Predictors of In-Hospital Death After Aneurysmal Subarachnoid Hemorrhage

Analysis of a Nationwide Database (Swiss SOS [Swiss Study on Aneurysmal Subarachnoid Hemorrhage])

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Background and Purpose—To identify predictors of in-hospital mortality in patients with aneurysmal subarachnoid hemorrhage and to estimate their impact.

Methods—Retrospective analysis of prospective data from a nationwide multicenter registry on all aneurysmal subarachnoid hemorrhage cases admitted to a tertiary neurosurgical department in Switzerland (Swiss SOS [Swiss Study on Aneurysmal Subarachnoid Hemorrhage]; 2009–2015). Both clinical and radiological independent predictors of in-hospital mortality were identified, and their effect size was determined by calculating adjusted odds ratios (aORs) using multivariate logistic regression. Survival was displayed using Kaplan–Meier curves.

Results—Data of n=1866 aneurysmal subarachnoid hemorrhage patients in the Swiss SOS database were available. In-hospital mortality was 20% (n=373). In n=197 patients (10.6%), active treatment was discontinued after hospital admission (no aneurysm occlusion attempted), and this cohort was excluded from analysis of the main statistical model. In the remaining n=1669 patients, the rate of in-hospital mortality was 13.9% (n=232). Strong independent predictors of in-hospital mortality were rebleeding (aOR, 7.69; 95% confidence interval, 3.00–19.71; $P<0.001$), cerebral infarction attributable to delayed cerebral ischemia (aOR, 3.66; 95% confidence interval, 1.94–6.89; $P<0.001$), intraventricular hemorrhage (aOR, 2.65; 95% confidence interval, 1.38–5.09; $P=0.003$), and new infarction post-treatment (aOR, 2.57; 95% confidence interval, 1.43–4.62; $P=0.002$).

Conclusions—Several—and among them modifiable—factors seem to be associated with in-hospital mortality after aneurysmal subarachnoid hemorrhage. Our data suggest that strategies aiming to reduce the risk of rebleeding are most promising in patients where active treatment is initially pursued.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT03245866.

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Key Words: cerebral infarction ■ infarction ■ intracranial aneurysm ■ mortality ■ survival

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Aneurysmal subarachnoid hemorrhage (aSAH) is a disease with considerable mortality and long-term morbidity despite maximal treatment.[1] Mortality rates after aSAH vary between 22% and 50% in modern series.[1–10] Thanks to advances in the understanding of the pathophysiology of aSAH and evidence-based recommendations concerning its

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*A list of all Swiss SOS study group participants is given in the Appendix.

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acute management, mortality rates have declined over recent decades.[2–5] It remains unclear, however, whether this decline in mortality can be attributed to a specific cause. The key to further improving survival after aSAH is to identify and eliminate factors or events that predict a negative outcome.[5]

In Switzerland, the nationwide Swiss SOS (Swiss Study on Aneurysmal Subarachnoid Hemorrhage; http://www.swiss-sos.ch) prospectively collects data on all patients admitted to 8 acute neurovascular care centers.[1] In a previous work, the incidence of aSAH in Switzerland was determined to be around 3.7 per 100 000 person-years between 2009 and 2013, with a mortality rate of about 20%.[11] Given that 1 in 5 Swiss patients succumbs during hospitalization, the present study aimed to identify factors associated with in-hospital mortality in a contemporary aSAH population.

Materials and Methods

The data that support the findings of this study are available from the corresponding author on reasonable request.

Patient Identification

This was a retrospective analysis of prospectively collected anonymized data within the framework of a nationwide multicenter registry (Swiss SOS).[1] Because of the healthcare regulations in Switzerland, each aSAH patient has to be transferred to one of the following neurosurgical departments: Cantonal Hospital Aarau, University Hospital Basel, University Hospital (Inselspital) Bern, University Hospital Geneva, University Hospital Lausanne, Cantonal Hospital Lugano, Cantonal Hospital St.Gallen, and University Hospital Zurich. Even if aSAH is diagnosed in a peripheral hospital, one of the listed departments is contacted for telemedical advice (radiological images of peripheral hospitals can be reviewed by the tertiary referral centers). Also patients in poor clinical status or higher age are transferred—at least for clinical evaluation by a neurosurgeon. Exceptions are made in rare circumstances only (eg, transfer denied by patient/next of kin). Patients with sudden death outside the hospital secondary to aSAH but undiagnosed are not recorded in the database (the rate of autopsy in these cases is low in Switzerland).[12] All registered aSAH patients from January 1, 2009, to December 31, 2015, were included. Patients with non-aSAH were not registered in the database. The study was registered.

Ethical Considerations and Data Collection

Ethics committee approval was obtained from all participating centers (under the supervision of the Geneva Ethics Committee Board no. 11-233R, NAC 11-085R). Prespecified uniform definitions are used for recorded variables, and data are collected in real time in parallel to patient care. Data are entered prospectively into a Secutrial data platform (provided by the Clinical Research Center of the University Hospital of Geneva, Switzerland) at time of patient discharge and follow-up. The responsibility for data correct and completeness lies with a dedicated principle investigator at each center (defined under: http://www.swiss-sos.ch), who is either specialized in cerebrovascular surgery or closely supervised by the department's senior cerebrovascular surgeon. In 1 to 2 annual meetings of the group, data quality and completeness is reviewed, and feedback is given to each center. All principle investigators are asked to provide data sets as complete as possible, but for the most important variables (eg, age, sex, World Federation of Neurosurgical Societies grading scale, outcome) we do not or only with clear justification accept missing data.

Variables and Definitions

The clinical variables collected were patient age and sex, modified Rankin Scale,[13] World Federation of Neurosurgical Societies grading scale at admission (before resuscitation),[14] uni- or bilateral pupil dilation, intubation status at admission, and complications as defined below.

Radiological variables on the admission computed tomographic (CT) scan comprised the Fisher grade,[15] aneurysm-bearing artery and maximum diameter in millimeters, intraventricular hemorrhage (IVH) other than sedimented blood, midline shift, acute subdural hematoma, and intracerebral hemorrhage.

Recorded treatment variables included the type of aneurysm occlusion performed, being microsurgical clipping, endovascular coiling, endovascular stenting, other (including [partial] trapping, wrapping, bypass, etc), or none. Decompressive hemicraniectomy was recorded.

Complications were defined as follows:

- Rebleeding: a sudden clinical deterioration with signs of increased hemorrhage on consecutive CT scans, or if no CT scan was obtained, sudden clinical deterioration suspected to be because of rebleeding with fresh blood in the ventricular drain. In addition, acute clinical deterioration suggestive of rebleeding (eg, acute neurological decline, bradycardia, or sudden hypertensive blood pressure) at the emergency department or before imaging was obtained was considered as a rebleed. Acute clinical deterioration before admission was not taken into account, in line with a recent study.[5]
- Clinical deterioration attributable to delayed cerebral ischemia (DCI): in accordance with the definition of Vergouwen et al.[16,17]
- Cerebral infarction attributable to DCI: in accordance with the definition of Vergouwen et al.[16,17]
- New infarction on the postoperative CT: hypodensity or intraparenchymal hematoma present in postoperative imaging. These must not have been present on the CT or magnetic resonance scan performed before aneurysm occlusion and should be suspected to result from the aneurysm occlusion therapy.

Study Cohort and Statistical Considerations

Patients who were admitted alive but died during hospitalization (ie, in-hospital mortality) were identified. The absolute number of analyzed variables was kept as low as possible to minimize the potential for type I errors because of multiple testing. The effect sizes of both clinical and radiological predictors of in-hospital mortality were estimated by calculating direct (odds ratio [OR]) and adjusted ORs (aORs) and 95% confidence intervals (CIs) using uni- and multivariate logistic regression analysis with forced entry modeling strategies. At the modeling stage, it was decided to remove patients based on the decision not to provide aneurysm occlusion treatment. This group is deemed unique and not homogenous with the rest of the cohort because once the decision is made not to treat the aneurysm, the patient's clinical course and prognosis are entirely different from the group where aneurysm occlusion therapy is attempted. Before entering them into the statistical model, all variables were assessed for collinearity. For collinear variables, only the most appropriate variable was selected (omitted were World Federation of Neurosurgical Societies grade, midline shift, Fisher grade, decompressive hemicraniectomy, and clinical deterioration attributable to DCI). Changes in the effect sizes before and after adjustment were reviewed to estimate the influence of confounding, and sensitivity analyses were performed. In addition, survival was demonstrated using Kaplan–Meier survival curves (day 0=day of aSAH). As the longest hospitalization time in the cohort was about 4 months, survival data were censored at 120 days. Statistical analysis and data visualization were performed with Stata version 14.2 (College Station, TX). With Bonferroni corrections made for the testing of 12 variables in the multivariate model, probability values of $P<0.0042$ (0.05/12) were considered statistically significant.

Results

The in-hospital mortality of 1866 admitted aSAH patients from the database was 20% (n=373; Figure 1). The mortality rate was relatively stable over the years of data collection (2009: 18.7%; 2010: 19.3%; 2011: 18.8%; 2012: 17.1%;

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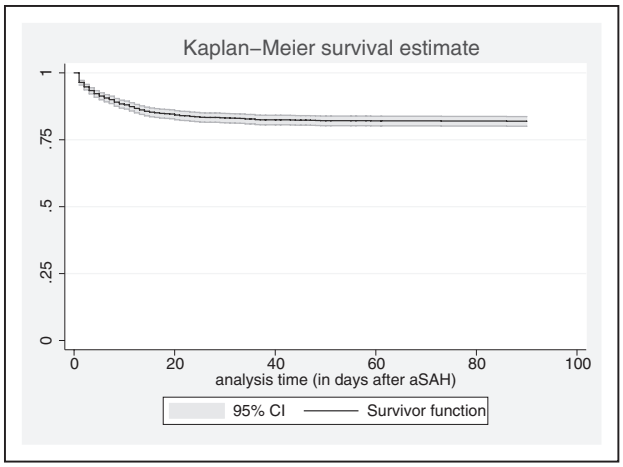

Figure 1. Kaplan–Meier survival estimate for all patients with aneurysmal subarachnoid hemorrhage (aSAH) in the Swiss SOS (Swiss Study on Aneurysmal Subarachnoid Hemorrhage) database,[1] time censored at 120 days. CI indicates confidence interval.

2013: 23.0%; 2014: 23.8%; 2015: 16.3%; *P*=0.289). Death occurred within 48 hours of ictus in 36% (n=133) of patients, and the median interval to in-hospital death was 7 days.

Of the complete cohort, n=197 patients (10.6%) in whom active treatment was discontinued after hospital admission (no aneurysm occlusion attempted) were excluded from further analysis (Table I in the online-only Data Supplement). In the remaining n=1669 patients, the rate of in-hospital mortality was 13.9% (n=232). The mean age of patients who died during hospitalization was 58.5 years (SD=14.4), and about two thirds were female (Table 1). The vast majority of patients was functionally independent before aSAH and presented with medium-to-large anterior circulation aneurysms and both high World Federation of Neurosurgical Societies and Fisher scores (Table 1).

Clinical and Radiological Predictors of In-Hospital Mortality

Table 2 illustrates the effect size of the relationship between selected clinical and radiological predictors of in-hospital mortality. A particularly strong independent predictor of in-hospital mortality was rebleeding (aOR, 7.69; 95% CI, 3.00–19.71; *P*<0.001) with a case fatality rate of 62%. Further independent predictors of in-hospital mortality were cerebral infarction attributable to DCI (aOR, 3.66; 95% CI, 1.94–6.89; *P*<0.001; case fatality, 25.0%), IVH (aOR, 2.65; 95% CI, 1.38–5.09; *P*=0.003; case fatality, 26.5%), and new infarction post-treatment (aOR, 2.57; 95% CI, 1.43–4.62; *P*=0.002; case fatality, 25.3%). Pupil dilation at admission was a predictor of in-hospital mortality in univariate analysis, but lost its predictive capacity once statistically adjusted for covariables (Table 2).

A goodness-of-fit analysis of the model showed an area under a receiver operating characteristics curve with good accuracy (0.8372; Figure I in the online-only Data Supplement).

Aneurysm Treatment

Patients in whom no aneurysm occlusion therapy was performed were ≈16× as likely to die, compared with patients

Table 1. Basic Characteristics of n=1669 Actively Treated aSAH Patients From the Swiss SOS (Swiss Study on Aneurysmal Subarachnoid Hemorrhage) Database, of Which n=232 (13.9%) Died During Hospitalization

Variable	In-Hospital Mortality	Discharged Alive	*P* Value
Age, y	58.5 (14.9)	54.7 (12.9)	<0.001
Sex			
Female	148 (63.8%)	954 (66.4%)	0.439
Male	84 (36.2%)	483 (33.6%)	
Pre-ictal mRS			<0.001
0	152 (65.5%)	1,160 (80.7%)	
1	35 (15.1%)	123 (8.6%)	
2 or higher	9 (3.9%)	42 (2.9%)	
Unspecified	36 (15.5%)	112 (7.8%)	
Admission WFNS grade			<0.001
1	30 (12.9%)	596 (41.5%)	
2	32 (13.8%)	299 (20.8%)	
3	16 (6.9%)	119 (8.3%)	
4	29 (12.5%)	143 (10.0%)	
5	121 (52.2%)	269 (18.7%)	
Unspecified	4 (1.7%)	11 (0.8%)	
Admission Fisher grade			<0.001
1	1 (0.4%)	50 (3.5%)	
2	6 (2.6%)	156 (10.9%)	
3	120 (51.7%)	821 (57.1%)	
4	105 (45.3%)	406 (28.2%)	
Unspecified	(0.0%)	4 (0.3%)	
Aneurysm-bearing artery			
ACA incl. Acom	88 (37.9%)	569 (39.6%)	0.664
ICA incl. Pcom	62 (26.7%)	335 (23.3%)	0.280
MCA	39 (16.8%)	338 (23.5%)	0.022
Posterior circulation	39 (16.8%)	191 (13.3%)	0.151
Other/unspecified	4 (1.7%)	4 (0.3%)	0.016
Maximal aneurysm diameter			0.008
2–5 mm	95 (41.0%)	622 (43.3%)	
6–9 mm	72 (31.0%)	493 (34.3%)	
10–14 mm	29 (12.5%)	193 (13.4%)	
15–24 mm	15 (6.5%)	46 (3.2%)	
≥25 mm	7 (3.0%)	12 (0.9%)	
Unspecified	14 (6.0%)	71 (4.9%)	
Aneurysm occlusion			<0.001
Surgical treatment	71 (30.6%)	558 (38.8%)	
Endovascular treatment	110 (47.4%)	748 (52.1%)	
Combined treatment	15 (6.5%)	119 (8.3%)	
Unspecified	36 (15.5%)	12 (0.8%)	
	n=232 (100%)	n=1437 (100%)	

Data are presented as count (percent) or mean (SD). ACA indicates anterior cerebral artery; Acom, anterior communicating artery; aSCH, aneurysmal subarachnoid hemorrhage; ICA, internal carotid artery; incl., including; MCA, middle cerebral artery; mRS, modified Rankin Scale; Pcom, posterior communicating artery; and WFNS, World Federation of Neurosurgical Societies.

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Table 2. Effect Size of the Relationship Between Clinical and Radiological Predictors of In-Hospital Mortality Was Estimated Using Logistic Regression Analysis

	Univariate Model			Multivariate Model		
	OR	95% CI	*P* Value	aOR	95% CI	*P* Value
Rebleeding	8.37	4.66–15.03	<0.001*	7.69	3.00–19.71	<0.001*
IVH	3.76	2.37–5.94	<0.001*	2.65	1.38–5.09	0.003*
New infarction post-treatment	3.52	2.44–5.09	<0.001*	2.57	1.43–4.62	0.002*
ITB at admission	3.13	2.19–4.46	<0.001*	1.80	0.99–3.25	0.050
Cerebral infarction attributable to DCI	3.10	2.02–4.74	<0.001*	3.66	1.94–6.89	<0.001*
Pupil dilation	3.10	1.80–5.35	<0.001*	1.41	0.65–3.04	0.384
Age ≥60 y	2.01	1.60–2.53	<0.001*	1.70	0.96–3.02	0.067
Acute SDH	1.99	1.21–3.30	0.007	1.18	0.57–2.47	0.654
Pre-ictal mRS (per 1-step increase in category)†	1.39	1.11–1.73	0.004*	0.67	0.33–1.39	0.287
Aneurysm size (per 1-step increase in category)†	1.11	1.01–1.23	0.037	1.16	0.91–1.47	0.230
PC aneurysm	0.96	0.70–1.31	0.645	0.96	0.50–1.85	0.902
ICH	0.28	0.24–0.32	<0.001*	1.67	0.87–3.21	0.125

Results of both the unadjusted model and the multivariate model are presented as odds ratio (OR)/adjusted odds ratio (aOR) with 95% confidence interval (CI). DCI indicates delayed cerebral ischemia; ITB, intubation; IVH, intraventricular hemorrhage; mRS, modified Rankin Scale; PC, posterior circulation; and SDH, subdural hematoma.

*Significant after Bonferroni correction.

†Categories are outlined in Table 1 (see above).

in whom the aneurysm was treated (OR, 15.6; 95% CI, 11.1–21.9; *P*<0.001). In treated patients, the rates of in-hospital mortality were 11.2% after a clipping (n=77/699), 12.6% after a coiling (n=119/948), and 14.9% after a stenting procedure (n=13/87). Clipped patients were as likely as coiled patients to die in hospital (OR, 0.85; 95% CI, 0.62–1.15; *P*=0.286; Figure II in the online-only Data Supplement).

Kaplan–Meier Survival Curves

When survival was stratified by the most important identified predictors, rebleeding was strongly associated with early mortality. This is evident from the clear drop in survival within the first days after aSAH (Figure 2A). As expected from a clinical point of view, DCI leads to delayed mortality, with the survival curves of these patients crossing the survival line of patients without DCI several days after aSAH (Figure 2B). Survival in patients with IVH showed a slow and continuous decrease over hospitalization time (Figure 2C), as did survival in patients experiencing new infarctions post-treatment, except for a certain drop in the second week after aSAH (Figure 2D).

Discussion

Using data from the nationwide Swiss SOS database allowed for the estimation of the impact of selected predictors on in-hospital mortality. Determining this in a relatively large and multicenter database sheds light on important aspects of patient care and can guide future research and funding.

A particularly strong independent predictor of in-hospital mortality was rebleeding. The effect sizes of the relationship between rebleeding and mortality were similar in the unadjusted and adjusted analyses (OR, 8.37; aOR, 7.69; Table 2), indicating only a slight influence of other covariables in the model. In a meta-analysis, the incidence of rebleeding was reported to range between 4% and 17% of aSAH patients, and mostly occurred within 6 hours of the initial hemorrhage.[18] A contemporary single-center study from Switzerland determined the case fatality rate after rebleeding to be as high as 71%,[19] which is comparable to the present series, with a case fatality rate of 62% after rebleeding. In more selected cohorts, mortality is even higher: ≈73% in a multicenter study on poor-grade aSAH patients.[20] All 3 reported rates are higher than the general 24% to 42% case fatality rates for aSAH reported in cooperative studies of various populations.[6,9,21–24] Of note, rebleeding may also occur at a much later stage of the disease and can be responsible for long-term excess mortality in patients without a treated ruptured aneurysm.[25]

Taking the recent literature and our present results into account, it seems that the importance of strategies that prevent rebleeding should be emphasized. Two concepts that may improve patient outcomes by reducing rebleeding have been investigated in recent decades[24]: the application of antifibrinolytic drugs[26,27] and the reduction of the time interval between the initial hemorrhage and aneurysm treatment (so-called ultra-early treatment). A third concept, reducing blood pressure to less extreme values, might also contribute; however, optimal target values for blood pressure control still need to be investigated.[28]

Concerning antifibrinolytic therapy, a recent Cochrane review demonstrated a reduced risk of rebleeding (relative risk, 0.65; 95% CI, 0.44–0.97), but without improvement in clinical outcome (relative risk for poor outcome, 1.02; 95% CI, 0.91–1.15).[29] Moreover, antifibrinolytic therapy leads to increased complications such as DCI (relative risk, 1.41; 95% CI, 1.04–1.91) and deep vein thrombosis,[30] although the rate of pulmonary embolism does not seem to be higher.[31] Most of the studies investigating antifibrinolytic therapy in aSAH patients began the administration late (ie, not in the timeframe of the highest risk of rebleeding) and proceeded with treatment until the DCI period. With the current knowledge that rebleeding occurs mainly within the first few hours and that antifibrinolytic therapy leads to an increase in DCI, these studies might have had some flaws in their design. Currently, a randomized, controlled trial (ULTRA study [Ultra-Early Tranexamic Acid After Subarachnoid Hemorrhage]) is enrolling patients in the Netherlands (URL: http://www.clinicaltrials.gov.

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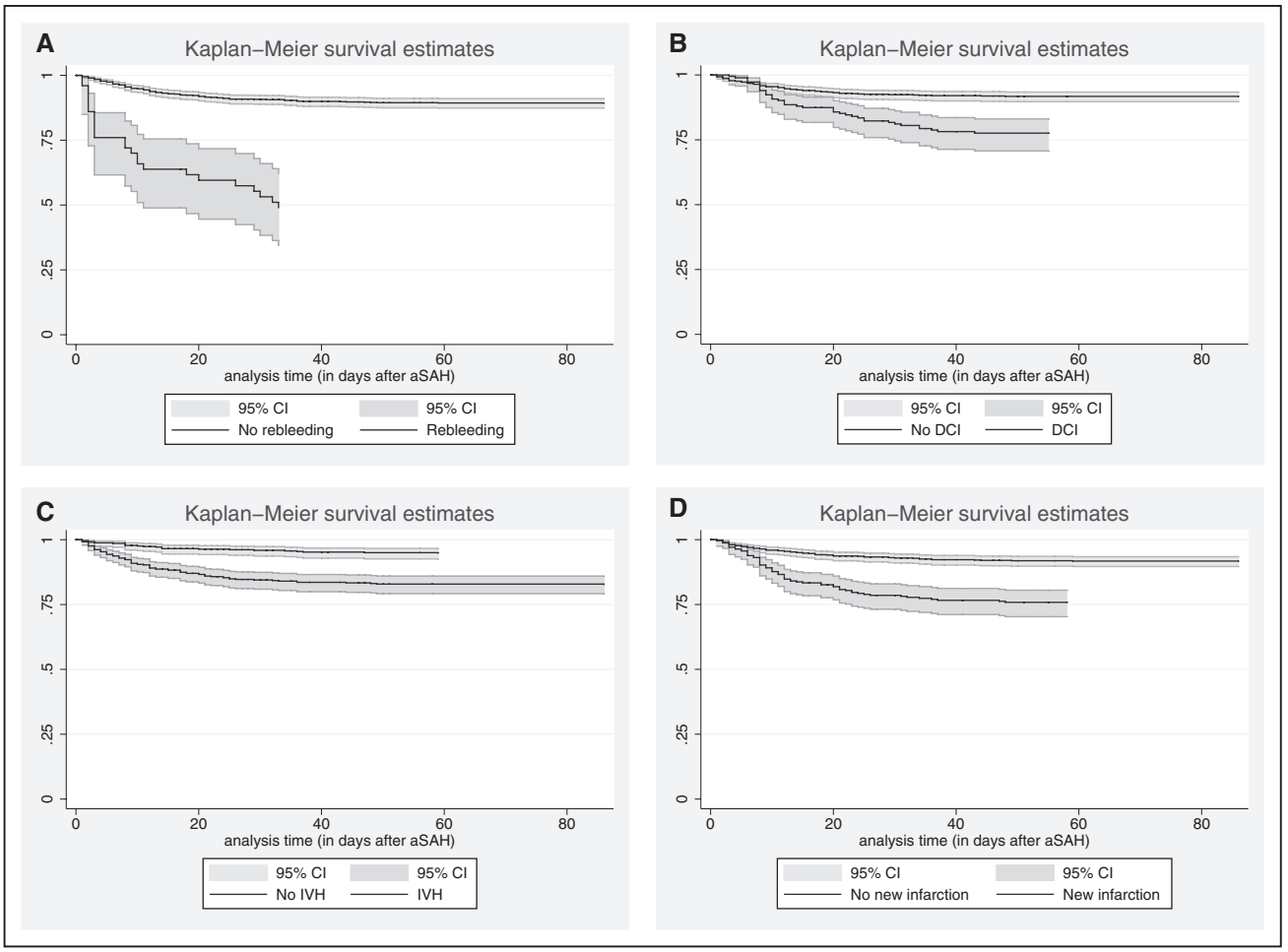

Figure 2. Unadjusted Kaplan–Meier survival estimate (time censored at 120 days) for all patients with aneurysmal subarachnoid hemorrhage (aSAH) in which the aneurysm was treated, stratified for the most important predictors of in-hospital mortality. **A**, Aneurysm rebleeding. **B**, Cerebral infarction attributable to delayed cerebral ischemia (DCI). **C**, Intraventricular hemorrhage (IVH). **D**, New infarctions post-treatment. CI indicates confidence interval.

Unique identifier: NCT02684812). This study should provide an answer to the question of whether ultra-early (as soon as possible after diagnosis) and short-term (until aneurysm treatment—with a maximum of 24 hours) tranexamic acid treatment leads to a better functional outcome. The results of this study are expected in 2019.[26]

Timing of aneurysm treatment has been subject to debate in recent decades, and current guidelines propose securing the ruptured aneurysm as early as possible.[28] With the goal of also reducing ultra-early rebleeding, an increasing number of physicians treat aneurysms as early as possible. The recent literature preponderantly indicates better outcomes after ultra-early aneurysm treatment (<24 hours) when compared with the standard timing of aneurysm occlusion—both for endovascular and surgical treatment.[32–38] In summary, previous and current data stress the importance of carrying out aneurysm treatment as early as possible to prevent rebleeding.[5,39] Moreover, our data suggest that the effect of rebleeding on mortality is about twice as strong as the effect of DCI.

Having said this, delayed brain injury attributable to DCI remains a major cause of death, as well as neurological and neuropsychological disability after aSAH.[28,40] Our data indicate that developing and establishing effective treatment for DCI remain a further important target for rescuing aSAH patients. In this study, the harmful effect of DCI, as demonstrated by cerebral infarcts seen in CT or magnetic resonance imaging studies (aOR, 3.66), was stronger than clinical deterioration attributable to DCI (OR, 1.63; 95% CI, 1.19–2.23; P=0.002).[17] The reason for this observation may be that infarcts detected in imaging studies are irreversible, whereas rescue treatment is quickly initiated as soon as clinical deterioration appears, possibly reversing cerebral ischemia and improving prognosis. Despite the disappointing results of randomized controlled trials with statins, endothelin-1 antagonists, and magnesium sulfate,[41] prophylactic measures taken with calcium antagonists seem to have a robust beneficial effect on outcomes and are recommended as standard therapy.[28] New therapies take into consideration the current understandings of the pathophysiology of DCI, including small-vessel thromboembolism, microcirculatory disturbances, cortical spreading depression, and delayed cell apoptosis.[10,41,42] Promising methods of reducing the rate of DCI and ischemic consequences are currently under investigation, including the intrathecal application of both thrombolytic infusions and calcium antagonists.[43–45]

The management of IVH in aSAH remains challenging.[46] In a previous report, strategies that cleared intraventricular blood

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faster by active lysis neither improved outcomes nor reduced shunt dependency.[44,47] Further ideas are required for this particularly vulnerable population of patients.

The results indicate that ischemic complications directly associated with the aneurysm occlusion therapy have a measurable and relevant impact on survival. As this is a modifiable risk factor, the finding stresses the important role of the team of care providers in choosing the most appropriate modality for aneurysm occlusion in the individual patients. It also points out the necessity of specialized cerebrovascular training and use of modern intraoperative techniques (eg, Doppler, indocyanine green or intraoperative digital subtraction angiography, electrophysiological monitoring, augmented reality) to provide high-quality patient care with low risk for cerebral ischemia.

Pupillary dilation is a sign of severe early brain injury after aSAH with transtentorial herniation secondary to large intracerebral and extra-axial hematomas, decompensated hydrocephalus, or generalized brain edema. In univariate analysis, it was indicative of the severity of the initial bleeding (OR, 3.10), but it lost its predictive capacity once the other variables were entered into the statistical model (Table 2). Vergouwen et al[5] found that initial bleeding remained a leading cause of in-hospital mortality and suggested that future intervention studies investigate the prevention of early brain injury from aneurysmal rupture. Our data confirm the association between the severity of early brain injury and in-hospital mortality, but indicate that this effect is likely conveyed by other variables included in the statistical model. Besides, reducing early brain injury outside the hospital—without having clearly established the diagnosis of aSAH—is challenging, whereas effective actions against rebleeding, cerebral infarction post-treatment, and even DCI can be taken as soon as diagnosis is confirmed.

Strengths and Weaknesses

A strength of the present study is that all major hospitals in Switzerland contributed to a clearly defined and prospective data collection. In contrast to highly selected data from randomized trials, our data are completely unselected, as also reflected by the high number of patients not curatively treated. Because of the multicenter, multicultural, and multilingual (German, French, and Italian, among others) nature of the data, these results can be generalized to other clinical settings and populations.[5] The observed associations and survival curves parallel our clinical observations, indicating that the data are valid.

Some data were missing and could not be obtained despite all efforts, as indicated by unspecified in Table 1. Furthermore, it can be difficult to determine the exact relationship between in-hospital death and certain complications in a patient who has several complications. By applying multivariate analysis, the effect size of each factor was estimated independently, but some inaccuracy may still remain. Determining the contribution of early withdrawal of life-sustaining therapy to case fatality was abstracted by the variable no aneurysm occlusion, as this was only rarely associated with continuation of active treatment. The OR for in-hospital mortality was 15.6, and the case fatality rate was exceptionally high with 71.6%. For the reasons mentioned above (Materials and Methods), we only considered patients in whom the aneurysm was treated for the main statistical model. Despite omitting those patients from analysis, rebleeding, cerebral infarction attributable to DCI, IVH, and new infarction after aneurysm treatment remained significant and strong independent predictors. Sensitivity analyses were performed and showed robustness of the model. The high likelihood to die in certain groups (eg, rebleeding) could still relate more to the decision not to pursue active treatment rather than to its true association with mortality, as abandonment of active treatment was also decided in some patients with dismal prognosis after aneurysm occlusion. Finally, this study did not aim to determine the cause of death of aSAH patients; however, this would be worth investigating. A better insight into the decision-making process of treating physicians that leads to the abandonment of active treatment may shine additional light on the factors that play a role in in-hospital mortality and which can potentially be optimized to enhance clinical outcomes.

Summary

Strong independent predictors for in-hospital mortality were aneurysm rebleeding (aOR, 7.69), cerebral infarction attributable to DCI (aOR, 3.66), IVH (aOR, 2.65), and new infarction post-treatment (aOR, 2.57) in patients where active treatment is initially pursued. Several—and among them modifiable—factors seem to be associated with in-hospital mortality after aSAH. Our data suggest that strategies aiming to reduce the risk of rebleeding are most promising in patients where active treatment is initially pursued.

Acknowledgments

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Disclosures

None.

Appendix

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