



Anticoagulation Therapy in Patients Suffering from Aneurysmal Subarachnoid Hemorrhage: Influence on Functional Outcome—a Single-Center Series and Multivariate Analysis

Patrick Schuss, Alexis Hadjiathanasiou, Simon Brandecker, Ági Güresir, Valeri Borger, Christian Wispel, Hartmut Vatter, Erdem Güresir

■ **INTRODUCTION:** Favorable outcome in patients presenting with aneurysmal subarachnoid hemorrhage (SAH) is determined by several factors. Nevertheless, data on the influence of prior use of oral anticoagulation drugs on functional outcome in patients suffering from SAH are scarce. We therefore analyzed our institutional data.

■ **METHODS:** From January 2009 to October 2015, 480 patients suffering from aneurysmal SAH were admitted to our institution. Information including patient characteristics, treatment modality, aneurysm size and location, radiologic features, and functional neurologic outcome was assessed and further analyzed. Outcome was assessed according to the modified Rankin Scale (mRS) at 6 months and stratified into favorable (mRS 0–2) versus unfavorable (mRS 3–6).

■ **RESULTS:** Overall, 17 of 480 patients suffering from aneurysmal SAH were on anticoagulation therapy before ictus (4%). Patients without anticoagulation therapy were significantly younger compared with patients with anticoagulation therapy before SAH ($P = 0.005$). Furthermore, patients without anticoagulation therapy presented in a significantly better clinical condition compared with patients with anticoagulation therapy before SAH ($P = 0.02$). Additionally, patients without anticoagulation therapy achieved significantly more often favorable functional outcome compared with patients with anticoagulation therapy before SAH ($P = 0.02$). However, anticoagulation therapy was not identified as a significant

and independent predictor for unfavorable outcome in the multivariate logistic regression analysis.

■ **CONCLUSION:** Anticoagulation therapy has not been identified as a significant and independent factor influencing functional outcome in patients suffering from SAH. Therefore treatment should not be omitted. Nevertheless, cautious management is necessary in patients with known anticoagulation therapy before SAH.

INTRODUCTION

Previous studies observed a potential increased risk of aneurysmal subarachnoid hemorrhage (SAH) in patients with anticoagulation therapy.¹ In addition, prescription of anticoagulant drugs is increasing for prevention and treatment of vascular pathologies, such as atrial fibrillation.² Favorable neurologic outcome in patients suffering from SAH is determined by several clinical and individual risk factors.³ However, influence of previous anticoagulation therapy on functional outcome in patients suffering from SAH remains unclear. Therefore we analyzed our institutional data to investigate a possible influence of anticoagulant usage before SAH on functional outcome in these critically ill patients.

METHODS

Patients

Between January 2009 and October 2015, 480 patients suffering from aneurysmal SAH were admitted to our institution. SAH was

Key words

- Anticoagulation
- Antithrombotic
- Intracranial aneurysm
- Subarachnoid hemorrhage

Abbreviations and Acronyms

- mRS:** Modified Rankin Scale
PCC: Prothrombin complex concentrate
SAH: Subarachnoid hemorrhage
SDH: Subdural hematoma
VKA: Vitamin K antagonist

WFNS: World Federation of Neurological Surgeons

Department of Neurosurgery, Rheinische Friedrich-Wilhelms-University, Bonn, Germany

To whom correspondence should be addressed: Patrick Schuss, M.D.

[E-mail: patrick.schuss@ukb.uni-bonn.de]

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diagnosed by computed tomography or lumbar puncture. Information including patient characteristics on admission and during treatment course, antiplatelet or antithrombotic therapy before hospitalization, aneurysm size and location, radiologic features, treatment modality, and functional neurologic outcome were collected and entered into a computerized database (SPSS, version 22, IBM Corp., Armonk, New York, USA). The World Federation of Neurological Surgeons (WFNS) scale was used to grade patients on admission.^{4,5} Patients suffering from aneurysmal SAH were divided into good grade (WFNS grades I–III) versus poor grade (WFNS grades IV–V) on admission. From 480 patients with aneurysmal SAH, 26 patients presented in devastated clinical condition that did not justify further aneurysm treatment. However, 454 patients were treated by surgical clipping or endovascular coiling on the basis of an interdisciplinary consensus in each individual case. We followed an early treatment strategy (within 24–48 hours) in patients suffering from SAH in all clinical grades.^{6–9} In order to rule out possible treatment-related complications, computed tomography scans were obtained 24 hours after aneurysm treatment. Patients with acute hydrocephalus were treated by ventriculostomy for external cerebrospinal fluid diversion. All patients received nimodipine from the day of clinical admission onwards. In cases of onset of symptomatic vasospasm, hypertension was induced with catecholamines during the course of the treatment.¹⁰ Patients with aneurysm-related SAH suffering from contemporaneous space-occupying acute subdural hematoma (SDH) or intracerebral hemorrhage were treated with surgical evacuation.^{6,8,9} In patients with intractable elevated intracranial pressure, decompressive craniectomy with subsequent autologous cranioplasty was performed in survivors as previously reported.^{11–15} In case of shunt-dependent hydrocephalus during treatment, a ventriculoperitoneal shunt was placed, primarily in the right frontal horn.¹⁴ Outcome was assessed according to the modified Rankin Scale (mRS) after 6 months and stratified into favorable (mRS 0–2) versus unfavorable (mRS 3–6). The present study is a retrospective analysis of data.

ANTICOAGULANT USAGE PRIOR SAH

In patients with aneurysmal SAH and known anticoagulant usage prior hospitalization, urgent reversal was carried out following our institutional guidelines due to controversial literature data. Besides withdrawal of the used agent, reversal of anticoagulation therapy with vitamin K antagonists (VKAs) was achieved through individual treatment approaches using vitamin K substitution (oral or parental), fresh frozen plasma, prothrombin complex concentrates (PCC), and recombinant factor VIIa.

STATISTICS

Retrospective data analyses were performed using the computer software package SPSS (version 22, IBM Corp., Armonk, New York, USA). The unpaired Student's *t*-test was used for parametric statistics. Categorical variables were analyzed in contingency tables using Fisher's exact test. Results with $P < 0.05$ were considered statistically significant.

Furthermore, a multivariate analysis was performed to find independent predictors of unfavorable functional outcome using binary logistic regression analysis in order to find confounding

factors between potentially independent predictors. Variables with significant *P* values in the univariate analysis were considered as potentially independent variables in a multivariate analysis. A backward stepwise method was used to construct a multivariate logistic regression model in relation to favorable outcome as a dependent variable with an inclusion criterion of $P < 0.05$.

RESULTS

Patient Characteristics

Between January 2009 and October 2015, 480 patients suffering from aneurysmal SAH were admitted to our institution. Overall, 454 patients with aneurysmal SAH underwent aneurysm treatment during treatment course. In detail, 184 of 454 patients were treated by surgical clipping (41%) and 270 patients underwent endovascular coiling (59%).

Overall, favorable outcome was achieved in 254 patients in the present series (53%).

Patient characteristics including age, gender, clinical admission status, information concerning the use of anticoagulation agents prior SAH, angiographic and radiologic findings, treatment modality, and clinical outcome of the present series are shown in **Table 1**.

Influence of Previous Anticoagulation Therapy

Overall, 17 patients (4%) were on anticoagulation therapy at the time of aneurysm rupture. All patients with known anticoagulant usage before SAH in the present series received anticoagulant medication. Patients with anticoagulant usage before SAH were significantly older compared with patients without previous anticoagulation therapy ($P = 0.005$, 95% CI 1.6–9.3). Four of 17 patients with previous anticoagulation therapy achieved favorable outcome compared with 250 of 463 patients without (24% vs. 54%; $P = 0.02$, OR 3.8, 95% CI 1.2–11.9). Further details concerning patient characteristics, laboratory data, and radiologic features for patients with and without anticoagulant usage before SAH are given in **Table 2**.

Neurologic Grading at Admission

Overall, 312 patients (65%) presented with good-grade SAH and 168 patients (35%) with poor-grade SAH on admission. Favorable outcome was achieved in 225 of 312 patients with good-grade SAH and in 29 of 168 patients with poor-grade SAH (72% vs. 17%; $P < 0.0001$, OR 12.4, 95% CI 7.7–19.8).

In patients with anticoagulation therapy before SAH, 6 patients (35%) presented with good-grade SAH and 11 patients (65%) with poor-grade SAH on admission. Therefore patients with anticoagulation therapy before SAH presented significantly more often with poor-grade SAH on admission compared with patients without anticoagulation therapy before SAH (65% vs. 34%; $P = 0.02$, OR 3.6, 95% CI 1.3–9.8).

Space-Occupying Hematoma

Overall, space-occupying hematoma was identified in 121 patients (25%) suffering from aneurysmal SAH in the present series. Favorable outcome was achieved significantly more often in patients without space-occupying hematoma when compared with patients with space-occupying hematoma (63% vs. 23%;

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