BRIEF REPORT

Incidence and Outcome of Aneurysmal Subarachnoid Hemorrhage

The Swiss Study on Subarachnoid Hemorrhage (Swiss SOS)

Bawarjan Schatlo[®], MD*; Christian Fung, MD*; Martin N. Stienen, MD*; Ali R. Fathi, MD; Javier Fandino[®], MD; Nicolas R. Smoll[®], MD; Daniel Zumofen, MD; Roy Thomas Daniel, MD; Jan-Karl Burkhardt, MD; David Bervini, MD; Serge Marbacher, MD, PhD; Michael Reinert, MD; Donato D'Alonzo, MD; Peter Ahlborn, MD; Vitor Mendes Pereira, MD; Michel Roethlisberger, MD; Martin Seule, MD; Hassen Kerkeni, MD; Luca Remonda, MD; Astrid Weyerbrock, MD; Kerstin Woernle, MD; Alice Venier, MD; Fabienne Perren, MD; Martin Sailer, MD; Thomas Robert, MD; Veit Rohde, MD; Daniel Schöni, MD; Johannes Goldberg, MD; Edin Nevzati[®], MD; Michael Diepers, MD; Jan Gralla, MD; Werner Z'Graggen[®], MD; Daniele Starnoni, MD; Christoph Woernle, MD; Nicolai Maldaner, MD; Zsolt Kulcsar, MD; Khaled Mostaguir, PhD; Rodolfo Maduri, MD; Christian Eisenring[®], MD; René Bernays, MD; Andrea Ferrari, MD; Hiroki Dan-Ura, MD; Sina Finkenstädt, MD; Yvan Gasche, MD; Asita Sarrafzadeh, MD; Stephan M. Jakob, MD; Marco Corniola, MD; Fabian Baumann, MD; Luca Regli[®], MD; Marc Levivier, MD; Gerhard Hildebrandt, MD; Hans Landolt, MD; Luigi Mariani, MD; Raphael Guzman, MD; Jürgen Beck[®], MD; Andreas Raabe, MD; Emanuela Keller[®], MD; Philippe Bijlenga, MD, PhD; Karl Schaller, MD

BACKGROUND AND PURPOSE: The purpose of this study was to assess nationwide incidence and outcomes of aneurysmal subarachnoid hemorrhage (aSAH). The Swiss SOS (Swiss Study on Subarachnoid Hemorrhage) was established in 2008 and offers the unique opportunity to provide this data from the point of care on a nationwide level.

METHODS: All patients with confirmed aneurysmal subarachnoid hemorrhage admitted between January 1, 2009 and December 31, 2014, within Switzerland were recorded in a prospective registry. Incidence rates were calculated based on time-matched population data. Admission parameters and outcomes at discharge and at 1 year were recorded.

RESULTS: We recorded data of 1787 consecutive patients. The incidence of aneurysmal subarachnoid hemorrhage in Switzerland was 3.7 per 100000 persons/y. The number of female patients was 1170 (65.5%). With a follow-up rate of 91.3% at 1 year, 1042 patients (58.8%) led an independent life according to the modified Rankin Scale (0–2). About 1 in 10 patients survived in a dependent state (modified Rankin Scale, 3–5; n=185; 10.4%). Case fatality was 20.1% (n=356) at discharge and 22.1% (n=391) after 1 year.

CONCLUSIONS: The current incidence of aneurysmal subarachnoid hemorrhage in Switzerland is lower than expected and an indication of a global trend toward decreasing admissions for ruptured intracranial aneurysms.

REGISTRATION: URL: https://www.clinicaltrials.gov. Unique identifier: NCT03245866.

Key Words: incidence = intracranial aneurysm = outcome = subarachnoid hemorrhage = patients = stroke = Switzerland

he reported incidence of aneurysmal SAH (aSAH) ranges from 3 to >20 per 100 000 persons/y.¹ Information on incidence and outcome of aSAH based on

direct data from healthcare providers remains scarce. In Switzerland, health care regulations resulted in a unique referral system for neurovascular emergencies to a

Correspondence to: Bawarjan Schatlo, MD, Department of Neurosurgery, University Hospital Göttingen, Germany. Email bawarjan.schatlo@med.uni-goettingen.de *Drs Schatlo, Fung, and Stienen contributed equally.

The Data Supplement is available with this article at https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.120.029538.

For Sources of Funding and Disclosures, see page 347.

^{© 2020} American Heart Association, Inc.

Stroke is available at www.ahajournals.org/journal/str

Nonstandard Abbreviations and Acronyms

aSAH	aneurysmal subarachnoid hemorrhage
Swiss SOS	Swiss Study on Aneurysmal Subarach- noid Hemorrhage

limited number of centers. These centers launched the Swiss SOS (Swiss Study on Aneurysmal Subarachnoid Hemorrhage) where neurovascular specialists contribute data on aSAH from the point of care with uniform dataentry and follow-up.²⁻⁴ This report contains the findings of the Swiss SOS on incidence rates and outcomes of aSAH on a nationwide level.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request. Ethics committee approval was obtained from all participating centers (Geneva Ethical Committee Board no. 11-233R, NAC 11-085R, and Bern [KEK-BE]). The study protocol was made public.² The present analysis includes patients admitted between January 1, 2009 and December 31, 2014. Only patients with imaging evidence of a proven intracranial aneurysm were included. Data collection and entry was performed by involved physicians at the point of care and included demographic characteristics, clinical and radiological information, treatment parameters, and outcome data (modified Rankin Scale at discharge and 1 year). Directly standardized incidence rates were calculated from 2010 to 2014 using the weighted average of the stratum-specific rates. The weighting used was based on the Swiss population distribution (Swiss age-standardization) from the Swiss Federal Bureau of Statistics (Neuchâtel, Switzerland). Statistical analysis and data visualization were performed with Stata version 13.1 (College Station, TX). Further details on data field definitions and methods are available in the Data Supplement.

RESULTS

N=1787 patients were admitted with a confirmed diagnosis of aSAH. Mean age was 56 years (95% CI, 34-79; Table). The overall incidence of aSAH in Switzerland between 2010 and 2014 was 3.7 per 100 000 persons/y (95% CI, 1.97-7.03; Figure 1). With a follow-up rate of 91.3% at1 year, 1042 patients (58.8%) led an independent life according to the modified Rankin Scale (0-2; Figure 2). The effect of the missing values for modified Rankin Scale at 1 year was minimal with a SE of 5.6%. Thus calculated, high World Federation of Neurosurgical Societies Score (3-5) predicted poor outcome with an odds ratio of 7.3 (95% Cl, 5.7-9.4; P<0.001). About one-third of cases remained dependent at the time of discharge (n=532; 30.0%) and 356 patients died in hospital (20.1%). At 1-year follow-up, 1042 (58.8%) patients led an independent life according to the modified Rankin

	Female (n=1170)		Male (n=617)		Total (n=1787)		P value
Age, y, mean (95% Cl)	57	(36–80)	54	(34–78)	56	(34–79)	<0.001
WFNS grade							
1	395	34.0%	236	38.8%	631	35.6%	0.091
2	222	19.1%	113	18.6%	335	18.9%	0.091
3	94	8.1%	44	7.2%	138	7.8%	0.091
4	118	10.2%	60	9.9%	178	10.1%	0.091
5	333	28.7%	156	25.6%	489	27.6%	0.091
Fisher grade							
1 and 2	147	12.6%	71	11.5%	218	12.2%	0.512
3 and 4	1020	87.4%	545	88.5%	1565	87.8%	0.512
Aneurysm location (ruptured only)							
Anterior circulation	972	83.1%	507	82.2%	1479	82.8%	0.666
Posterior circulation	168	14.4%	82	13.3%	250	14.0%	0.666
Other	30	2.6%	28	4.5%	58	3.2%	0.666
Aneurysm size (ruptured only)							
≤7 mm	689	63.7%	342	61.0%	1031	62.8%	0.280
>7 mm	393	36.3%	219	39.0%	612	37.2%	0.280
Multiple aneurysms							
Patients with one aneurysm	829	70.9%	484	78.4%	1313	73.5%	0.001
Patients with multiple aneurysms	341	29.1%	133	21.6%	474	26.5%	0.001

Missing values: WFNS: n=16, Fisher grade: n=4, Aneurysm size: n=144. Results are presented in count and percentage or mean (95% CI). WFNS indicates World Federation of Neurosurgical Societies.

Table 1. Baseline Parameters

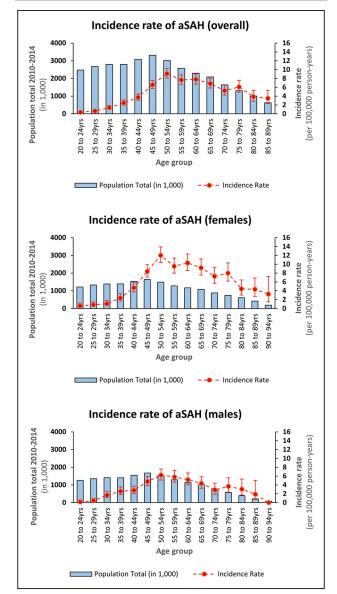


Figure 1. Incidence of aneurysmal subarachnoid hemorrhage (aSAH) in Switzerland.

Population distribution (blue bars; **left** *y* axis) in Switzerland stratified by age group (in increments of 5 y). Dotted line: incidence rates (**right** *y* axis). Error bars: 95% Cls. The overall peak incidence of 9.1 per 100 000 persons/y is reached between ages 50 and 54 y (**top**). Incidence rates for women (**middle**) range above those of men (**bottom**). The sex-specific peak incidence in the most affected age group was 12.0 for women and 6.2 per 100 000 persons/y for men.

Scale, whereas about 1 in 10 patients remained dependent (n=185; 10.4%).

DISCUSSION

Reported worldwide incidence rates of aSAH range from 3 to 23 per 100000 persons/y.¹ Some of the higher incidence numbers have recently been questioned. A metaanalysis confirmed that incidence of aSAH decreases, with reduction of cardiovascular risk factors cited as a likely driver.⁵ Our study's calculation of incidence is unique in requiring imaging evidence of an aneurysm before inclusion. Based on this prerequisite, the overall incidence of aSAH in Switzerland is 3.7 per 100000 persons/y. Nonetheless, there may be missing cases that led to an underestimation of the true incidence of aSAH. The first cause for missing cases is death before arrival and therefore lack of diagnosis. It is estimated to occur in 12%^{6,7} to 21%⁸ of patients. Furthermore, misdiagnosis of aSAH in milder cases cannot be ruled out and was previously reported to account for one in twenty cases of aSAH.9 A correction for these 2 limitations might yield an incidence rate closer to 4.6 per 100000 persons/y at most. In addition to incidence, mortality due to aSAH is decreasing.¹⁰ An independent outcome was achieved by almost two-thirds of affected patients at the one-year follow-up. Although mortality has declined over time, 1 in 5 patients still succumb to aSAH. One major weakness is that the initial Swiss SOS data fields did not specifically include the cause of death. This important information will be collected going forward in accordance with the common data element recommendations.11

Our study data serve as a benchmark to help design studies aimed at (1) assessing incidence of aSAH over time and at (2) addressing outcomes after aSAH. As this cooperative effort moves forward, the study group will incorporate the common data elements proposed for aSAH.¹¹

ARTICLE INFORMATION

Received December 12, 2019; final revision received July 20, 2020; accepted September 29, 2020.

Affiliations

Neurosurgery (B.S., A.S., M.C., P.B., K.S.), Neurology (F.P.), Clinical Research Centre, (K.M.), and Intensive Care Medicine (Y.G.), University Hospital Geneva, Switzerland. Department of Neuroradiology, University Hospital Zürich, Switzerland (Z.K.). Neurosurgery (B.S., J.F., S.M., D.D., K.W., H.D.U., H.L.), Neurology (H.K.), and Neuroradiology (L.R., M.D.), Kantonsspital Aarau Switzerland. Neurosurgery, University Hospital Göttingen Germany (B.S., V.R.). Neurosurgery (C.F., D.B., D. Schöni, J. Goldberg, C.E., J.B., A.R.), Neuroradiology (J. Gralla, W.Z.), and Intensive Care Medicine (S.M.J.), University Hospital Bern Switzerland. Neurosurgery (M.N.S., J.-K.B., C.W., N.M., R.B., S.F., L.R.) and Intensive Care Medicine (E.K.), University Hospital Zürich Switzerland. Neurosurgery, Hirslanden Klinik Aarau Switzerland (A.R.F.). School of Population and Global, University of Melbourne Australia (N.R.S.). Neurosurgery, University Hospital Basel Switzerland (D.Z., M. Roethlisberger, M. Sailer, L.M., R.G.). Neurosurgery, University Hospital Lausanne Switzerland (R.T.D., D. Starnoni, R.M., M.L.). Neurosurgery, Ospedale Civico Lugano Switzerland (M. Reinert, A.V., T.R.). Neurosurgery, Kantonsspital St. Gallen Switzerland (P.A., M. Seule, A.W., A.F., G.H.). Neuroradiology, University of Toronto Canada (V.M.P.). Neurosurgery, Kantonsspital Luzern Switzerland (E.N., F.B.). Department of Neurosurgery, Faculty of Medicine, Medical Center, University of Freiburg, Germany (J.B., C.F.).

Acknowledgments

We acknowledge the support of Mr Erwin Wüest (Federal Statistics Bureau Neuchâtel). All aforementioned individuals are contributors to the present study in that they have contributed substantially. Drs Bernays, Jakob, Woernle [born Winkler], Woernle, Levivier, Hildebrandt, Landolt contributed to conception or design; Drs Venier, Robert, Schöni, Goldberg, Nevzati, Diepers, Gralla, Z'Graggen, Starnoni, Maldaner, Kulcsar, Ferrari, Dan-Ura, Finkenstädt, D'Alonzo, Kerkeni, Perren, Mostaguir, Eisenring, Sarrafzadeh, Baumann, Woernle [born Winkler], Woernle, Levivier, Hildebrandt, Landolt contributed to acquisition; Drs Rohde, Jakob, D'Alonzo, Kerkeni, Perren, Mostaguir, Eisenring, Sarrafzadeh, Baumann contributed to interpretation

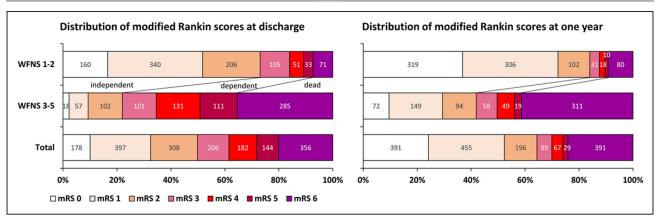


Figure 2. Distribution of admission status and outcome after aneurysmal subarachnoid hemorrhage.

Outcomes stratified by World Federation of Neurosurgical Societies (WFNS) score at time of admission. Favorable admission status (WFNS scores 1–2) was associated with lower rates of dependent outcome (modified Rankin Scale [mRS] score of 3–5) or death (mRS score of 6) at discharge and after 1 y.

of data; and Drs Schatlo, Fung, Stienen, Fathi, Fandino, Smoll, Zumofen, Daniel, Burkhardt, Bervini, Marbacher, Reinert, Ahlborn, Mendes-Pereira, Roethlisberger, Seule, Remonda, Weyerbrock, Sailer, Maduri, Gasche, Corniola, Regli, Mariani, Guzman, Beck, Raabe, Keller, Bijlenga, Schaller contributed to conception or design, acquisition, and interpretation of data. In addition, all contributors were involved in drafting and critically revising the manuscript for important intellectual content. Finally, all contributors agree to be held accountable for all aspects of this work.

Sources of Funding

There is no funding to declare. Dr Dan-Ura received funding from the Wellcome Trust unrelated to the present study.

Disclosures

The following authors reported funding outside of the current work: Drs Burkhardt (Longeviti Neuro Solutions), Gralla (Medtronic), Kulcsar (Stryker Neurovascular, Cerenevous, Medtronic), Regli (B Braun), Schaller (Swiss National Fund). The other authors report no conflicts.

REFERENCES

- de Rooij NK, Linn FH, van der Plas JA, Algra A, Rinkel GJ. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. *J Neurol Neurosurg Psychiatry*. 2007;78:1365– 1372. doi: 10.1136/jnnp.2007.117655
- Schatlo B, Fung C, Fathi AR, Sailer M, Winkler K, Daniel RT, Bijlenga P, Ahlborn P, Seule M, Zumofen D, et al. Introducing a nationwide registry: the Swiss study on aneurysmal subarachnoid haemorrhage (Swiss SOS). *Acta Neurochir (Wien)*. 2012;154:2173–2178. doi: 10.1007/s00701-012-1500-4
- Stienen MN, Smoll NR, Fung C, Goldberg J, Bervini D, Maduri R, Chiappini A, Robert T, May A, Bijlenga P, et al; Swiss SOS Study Group. home-time as a surrogate marker for functional outcome after aneurysmal subarachnoid hemorrhage. *Stroke*. 2018;49:3081–3084. doi: 10.1161/ STROKEAHA.118.022808

- Stienen MN, Germans M, Burkhardt JK, Neidert MC, Fung C, Bervini D, Zumofen D, Röthlisberger M, Marbacher S, Maduri R, et al; Swiss SOS Study Group. Predictors of in-hospital death after aneurysmal subarachnoid hemorrhage: analysis of a nationwide database (swiss sos [swiss study on aneurysmal subarachnoid hemorrhage]). *Stroke.* 2018;49:333–340. doi: 10.1161/STROKEAHA.117.019328
- Etminan N, Chang HS, Hackenberg K, de Rooij NK, Vergouwen MDI, Rinkel GJE, Algra A. Worldwide incidence of aneurysmal subarachnoid hemorrhage according to region, time period, blood pressure, and smoking prevalence in the population: a systematic review and meta-analysis. *JAMA Neurol.* 2019;76:588–597. doi: 10.1001/jamaneurol.2019.0006
- Huang J, van Gelder JM. The probability of sudden death from rupture of intracranial aneurysms: a meta-analysis. *Neurosurgery*. 2002;51:1101– 1105. doi: 10.1097/00006123-200211000-00001
- Koffijberg H, Buskens E, Granath F, Adami J, Ekbom A, Rinkel GJ, Blomqvist P. Subarachnoid haemorrhage in Sweden 1987-2002: regional incidence and case fatality rates. *J Neurol Neurosurg Psychiatry*. 2008;79:294–299. doi: 10.1136/jnnp.2007.123901
- Korja M, Lehto H, Juvela S, Kaprio J. Incidence of subarachnoid hemorrhage is decreasing together with decreasing smoking rates. *Neurology*. 2016;87:1118–1123. doi: 10.1212/WNL.000000000003091
- Vermeulen MJ, Schull MJ. Missed diagnosis of subarachnoid hemorrhage in the emergency department. *Stroke*. 2007;38:1216–1221. doi: 10.1161/01. STR.0000259661.05525.9a
- Nieuwkamp DJ, Setz LE, Algra A, Linn FH, de Rooij NK, Rinkel GJ. Changes in case fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex, and region: a meta-analysis. *Lancet Neurol.* 2009;8:635– 642. doi: 10.1016/S1474-4422(09)70126-7
- 11. Bijlenga P, Morita A, Ko NU, Mocco J, Morel S, Murayama Y, Wermer MJH, Brown RD Jr; Unruptured Cerebral Aneurysms and SAH CDE Project Investigators. Common data elements for subarachnoid hemorrhage and unruptured intracranial aneurysms: recommendations from the working group on subject characteristics. *Neurocrit Care*. 2019;30(suppl 1):20–27. doi: 10.1007/s12028-019-00724-5