anterior circulation aneurysms (38.4%). Interestingly, patients with ruptured MCAAs had an almost 8-fold higher chance of undergoing surgical treatment than patients with aneurysms in other locations, even after adjusting for covariables. Table 3 indicates that the decision to clip an MCAA was somewhat influenced by factors such as WFNS grade and the presence of ICH. However, an MCA location remained a strong independent predictor of surgical treatment despite statistical adjustment for variables that are traditionally thought of as main drivers of surgical treatment, such as (space-occupying) ICH. It is likely that additional variables that were not routinely recorded in the Swiss SOS data set influenced decision-making, including the detailed vascular anatomy (aneurysm shape, proximal vessel anatomy, perforating vessels), patient comorbidity, patient or physician preference, and local availability of care, but it is interesting to note that the choice for or against clipping of MCAAs cannot entirely be explained by the covariables included in the model.[17,18,22]

Despite a continuing high tendency for care providers to opt for surgical treatment for MCAAs in the post-ISAT/post-BRAT era, around 20% of patients in our cohort underwent either endovascular or combined treatment. With the introduction of new intrasaccular devices that can be used in cases with wide-necked bifurcation aneurysms, the share of endovascularly treated MCAAs is likely to increase.[1,28] Devices like the Woven EndoBridge (WEB) have already shown promising results in complex unruptured bifurcation aneurysms, but a higher thromboembolic complication rate in ruptured IAs demands further investigation with regard to the safety profile and management of anticoagulation or antiaggregation.[3,4] The same applies to the somewhat counterintuitive approach of endovascular aneurysm occlusion followed by minimally invasive ICH evacuation, as described by Turner et al.[37]

There was a particularly low representation of MCAAs in two of the largest RCTs on aSAH treatment today, the BRAT and ISAT, representing a lack of perceived clinical equipoise at the time of the trial and therefore further limiting an adequate comparison of endovascular and microsurgical treatment strategies for this aneurysm subgroup.[20,22,33]

In our cohort, it is notable that the likelihood of surgically or endovascularly treated patients to experience a favorable or an unfavorable outcome at discharge or the 1-year follow-up was similar (Fig. 1A and B). This may indicate that both treatment modalities can be reasonable options in an individual patient in hospitals that do not follow a rigid "clip first" or "coil first" strategy.[30,34] Because the Swiss SOS was designed to monitor the quality of care in Switzerland and the decision for aneurysm occlusion therapy was patient specific, individualized, and thus selected, we could not evaluate the superiority of one treatment modality over the other. Nevertheless, our study substantially adds data from a real-world scenario outside an RCT to the existing literature.

Outcome in MCAA Patients

Substantial variability in the timing, use of outcome measures or endpoints, and selection of patients in aSAH research has impeded comparison across cohorts. Our methods for outcome assessment and dichotomization are in agreement with the recent recommendations of the National Institutes of Health (NIH)/National Institute of Neurological Disorders and Stroke (NINDS)/National Library of Medicine Unruptured Intracranial Aneurysm and SAH Common Data Elements Group.[36] In the Swiss SOS cohort, 56% of patients with MCAAs showed a favorable outcome (mRS score ≤ 3) at discharge and 69% at the 1-year follow-up. It is particularly interesting that the proportion of favorable outcomes at discharge was significantly lower for patients with MCAAs than for those with IAs in non-MCA locations (55.7% vs 63.7%), whereas both groups had similar rates of favorable outcomes at the 1-year follow-up (68.5% vs 69.6%, $p = 0.676$).

These reasonably good functional outcomes and the trend toward a relevant improvement especially in surgically treated MCAA patients compares well with results presented in the BRAT: among a cohort of 46 patients with ruptured MCAAs who had undergone microsurgical clipping, 32% had a good outcome at discharge (defined as mRS score 0–2) and 57% at the 1-year follow-up.[22] In a series of 282 ruptured MCAAs treated with microsurgical clipping, Rodríguez-Hernández et al. reported good outcomes (mRS score 0–2) in 70.2% of patients at the last available follow-up (mean follow-up not specified).[30] Mortimer et al. reported a favorable outcome (defined as Glasgow Outcome Scale [GOS] score 4–5) at 3–6 months' follow-up in 79.8% of 242 consecutive patients who had undergone coiling for a ruptured MCAA.[23] While theirs is one of the largest published cohorts of MCAA patients treated via coiling, Mortimer et al. did not report on patients in whom aneurysm occlusion therapy was not initiated, and 51 patients were treated with primary clipping during roughly the same period despite their "coil first" policy, likely constituting strongly selected cases.[23]

The overwhelming majority of patients (88%) included in the ISAT presented with a good clinical grade (WFNS grade I–II) at the time of enrollment, which is in contrast to our series (48.4% of MCAA patients and 55.9% of patients with IAs in non-MCA locations).[21] The current results of the Swiss SOS may be more comparable to a real-world scenario than the carefully selected patients enrolled in those aforementioned RCTs and thus may serve as a reference for benchmarking purposes. Nonetheless, our results are in line with the disability outcomes of other large referral centers. This indicates the high quality of patient care in Switzerland and may support the practice of centralized management in aSAH at specialized neurovascular centers that are staffed with both neurosurgeons and interventional neuroradiologists 24/7.

Factors Influencing Functional Disability in MCAA Patients

To further analyze the predictors of outcome in the patients with ruptured MCAAs, we performed logistic regression analysis. Strong independent predictors of an unfavorable outcome at discharge and the 1-year follow-up were age > 55 years and WFNS grade. Both variables have previously been shown to be associated with a poor outcome for aSAH patients in general (as opposed to patients with MCAAs) and are part of a core prediction model recently developed by the SAH International Trialists (SAHIT) collaborations within the framework of a multinational cohort study.[15] Interestingly, while ICH and DCI presented as the most important independent predictors of an unfavorable outcome at discharge (aOR 4.80 and aOR 3.19, respectively) in our current study, both variables lost their predictive capacity at the 1-year follow-up. While ICH and DCI have reliably been shown to worsen outcome, especially within a short time frame after aSAH, the current results may indicate that other factors, such as the social and financial situation of the patient, family support, and complications after discharge (including rebleeding and shunt dependency), contribute considerably to the long-term outcome.[5,14,25,26,35] Further research is required to substantiate the factors influencing long-term outcome in patients with MCAAs since our data set, unfortunately, does not provide more detailed information about the patients' health and social status in the months following aSAH.

Study Strengths and Weaknesses

The inherent strength of this Swiss SOS study is that all neurovascular centers in Switzerland contributed to the prospective nationwide data collection. The unselected collection of all aSAH patients allows for a realistic view of modern neurovascular patient care, which is difficult to obtain with highly selected data from RCTs. In addition, the multicenter and multicultural framework increases the likelihood that our observations and results can be generalized to other settings and populations. Despite all efforts for rigorous data collection, some data were missing, as indicated in Table 1. We also cannot account for patients who suddenly died outside the hospital as a result of undiagnosed aSAH, which may have influenced the results. Lastly, despite all efforts to analyze and discuss treatment choices in our cohort, we can only illustrate final results; the underlying decision-making process of treating physicians remains uncertain.[17]

Conclusions

Data from the nationwide Swiss SOS registry shed light on the epidemiology, patterns of care, and contemporary disability outcomes of MCAA patients in a small but well-developed European country. Microsurgical occlusion remains the dominant treatment choice, whereas endovascular or combined treatment was performed in selected cases. Although MCAA patients presented with worse admission grades and higher rates of concomitant ICH than the patients with ruptured IAs at non-MCA locations, similarly good long-term disability outcomes could be achieved. More than two-thirds of MCAA patients showed a favorable outcome at the 1-year follow-up, supporting the practice of national centralized care at specialized neurovascular centers.

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Appendix

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Disclosures

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