Acta Neurochirurgica (2019) 161:1763–1773
https://doi.org/10.1007/s00701-019-03992-4

ORIGINAL ARTICLE - VASCULAR NEUROSURGERY - ANEURYSM

Early clinical course after aneurysmal subarachnoid hemorrhage: comparison of patients treated with Woven EndoBridge, microsurgical clipping, or endovascular coiling

Thomas Sauvigny[1] · Marie Teresa Nawka[2] · Nils Schweingruber[3] · Marius Marc-Daniel Mader[1] · Jan Regelsberger[1] · Nils Ole Schmidt[1] · Manfred Westphal[1] · Patrick Czorlich[1]

Received: 10 April 2019 / Accepted: 25 June 2019 / Published online: 6 July 2019

Abstract

Background The Woven EndoBridge (WEB) device has been increasingly used for the treatment of intracranial aneurysms after aneurysmal subarachnoid hemorrhage (SAH). Still, recent major clinical trials on patient management after SAH have defined WEB embolization as an exclusion criterion. In an analysis of an unselected patient cohort, we evaluate the early clinical course of SAH patients after WEB treatment compared to those treated with endovascular coiling or surgical clipping.

Methods Data of all patients with proven SAH who were either treated with a WEB device, coil embolization, or neurosurgical clipping between March 2015 and August 2018 was systematically reviewed. Clinical parameters on intensive care unit (ICU), medical history and mortality rates were evaluated and compared between the different treatment approaches.

Results Of all 201 patients included, 107 patients received endovascular coil embolization, 56 patients were treated with clipping and in 38 cases a WEB device was placed. The overall mortality was 17.9%. Thirteen patients (34.2%) in the WEB group had a Hunt and Hess grade > 3. Essential medical factors showed no clinically relevant differences between the treatment groups, and the analyzed blood parameters were predominantly within physiological limits without any relevant outliers. The Hunt and Hess grade but not the treatment modality was identified as independent risk-factor associated with ICU-mortality in the overall cohort ($p < 0.001$).

Conclusion In this study, there was no difference in the early clinical course between those treated with WEB embolization, coil embolization, or neurosurgical clipping. Since WEB embolization is a valuable treatment alternative to coiling, it seems not justified to exclude this procedure from upcoming clinical SAH trials, yet the clinical long-term outcome, aneurysm occlusion, and retreatment rates have to be analyzed in further studies.

Clinical trial registration number not applicable.

Keywords Subarachnoid hemorrhage · WEB · Mortality · Neurocritical care · Clipping · Coiling

Abbreviations

ACA	Anterior cerebral artery complex
ACOM	Anterior communicating artery
aPTT	Activated partial thromboplastin time
ASA	Acetylsalicylic acid
CSF	Cerebrospinal fluid

This article is part of the Topical Collection on *Vascular Neurosurgery-Aneurysm*

Presentation at a conference: Parts of the manuscript were presented at the 70th annual meeting of the German Society for Neurosurgery (DGNC) held in Würzburg, Germany, May 12–15 2019.

✉ Patrick Czorlich
p.czorlich@uke.de

[1] Departments of Neurosurgery, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany

[2] Diagnostic and Interventional Neuroradiology, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany

[3] Institute of Neuroimmunology and Multiple Sclerosis, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany

DCI	Delayed cerebral ischemia
IA	Intracranial aneurysm
ICA	Internal carotid artery
ICU	Intensive care unit
MCA	Middle cerebral artery
mRS	Modified Rankin Scale
SAH	Subarachnoid hemorrhage
SD	Standard deviation
TISS	Therapeutic Intervention Scoring System
VP	Ventricular-peritoneal
WEB	Woven EndoBridge
WFNS	World Federation of Neurosurgical Societies

Introduction

Aneurysmal subarachnoid hemorrhage (SAH) still remains a life-threatening disease with high rates of mortality and morbidity [21]. In patients presenting with SAH due to ruptured IAs, prompt therapy is indispensable as approximately 80% of patients suffer death or remain disabled if rebleeding occurs [32]. To achieve complete and long-term occlusion of ruptured IAs, endovascular coiling and neurosurgical clipping have been established as suitable treatment options [5, 28]. However, endovascular aneurysm treatment is a constantly developing field with improvement of accessible techniques and devices. As treatment of wide-neck aneurysms is one of the major challenging scenarios and clipping is not always feasible in these patients [27, 33], distinct endovascular devices including flow diverters and Woven EndoBridge (WEB) have been introduced into clinical practice recently [26, 28, 29]. Aneurysm therapy with the WEB device has been proven as a potentially safe option in SAH patients since being introduced [1, 3, 19, 29]. Various retrospective single- and multicenter studies evaluating initial management strategies and new treatment options of the acute disease stage have contributed information and recommendations for the respective clinical scenarios, but most recent major clinical trials have been excluding SAH patients treated with the WEB device [14, 20]. The rationale why SAH patients treated with the WEB device are excluded in these trials remains unclear. However, it can be assumed that this is due to the lack of randomized prospective trials available for this new treatment method. Furthermore, the aforementioned previous studies lack comparative data for the critical care period distinguishing well-established aneurysm securing procedures like microsurgical clipping or endovascular coiling. We therefore aimed to assess the clinical course on the intensive care unit (ICU) as well as ICU mortality in SAH patients treated with the WEB device. We hypothesized (null hypothesis) that endovascular WEB treatment does not have a clinically relevant impact on the early clinical course, and parameters, mortality as well as 6 months outcome do not differ between patients treated with endovascular coiling, WEB placement, or neurosurgical clipping.

Materials and methods

Study population

The study was reported to the local ethics committee (WF-069/18) and was performed in accordance with the ethical standards laid down in the Declaration of Helsinki. We retrospectively evaluated anonymous data of patients presenting with SAH due to acutely ruptured intracranial aneurysms in our tertiary center between March 2015 and August 2018 (n = 226). The time span available for analysis was predefined starting when WEB treatment became routinely available in our institution. For this type of study, formal consent is not required. Patients who did not receive any endovascular or neurosurgical treatment due to clinical conditions were excluded from the study. Furthermore, the implantation of additional devices (i.e., flow diverter, stent) and a combined treatment of WEB placement, coiling, and clipping were exclusion criteria.

Data analysis

All clinical data were reviewed anonymously. The decision between surgical and endovascular treatment was individually discussed between the attending neurosurgeon and neuroradiologist based on aneurysm shape, localization, and logistic circumstances. Aneurysm locations were subdivided according to their location: internal carotid artery (ICA), middle cerebral artery (MCA), anterior cerebral artery complex (ACA), including the anterior communicating artery (ACOM) and the pericallosal artery and aneurysms of the vertebrobasilar circulation.

Basic clinical characteristics of our study population including clinical parameters and SAH-relevant events on ICU at admission and during hospitalization as well as medical history were collected. Data collection included demographic information, comprising age and sex, aneurysm information including location and size, antiplatelet information, acute hydrocephalus and initial coma rates, pre-existing conditions, and distinct clinical evaluation scores (Glasgow Coma Scale, Hunt and Hess grading system, WFNS grading system, modified Graeb scale, Fisher score). Ventriculitis was defined as clinical signs of ventriculitis/meningitis (like fever above 38.5 °C and meningism and neurological deterioration) and at least three or more pathological CSF findings as described before [7]. Delayed cerebral ischemia (DCI) was defined as previously described by Vergouwen et al. as the occurrence of a new focal neurological impairment or a decrease of at least 2 points on the Glasgow Coma Scale for at least 1 h and cannot be attributed to other causes by means of clinical assessment, CT, or MRI scanning or the presence of cerebral infarction on CT or MR scan not present on the CT or MR scan between 24 and 48 h after early aneurysm occlusion, and not attributable to other causes such as surgical clipping or endovascular treatment [35].

Vital signs, laboratory parameters, blood gas values, and the Therapeutic Intervention Scoring System (TISS) were extracted from the intensive care unit's electronic documentation system and bioinformatically processed. Mean arterial pressure, body temperature measurements from bladder catheter and peripheral oxygen saturation were analyzed in the treatment groups (number of analyzed values clip (n) = 21,000–29,000 values, coil (n) = 35,000–56,000 values, WEB (n) = 10,000–17,000 values). Additionally, relevant blood laboratory findings (hemoglobin, thrombocytes, leucocytes, coagulation parameters) were calculated (clip (n) = 1000–1150 values, coil (n) = 1920–1950 values, WEB (n) = 590–600 values). To get a further impression of metabolic and respiratory changes blood gas analyses were taken in account (clip (n) = 5590–5660 values, coil (n) = 11,120–11,190 values, WEB (n) = 3470–3540 values). The data was processed in a standardized script-based manner with R [11].

Mortality rates at discharge from ICU were evaluated according to the treatment procedure. Outcome was assessed at 6 months using the modified Rankin scale (mRS). A favorable outcome was defined as an mRS of 0–2. Parameters were associated with the different treatment modalities neurosurgical clipping, endovascular coiling, and WEB placement.

WEB embolization

The Woven EndoBridge (WEB; MicroVention, Tustin, CA, USA) is an intrasaccular braided wire device designed to embolize intracranial aneurysms with anatomies unfavorable for coiling (large aneurysms, wide-necked aneurysms) [8, 24]. Once detached inside the aneurysmal sac, flow disruption is provided by fine nitinol meshes, leading to thrombus formation and thus subsequent occlusion of the aneurysm [8]. In our institution, the standard antiplatelet regime in acutely ruptured intracranial aneurysms treated with the WEB device comprises a perioperative dose of 250 mg i.v. of ASA (acetylsalicylic acid) and a daily dose of 100 mg of ASA 6 weeks postprocedural, which is similar to the regime applied in elective cases and generally due to the pathoanatomy, i.e., more frequently wide-neck aneurysms than in the coiling collective. Antiplatelet regime in acutely ruptured intracranial aneurysms treated with coil embolization alone consists of periprocedural dose of 250 mg i.v. of ASA, per default no postprocedural antiplatelet therapy; however, ASA is continued in a certain percentage (app. 30%).

Statistical analysis

Quantitative variables were described as mean ± standard deviation (SD), qualitative variables are outlined as number and percentage. Statistical analysis of the data was performed by a univariate analysis using χ^2 tests, independent-samples Kruskal-Wallis tests or ANOVA tests depending on the scale of the measurements and equality of variances, to examine correlations between the parameters using IBM® SPSS® Statistics 22 (IBM Corporation, Armonk, NY, USA). A univariate logistic regression followed by a multivariate logistic regression analysis including all factors with a $p < 0.1$ in the univariate analysis was used to identify independent factors for ICU mortality, DCI and 6-month outcome. The level of statistical significance was set at $p < 0.05$. To ascertain whether the number of patients in our study was sufficient to detect differences between groups, the minimum detected effect size was computed using G*power v3.1.9.3 for χ^2 test, Kruskal-Wallis test, and ANOVA test given a power of 0.8, respectively. Since this was a retrospective analysis of a predefined period of SAH cases, the mentioned power calculations were performed ex post. To visualize the parameters from the digital patient record, we tiled the time since ICU admittance and calculated the mean (point) and standard error of mean (error bar). To get a better impression on trends in the data, a regression model was fitted over the aforementioned intervals. Data transformation, calculation, and visualization were done in R (main packages: dplyr, tidyverse, stringr, ggplot2).

Results

Patient and clinical characteristics

Two hundred one patients including 127 women (63.2%) and 74 men (36.8%) were finally enrolled in this study. Twenty-five of 226 patients were excluded because of the following: in 10 patients, no aneurysm treatment was conducted after hospitalization and in 15 cases, either adjunctive devices were placed or a combined therapy of different treatment options was performed. One hundred seven (53.2%) patients were treated with endovascular coil embolization, 56 patients received neurosurgical clipping (27.9%) and in 38 patients (18.9%) endovascular WEB placement was performed. Figure 1 illustrates patient flowchart inclusion into our study population.

Mean age was 55.6 ± 13.3 years, range 21–90 years. Significant differences between aneurysm locations according to the three different treatment groups could be observed (ACA 93; 46.3% vs. MCA 38; 18.9% vs. ICA 49; 24.4% vs. vertebrobasilar circulation 21; 10.4%, $p < 0.001$). Development of acute hydrocephalus defined as an indication for placement of an external ventricular drainage by the attending neurosurgeon was observed in 137 cases (68.2%), showing significantly higher rates in patients treated with coils

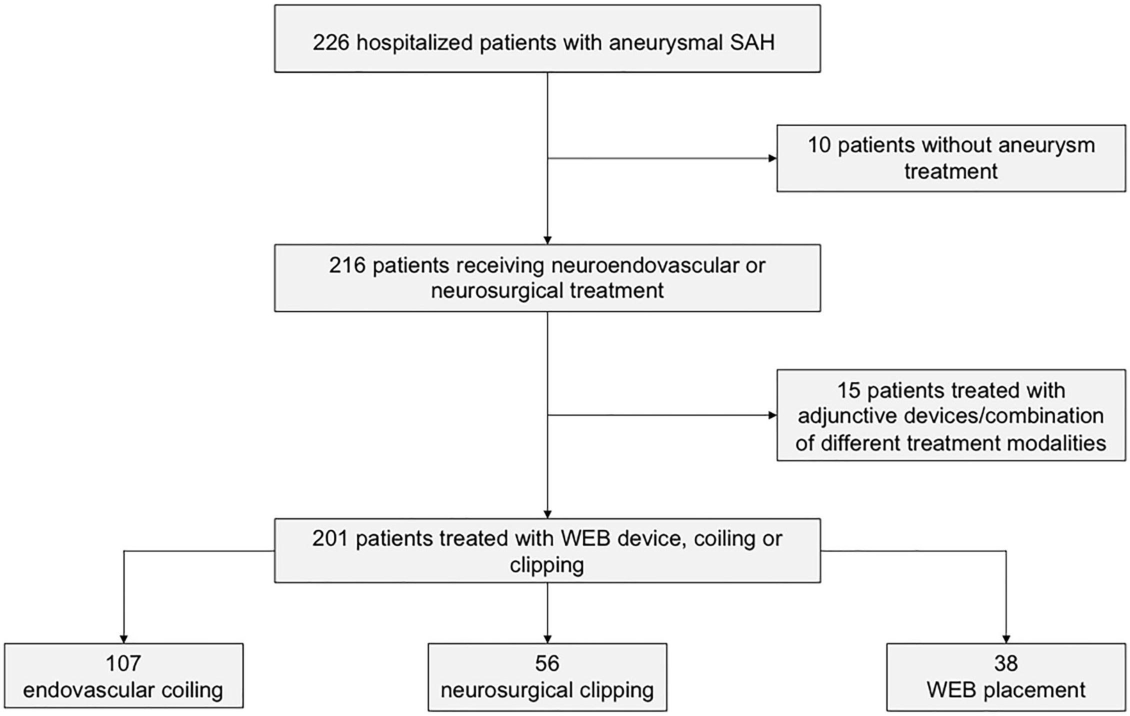

Fig. 1 Patient flowchart derivation and final study cohort

and the WEB device compared to patients who received microsurgical clipping (74.8% vs. 68.4% vs. 55.4%, $p = 0.041$). Further clinical parameters including arterial hypertension, nicotine abuse, pre-existing conditions, and the different intensive care unit scoring systems did not differ between the groups. Basic clinical characteristics of the study population are presented in Table 1.

Table 2 shows clinical parameters during ICU hospitalization. The overall length of stay on ICU accounted for 18.1 ± 10.3 days, range 1–61 days. TISS showed no clinical nor statistically significant differences between the treatment modalities. No significant difference between rates of ventricular-peritoneal shunt-implantation, ventriculitis, tracheotomy, stay on ICU, and hours of ventilation occurred. Delayed cerebral ischemia showed no significant difference between the treatment groups. Dexamethasone dose was significantly higher in neurosurgical patients who underwent clipping compared to patients who underwent endovascular treatment (61.9 mg ± 63.4 vs. 29.8 mg ± 70.1, and 23.3 mg ± 54.7, $p = 0.005$). Additionally, post-interventional antiplatelet therapy including acetylsalicylic acid and/or clopidogrel differed significantly between the three treatment groups (see Table 2). Figure 2 shows the continuous course of the most important clinical laboratory parameters, blood pressure, oxygen saturation, and body temperature during the intensive care stay. The vital parameters run uniformly and within narrow, mainly physiological limits (Fig. 2a). The laboratory blood values show a continuous, homogeneous drop in hemoglobin values in all groups, which is characteristic of an intensive care patient group (Fig. 2b). Furthermore, we observed a constant leucocytosis during the entire treatment on ICU. An increase of leukocytes during the second week on ICU in patient after surgical clipping can be observed in this group. Additionally, a simultaneous lactate increase (Fig. 2c) as well as temporarily increased glucose values are plotted in the surgically treated group presumably as an effect of the increased cortisone administration. The slight initial increase in aPTT in endovascular patients can be explained by the intraprocedural administration of heparin.

Aneurysm characteristics

Aneurysm locations were divided into aneurysms of the anterior circulation (internal carotid artery including the posterior communicating artery, middle cerebral artery, anterior cerebral artery complex including the anterior communicating artery and the pericallosal artery) and aneurysms of the posterior circulation including the basilar artery and its branches. As aneurysm locations differed significantly between the three treatment groups ($p < 0.001$) with the majority of all aneurysms located in the anterior cerebral artery complex (93; 46.3%), an additional analysis for this subgroup was performed. Therefore, all clinical and outcome parameters as shown in Tables 1, 2, 3, and 4 were evaluated separately. There was a significant difference in the use of antiplatelet therapy for the three treatment approaches, as this parameter originally differed between the treatment groups ($p = 0.001$). Besides, all remaining parameters showed no significant differences between the three treatment modalities.

Table 1 Basic clinical characteristics of the study population

Characteristic	Overall ($n = 201$)	Clip ($n = 56$)	Coiling ($n = 107$)	WEB ($n = 38$)	p value
Aneurysm location (%)					
ICA	49 (24.4)	12 (21.4)	29 (27.1)	8 (21.1)	< 0.001
ACA	93 (46.3)	13 (14.0)	58 (54.2)	22 (57.9)	< 0.001
MCA	38 (18.9)	31 (55.4)	4 (3.7)	3 (7.9)	< 0.001
Posterior circulation	21 (10.4)	0 (0.0)	16 (15.0)	5 (13.2)	< 0.001
Arterial hypertension (%)	90 (44.8)	22 (39.3)	51 (47.7)	17 (44.7)	0.593
Nicotine abuse (%)	42 (20.9)	12 (21.4)	23 (21.5)	7 (18.4)	0.917
Cardiovascular disease (%)	25 (12.4)	6 (10.7)	18 (16.8)	1 (2.6)	0.067
Neurological disease (%)	19 (9.5)	4 (7.1)	11 (10.3)	4 (10.5)	0.784
Aneurysm diameter (mm, mean ± SD, range)	6.6 ± 4.2 (1.0–26.0)	6.2 ± 3.6 (1.0–18.0)	6.8 ± 4.9 (1.3–26.0)	6.6 ± 2.9 (1.0–16.0)	0.690
Fisher–median (range)	4 (1–4)	4 (1–4)	4 (1–4)	4 (1–4)	0.769
GCS–median (range)	15 (3–15)	15 (3–15)	15 (3–15)	15 (3–15)	0.747
Hunt and Hess–median (range)	2 (1–5)	2 (1–5)	2 (1–5)	2 (1–5)	0.557
Number of Hunt and Hess IV–V	66 (32.8)	15 (26.7)	38 (35.5)	13 (34.2)	0.519
WFNS–median (range)	2 (1–5)	2 (1–5)	1 (1–5)	2 (1–5)	0.729
Graeb–median (range)	2 (0–12)	1 (0–12)	2 (0–12)	2 (0–12)	0.158
Acute hydrocephalus (%)	137 (68.2)	31 (55.4)	80 (74.8)	26 (68.4)	0.041
Age (years, mean ± SD, range)	55.6 ± 13.3 (21–90)	56.1 ± 12.0 (35–80)	54.8 ± 13.8 (21–90)	56.7 ± 13.7 (29–86)	0.701
Sex (female)	$n = 127$ (63.2%)	$n = 31$ (55.4%)	$n = 70$ (65.4%)	$n = 26$ (68.4%)	0.341

ICU mortality rates

Overall ICU mortality was 17.9% ($n = 36$) with rates of 12.5% ($n = 7$) for microsurgical clipping, 19.6% ($n = 21$) in endovascular coiled patients and 21.1% ($n = 8$) in WEB-secured aneurysms. An additional multivariate regression analysis identified only the Hunt and Hess grade ($p < 0.001$) as an independent predictor for mortality. The modality of treatment showed no significant influence in this multivariate analysis. Variables included in the regression analysis and results are displayed in Table 3.

DCI rates

A delayed cerebral ischemia was documented in 40.8% percent of the entire cohort with a range of 28.6% in clipped patients up to 47.7% in coil-embolized patients showing no statistically significant differences ($p = 0.061$). The only independent factor associated with the occurrence of DCI in an adjusted multivariate analysis was acute hydrocephalus ($p = 0.006$). MCA aneurysms in contrast were associated with a lower chance for DCI ($p = 0.023$). Again, the treatment modality had no statistically significant impact on the DCI rates (details in Table 4).

Table 2 Clinical parameters on the intensive care unit

Characteristic	Overall ($n = 201$)	Clip ($n = 56$)	Coiling ($n = 197$)	WEB ($n = 38$)	p value
VP shunt implantation (%)	22 (10.9)	7 (12.5)	11 (10.3)	4 (10.5)	0.907
DCI (%)	82 (40.8)	16 (28.6)	51 (47.7)	15 (39.5)	0.061
Ventriculitis (%)	42 (20.9)	10 (17.9)	25 (23.4)	7 (18.4)	0.654
Tracheotomy (%)	41 (20.4)	11 (19.6)	23 (21.5)	7 (18.4)	0.909
Antiplatelet medication (%)	84 (41.8)	4 (7.1)	54 (50.5)	26 (68.4)	< 0.001
Stay on ICU (d, mean ± SD, range)	18.1 ± 10.3 (1–61)	18.9 ± 10.2 (7–49)	18.2 ± 10.0 (1–49)	16.6 ± 11.5 (3–61)	0.585
Hours of ventilation (mean ± SD, range)	173 ± 239 (0–1039)	168 ± 229 (1–850)	182 ± 251 (0–1039)	151 ± 222 (0–854)	0.776
TISS (daily mean ± SD)	12.7 ± 6.53	12.2 ± 6.36	13 ± 6.68	12.7 ± 6.22	0.051
Dexamethasone dose (mg, mean ± SD, range)	37.5 ± 67.1 (0–446)	61.9 ± 63.4 (0–216)	29.8 ± 70.1 (0–446)	23.3 ± 54.7 (0–228)	0.005

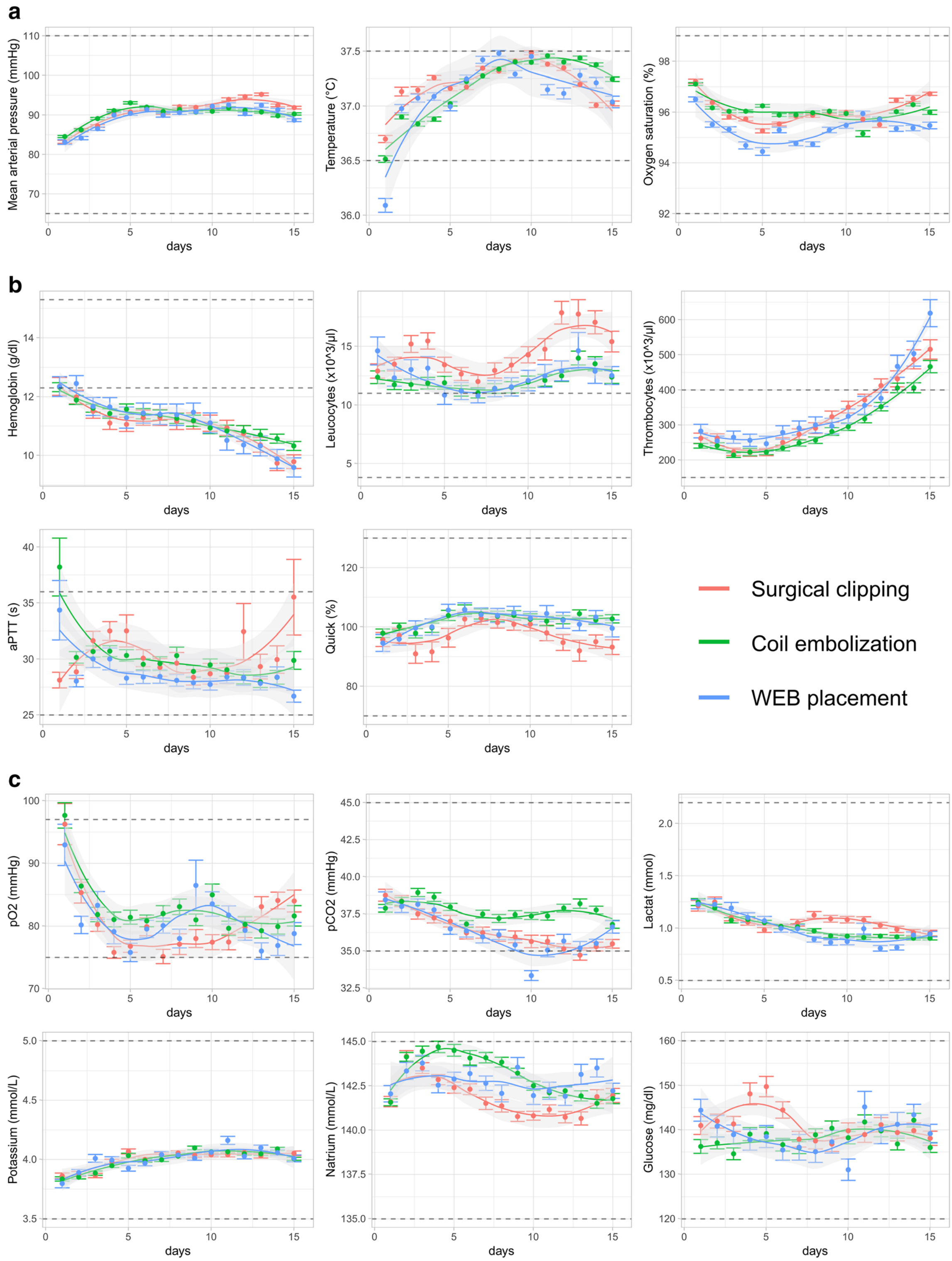

Fig. 2 Data of SAH patients after the first ICU admittance was collected for 20 days. SAH patients were further subdivided according to their aneurysm treatment. The same cohort which was described before was used; surgical clipping (red) $n = 55$ patients, endovascular coiling (green) $n = 106$, and WEB device (blue) $n = 38$. The lines represent a generalized additive model and in gray the confidence interval. **a** Depicted are mean arterial pressure (MAP), temperature measurements from bladder catheter and peripheral oxygen saturation (clip $(n) = 21{,}000$–$29{,}000$, coil $(n) = 35{,}000$–$56{,}000$, WEB $(n) = 10{,}000$–$17{,}000$). **b** To evaluate intervention relevant blood laboratory testings, we analyzed hemoglobin, thrombocytes, and leucocytes. To display potential effects on the coagulative effect of the treatment, we depicted Quick and ptt as read out (clip $(n) = 1000$–1150, coil $(n) = 1920$–1950, WEB $(n) = 590$–600). **c** To get a further impression of metabolic and respiratory changes, we decided to also take some blood gas analysis in account (clip $(n) = 5590$–5660, coil $(n) = 11{,}120$–$11{,}190$, WEB $(n) = 3470$–3540)

Table 3 Regression analysis for mortality

	Univariate model			Multivariate model		
Characteristic $N = 201$	OR	CI	*p*	OR	CI	*p*
Age	1.04	1.01–1.07	.011	1.02	0.99–1.06	.130
Male sex	1.48	0.71–3.07	.297			
Aneurysm location (%)						
ACA	ref	ref	ref			
MCA	1.06	0.37–3.00	.915			
ACI	1.63	0.68–3.94	.274			
Posterior circ.	1.76	0.56–5.59	.335			
Hunt and Hess	2.13	1.58–2.87	< .001	1.87	1.34–2.57	< .001
Acute hydrocephalus	10.23	2.38–44.08	.002	4.12	0.88–19.32	.073
Antiplatelet	0.99	0.48–2.07	.987			
Treatment modality (%)						
Clip	Ref	Ref	Ref			
Coil	1.71	0.68–4.31	.256			
WEB	1.87	0.61–5.73	.271			
DCI	2.39	1.15–4.97	.020	1.88	0.85–4.20	.121
Dexamethasone dosis	1.00	1.00–1.01	.313			

6-month outcome

Follow-up at 6 months was available for 176 patients (87.6%). One hundred patients (56.8%) had a favorable outcome and 76 patients (43.2%) did not. Favorable outcome was reached in 54.8% of WEB-embolized patients, 56.3% of microsurgical clipped patients, and 57.7% of coil-embolized patients. Neither treatment modality was associated with a higher chance for a favorable outcome nor a higher risk for an unfavorable outcome. Details are presented in Table 5.

Minimum detected effect size

Subsequently, the probability of the erroneous assumption of the null hypothesis (i.e., that there is no significant difference between the treatment modalities examined) was determined

Table 4 Regression analysis for DCI

	Univariate model			Multivariate model		
Characteristic $N = 201$	OR	CI	*p*	OR	CI	*p*
Age	0.99	0.97–1.01	.369			
Male sex	1.17	0.66–2.10	.590			
Aneurysm location (%)						
ACA	Ref	Ref	Ref	Ref	Ref	Ref
MCA	0.33	0.14–0.78	.011	0.37	0.16–0.87	.023
ACI	0.62	0.31–1.26	.185			
Posterior circ.	0.97	0.38–2.50	.949			
Hunt and Hess	1.22	0.99–1.49	.057	1.09	0.86–1.38	.499
Acute hydrocephalus	2.50	1.31–4.77	.006	2.50	1.31–4.77	.006
Antiplatelet	0.98	0.55–1.73	.938			
Treatment modality (%)						
Clip	Ref	Ref	Ref	Ref	Ref	Ref
Coil	2.28	1.14–4.55	.020	1.43	0.61–3.37	.415
WEB	1.63	0.68–3.90	.272			
Dexamethasone dosis	1.00	1.00–1.01	.554			

Table 5 Regression analysis for a favorable outcome at 6 months

Characteristic $N = 176$	Univariate model OR	CI	p	Multivariate model OR	CI	p
Age	0.95	0.92–0.97	< .001	0.94	0.91–0.97	.001
Male sex	0.75	0.40–1.39	.356			
Aneurysm location (%)						
ACA	Ref	Ref	Ref			
MCA	1.20	0.53–2.75	.664			
ACI	1.44	0.68–3.05	.343			
Posterior circ.	0.66	0.24–1.84	.424			
Hunt and Hess	0.37	0.27–0.49	< .001	0.46	0.33–0.63	< .001
Acute hydrocephalus	0.06	0.02–0.17	< .001	0.18	0.05–0.62	.007
Antiplatelet	1.01	0.55–1.85	.978			
Treatment modality (%)						
Clip	ref	ref	ref			
Coil	1.062	0.53–2.14	.865			
WEB	0.94	0.38–2.34	.902			
DCI	0.56	0.30–1.02	.059	0.56	0.24–1.29	.172
Dexamethasone dosis	1.00	0.99–1.00	.030	0.99	0.99–1.00	.003

in more detail [6]. For this purpose, a minimum effect size was calculated for the clinical characteristics for a postulated power of 0.8 and the given number of patients for the statistical tests used, above which a difference would have been detected with the specified safety. In detail, the χ^2 test showed an effect size of $w = 0.22$–0.26, the Kruskal-Wallis test an effect size of $d = 0.48$–0.61 and the ANOVA test an effect size of $f = 0.22$.

In summary, it results from these values that already medium-sized effects would have been detected with sufficient certainty and that only small, clinically presumably irrelevant effects could not have been recorded [10]. The effect sizes calculated from our data thus correspond approximately to a number needed to treat (NNT) of 4. In comparison to this, for example, the values for the use of oral nimodipine in SAH to avoid a poor outcome are in the range of a NNT of 5.20 [9]. For vital signs, laboratory parameters and blood gas values extracted from the electronic documentation system generally a high power of at least 0.9 was achieved due to the large number of values.

Discussion

In this retrospective analysis, we assessed the early clinical course using neurosurgical clipping, endovascular coiling, or WEB placement as different treatment modalities in aneurysmal SAH patients considering distinct intensive care parameters and early neurological outcome.

Up until now, most studies have been relying on the technical feasibility of WEB embolization in ruptured (and unruptured) IAs, but no study has been implemented evaluating clinical parameters after aneurysm treatment comparing the three different treatment modalities. Thus, only very few data on the early clinical course after WEB implantation in an unselected SAH cohort is available, as most recent trials have been excluding patients treated with the WEB device for no apparent reason.

Our detailed analysis of laboratory parameters and clinical characteristics on ICU (Fig. 2 and Table 2) confirms that these are predominantly in the physiological range with overall small and unsystematic differences in all treatment groups. The leukocytosis of the surgically treated patients observed during the second week is most probably due to the administration of dexamethasone in this group (see Table 2). Evaluating mortality rates according to their treatment modality (clipping, coiling, WEB embolization), we did not observe any differences between the three treatment approaches. Additionally, we found no difference at 6-month outcome between the treatment modalities. Interestingly, a higher dexamethasone dosage was associated with a higher risk for an unfavorable outcome in this cohort which is in line with our previous finding that endovascular-treated patients do not benefit from dexamethasone administration [7].

Correct and immediate diagnosis, technical aspects of treatment and postoperative care are known parameters affecting intensive care course and clinical outcome in patients suffering aneurysmal SAH [15]. As recently reported, dexamethasone treatment in SAH patients undergoing clipping might be associated with a reduced risk for an unfavorable outcome [7] but with higher leucocyte count during the ICU course. These findings matched with our analyses, showing significantly higher doses of dexamethasone in patients who underwent clipping compared to patients who underwent neuroendovascular treatment. Furthermore, the Hunt and Hess grade was detected a known independent predictor for ICU mortality after aneurysmal SAH and was the only independent predictor for hospital mortality in this analysis [2, 12, 16]. As described by Li et al. in 2013, the development of shunt-dependent hydrocephalus after aneurysmal SAH seems to be independent of treatment with coiling or clipping and is also independent for WEB embolized aneurysm. [17]. Further intracranial complications of aneurysmal SAH include the development of DCI and rebleeding [15, 30]. Besides, extracranial consequences in SAH patients including fever, anemia, blood pressure irregularities, and changes in metabolic and electrolyte levels must be taken into account at admission and during intensive care stay as these parameters influence clinical outcome directly [13]. The increase of leukocytes during the second week on ICU in patient after surgical clipping is well explained by the increased administration of dexamethasone in this group. We also interpret the simultaneous lactate increase as an effect of the increased cortisone administration as well as the temporarily increased glucose values in the surgically treated group. But again, no relevant differences were observed between the treatment modalities. All in all, a surprisingly similar course of values can be observed in relation to the treatment modality in this seriously affected patient group on ICU. The differences to be detected are within physiological limits and arise from the extremely high power of the analysis, which is based on tens of thousands of individual values. This data are supported by the TISS which showed no clinically or statistically significant differences between the treatment modalities as described before between endovascular and surgical treatment in aSAH patients [22].

If both clipping and endovascular treatment can be considered as treatment options in aneurysmal occlusion, the ongoing debate on advantages and disadvantages for either method becomes an issue. In this study, no significant differences in mortality rates between the treatment groups were detected. This finding is supported by a recently published work from the Swiss SOS database analyzing 1.866 patients, showing no statistically significant difference of in-hospital death after aSAH between clipped and coiled patients [34].

Apart from aneurysm location, aneurysm configuration is another essential factor to consider, and especially, the treatment of wide-neck IAs is often challenging [33]. The WEB device has been shown to provide satisfying aneurysm occlusion rates with adequate aneurysm occlusion of 79.3% after 1 year in the French Observatory [25] and 85.4% at mid-term follow-up (6 months) in the WEBCAST study [28]. Results of major WEB studies (WEBCAST, WEBCAST 2 and the French Observatory) did not consider the distinction between incidental and ruptured IAs as the included number of aneurysmal SAH patients was rather small (three patients in WEBCAST and four patients in WEBCAST 2, respectively) [23, 25, 28]. As those studies were performed during the initial experience of WEB treatment, they lack a satisfying amount of aneurysmal SAH patients and reliable data on neurological outcome after intensive care treatment [28]. In a multicenter retrospective study conducted by Liebig et al. in 2015, WEB embolization has been proven to be a suitable and safe treatment option in acutely ruptured IAs [18]. Emphasis must be placed on the high rate of patients with a Hunt and Hess grade 4–5 in terms of a slightly higher mortality in our cohort (17.9%) compared with other studies [18]. Recently, a retrospective observational study evaluated neurological outcome in 33 Finnish patients (only 21% high-grade SAH patients, Hunt and Hess IV and V vs. 34.2% high-grade SAH in this study) after WEB treatment of ruptured intracranial aneurysms with a mortality rate of 18.2% (6/33) [31]. Nevertheless, these studies did not evaluate intensive care parameters nor did they compare their treatment approach to available alternatives such as coiling and clipping [4, 18, 31]. Clinical assessment of WEB device in ruptured aneurysms (CLARYS, NCT02687607) is an ongoing non-randomized, prospective registry measuring rebleeding rates and aneurysm occlusion after 1 year [4].

One of the major limitations of our study is the retrospective character and the short time range of data acquisition. We acknowledge that additional long-term follow-up data might be more conclusive to support our findings. However, we aimed to analyze the early clinical course, while long-term outcome, aneurysm occlusion rates, and retreatment rates should be analyzed in further studies. In addition, it can be argued that the displayed sensitivity is not sufficient for the detection of inferiority. Our statistical evaluation, however, allows us to prove that the power of our analysis is sufficient to detect effects in clinically relevant orders of magnitude. In order to detect possible smaller effects, larger case numbers of SAH patients who have been treated with a WEB device have to be analyzed.

Conclusion

Intensive care course, laboratory parameters, DCI-rate, ICU-mortality, and 6-month outcomes did not show relevant differences between aneurysmal SAH patients treated with neurosurgical clipping, endovascular coil embolization, or WEB treatment. As WEB placement therefore seems to be a safe and feasible treatment option in acutely ruptured IAs, it cannot be justified to exclude these patients from upcoming clinical SAH trials. Nevertheless, imminent mortality, clinical long-term outcome, and aneurysm occlusion rates as well as retreatment rates in aneurysmal SAH patients treated with the WEB device have to be analyzed in further studies.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study, formal consent is not required.

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