Aneurysm Location as a Prognostic Outcome Factor After Subarachnoid Hemorrhage From Internal Carotid Artery Aneurysms and Potential Impact for Further Experimental Subarachnoid Hemorrhage Models

Juergen Konczalla, Nina Brawanski, Johannes Platz, Christian Senft, Sepide Kashefiolasl, Volker Seifert

■ OBJECTIVE: **Prognostic factors of favorable and unfavorable clinical outcome after aneurysmal subarachnoid hemorrhage (SAH) are still not completely known. We retrospectively analyzed the aneurysm location as a factor for patients' outcome after aneurysmal SAH.**

■ METHODS: **We retrospectively selected patients from our prospectively collected database with aneurysm at the carotid bifurcation artery ($n = 23$) and posterior communicating artery ($n = 170$). Outcome was assessed using the modified Rankin Scale (mRS) (favorable [mRS score, 0–2] vs. unfavorable [mRS score, 3–6]) 6 months after SAH.**

■ RESULTS: **A good clinical admission status (World Federation of Neurological Surgery grade I–III) has a significant influence on mRS score after SAH. In univariate analysis, advanced age, Fisher grade 3, early hydrocephalus, severity of cerebral vasospasm (CVS), longer stay on the intensive care unit, and posterior communicating artery aneurysms were associated with an unfavorable outcome. Multivariate analysis showed 4 prognostic factors for a favorable outcome: good admission status (odds ratio [OR], 10.8); aneurysms of carotid bifurcation artery (OR, 4.3); absence of mild or severe CVS (OR, 3.4); and patients age less than 55 years (OR, 2.1).**

■ CONCLUSIONS: **Despite the usual prognostic factors (good admission status, younger age, absence of CVS) for a favorable outcome after SAH, the aneurysm location (carotid bifurcation artery) itself seems to be a prognostic factor. Also, aneurysms of the carotid bifurcation artery showed less occurrence of an early hydrocephalus, which is an indicator for the presence of an early brain injury. According to these results, we question if experimental animal models (especially the endovascular model using the perforation of the carotid bifurcation artery) have to be re-evaluated.**

INTRODUCTION

Prognostic factors for favorable or unfavorable clinical outcome after aneurysmal subarachnoid hemorrhage (SAH) are still not completely known. We retrospectively analyzed factors associated with favorable clinical outcome of patients with SAH caused by aneurysms of the internal carotid artery. A recently published article[1] detected a relatively favorable outcome for carotid bifurcation aneurysms. We therefore analyzed if the aneurysm location had an influence on patients' outcome. We included patients with an SAH out of an aneurysm of the carotid bifurcation artery and posterior communicating (Pcom) artery and compared both aneurysm locations.

Furthermore, in experimental SAH models, the endovascular perforating model is often used. A rupture of the carotid bifurcation aneurysm should have similar effects in humans. We

Key words
- Aneurysm location
- Early brain injury
- Internal carotid artery
- Outcome
- Prognostic factor
- Subarachnoid hemorrhage
- Translational research

Abbreviations and Acronyms
CVS: Cerebral vasospasm
DIND: Delayed ischemic neurologic deficit
EBI: Early brain injury
ICU: Intensive care unit
mRS: Modified Rankin Scale
OR: Odds ratio
PCom: Posterior communicating
SAH: Subarachnoid hemorrhage
WFNS: World Federation of Neurological Surgery

Department of Neurosurgery, Johann Wolfgang Goethe University Hospital, Frankfurt am Main, Germany

To whom correspondence should be addressed: Nina Brawanski, M.D. [E-mail: N.Brawanski@web.de]

Jürgen Konczalla and Nina Brawanski contributed equally and are considered to be co–first authors.

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therefore analyzed our results against this background to detect implications for translational research, but this time from bedside to bench.

METHODS

Statistical analyses were performed with commercially available software (IBM SPSS Statistics version 22 [IBM Inc., Armonk, New York, USA]). Categorial variables were analyzed using the Fisher exact test and the unpaired t test with Welch correlation for parametric values. Furthermore, multivariate analysis and binary regression analysis were performed. Factors included were patient age, World Federation of Neurological Surgery (WFNS) grade, Fisher grade at time of admission, modified Rankin Scale (mRS) score 6 months after SAH, the occurrence of an early hydrocephalus, and aneurysm location. Probability values <0.05 were considered statistically significant. The study was approved by the local ethics committee.

Study Population

Between 1999 and 2013, 1493 patients with aneurysmal SAH were entered into a prospectively conducted database (SPSS). Retrospectively, we selected patients with aneurysms of the Pcom artery and of the carotid bifurcation artery. In total, 193 patients were selected (23 patients with an aneurysm of the carotid bifurcation and 170 patients with an aneurysm of the Pcom artery). All patients were monitored in the intensive care unit (ICU). Digital subtraction angiography was performed, and then the aneurysm was treated based on ISAT (International Subarachnoid Aneurysm Trial) data and patients' characteristics. All patients received nimodipine initiated at time of admission (60 mg 6 times per 24 hours). In case of an early hydrocephalus, affected patients received an external ventricular drainage. Outcome was assessed by mRS 6 months after aneurysmal SAH.

RESULTS

Patient Characteristics

In 170 cases, SAH occurred from an aneurysm of the PCom artery and in 23 patients from an aneurysm of the carotid bifurcation artery (carotid T). Patients' characteristics are detailed in Table 1. A total of 114 patients (59%) had good admission status at the time of SAH detected by WFNS grade I–III. A total of 108 patients (55%) had early hydrocephalus, and over the course of time, 37 of the patients (19%) needed implantation of a ventricular peritoneal shunt. No case of ruptured aneurysm of the carotid bifurcation showed a concomitant intraparenchymatous bleeding.

Outcome Characteristics

In total, 117 of 193 patients (61%) had a favorable outcome 6 months after SAH. These patients had a mean age of 51.77 ± 12.76 years. In univariate analysis, good clinical status at admission (WFNS grade I–III) has a significant positive influence on outcome ($P < 0.001$). Also, advanced age, Fisher grade 3 ($P = 0.04$), early hydrocephalus ($P < 0.001$), severity of cerebral vasospasm (CVS) (CVS >33%, $P < 0.001$; CVS >66%, $P < 0.001$), longer stay on ICU ($P < 0.001$), and Pcom aneurysm ($P = 0.02$) were associated with an unfavorable outcome (Table 2).

Table 1. Patients' Characteristics

Patient Characteristics	Number of Aneurysms of Carotid Bifurcation and Posterior Communicating Artery	Percentage of Total Patients
Number of patients	193	
Posterior communicating artery	170	88
Carotid bifurcation artery	23	12
Mean age (years)	55.2	
Female sex	156	80
World Federation of Neurological Surgery I–III at admission	114	59
Early hydrocephalus	108	55
Shunt dependence	37	19
Fisher grade 3	141	72
Clip	75	39
Coil	118	61

Therefore, additional multivariate analysis was performed to identify independent prognostic factors (Nagelkerke $R^2 = 0.427$). In our analysis, these factors were admission status (odds ratio [OR], 10.8; $P < 0.001$), aneurysms of the carotid bifurcation artery (OR, 4.3; $P = 0.02$), absence of mild or severe CVS (OR, 3.4, $P < 0.001$) and patients' age <55 years (OR, 2.1; $P = 0.05$). In total, 72 of 193 patients (37%) had CVS with a radiologically detected vessel narrowing more than 33%, which influenced the outcome significantly (Table 2). In addition, we analyzed the occurrence of ischemic infarctions in all patients included in this study. Three patients with SAH from an aneurysm of the Pcom artery and 1 patient with a ruptured aneurysm of the carotid bifurcation artery had cerebral infarctions without the detection of CVS on radiologic imaging during their stay in the ICU.

Aneurysm Treatment

In subgroup analysis, 19 patients (83%) with an aneurysm of the internal carotid bifurcation had a favorable clinical outcome compared with 4 (17%) patients with an unfavorable outcome 6 months after SAH ($P = 0.02$). A total of 98 patients (58%) of patients with an aneurysm of the PCom artery had a favorable outcome compared with 72 patients (42%) with an unfavorable outcome ($P = 0.02$). A total of 118 aneurysms (61%) were treated with endovascular coiling and 75 aneurysms (39%) with surgical clipping. Statistical analysis showed no influence on patient outcome compared with aneurysm treatment modality.

Comparison of Aneurysms of the PCom Artery and Carotid Bifurcation Artery

Furthermore, we directly compared aneurysms of the PCom artery and carotid bifurcation artery (Table 3). This analysis showed a significantly better outcome in patients with aneurysms of the