Stent-assisted treatment of ruptured intracranial aneurysms in the acute phase: A single center experience

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ABSTRACT

Introduction: The purpose of this study was to analyze the results of patients with ruptured aneurysms who were treated with a specific microstent in the acute phase of subarachnoid hemorrhage.
Methods: Data from patients with acutely-ruptured intracranial aneurysm treated with the Neuroform stent in the period between 2003 and 2016 were retrospectively assessed, addressing aneurysm occlusion and clinical outcome with a focus on periprocedural complications.
Results: Twenty-nine consecutive patients with ruptured intracranial aneurysms were included in the analysis. Periprocedural hemorrhagic complications were stated in six patients, leading to death in four. Thromboembolic complications were observed in seven patients, among whom only one affected the clinical outcome with death due to basilar thrombosis. Immediate complete occlusion and occlusion with residual neck was achieved in 79.3% of cases.
Conclusion: Stent-assisted coiling of acutely-ruptured aneurysms achieves good immediate aneurysm occlusion. Rates of intra- and periprocedural adverse events observed in this series were significant, but did not translate to corresponding morbidity and mortality in all cases. The retrospective analysis did not allow assessing the overall risks of endovascular therapy with stent use in ruptured and complex aneurysm when compared to the overall risks with other alternative options.

1. Introduction

Stent-assisted coiling has become an established treatment option for intracranial aneurysms, enabling endovascular treatment (EVT) for complex ruptured aneurysms with good occlusion rates [1–3]. However, dual antiplatelet therapy is required to avoid thromboembolic complications. Previous studies have shown that dual antiplatelet therapy is associated with an increased risk of hemorrhagic complications, which might be further aggravated in the setting of subarachnoid hemorrhage (SAH) with an abnormal coagulation status [4]. The purpose of this study was to retrospectively analyze the consecutive series of patients who underwent attempted stent-assisted coil embolization with a Neuroform stent (Neuroform, Stryker Neurovascular, Kalamazoo, MI, USA) between January 2003 and January 2016 at the Institute of Diagnostic and Interventional Radiology and Neuroradiology at the University Hospital of the University Duisburg - Essen to evaluate this treatment strategy for acutely-ruptured aneurysms.

2. Materials and methods

2.1. Patient selection

Data for patients who underwent attempted stent-assisted treatment of acutely-ruptured intracranial wide-neck and fusiform aneurysms with a Neuroform I, II or III microstent between January 2003 and January 2016 was retrieved from the institutional aneurysm databank.

An acutely-ruptured intracranial aneurysm was defined as an aneurysm treated no > 30 days after the initial rupture. A vascular neurosurgeon and a neuroendovascular specialist jointly made the decision concerning whether EVT or surgical clipping of the ruptured aneurysm was the appropriate treatment option on a patient-by-patient basis [5]. Whenever a high-surgical risk (esp. in posterior circulation aneurysms or with patients in the vasospastic period between day 4 and 14) existed or aneurysm occlusion by coiling alone was considered too risky, the decision was made to perform EVT with stent-assisted coil embolization. Stent deployment was also performed as bailout procedure where coil protrusion into the parent artery would have posed a risk of vessel occlusion. Demographic data, aneurysm occlusion grades, clinical outcome, procedural and periprocedural complications were retrospectively analyzed by an independent reviewer (MH). Approval for data collection and the retrospective analysis of all interventional procedures and follow-up reported in this study was given by the ethical board of the University Duisburg - Essen, Germany (reference no: Z-14-57744-BO).

2.2. Endovascular procedures

If necessary, external ventricular drainage (EVD) was usually placed prior to the procedure. EVT was performed via a femoral approach and under general anesthesia. A triaxial approach was applied using a long femoral introducer, a guiding catheter and a microcatheter under the guidance of roadmaps. Using a coil-through technique, coils were deployed over a microcatheter, which was positioned through the stent interstice into the aneurysm sac after releasing the stent from the stent delivery system across the neck of the ruptured aneurysm. Alternatively, coils were deployed using the jailing technique, releasing the stent after positioning the microcatheter within the sac of the aneurysm.

2.3. Anticoagulation/antiplatelet regimen

In all patients, shortly before or during the procedure, a combination of an intravenous bolus of aspirin (500 mg) followed by clopidogrel (300 mg) through the gastric tube was administered. The clopidogrel treatment (75 mg) was continued for 6–12 weeks. Aspirin (100 mg/day) was continued indefinitely. Due to the emergency situation, responsiveness to antiplatelet therapy was not tested. During the procedure, patients received a bolus dose of heparin 2–3 times above the baseline for anticoagulation to maintain an activated clotting time (ACT) or alternatively a body-weight adjusted bolus without ACT control.

2.4. Follow-up protocol

As a baseline examination for the non-invasive evaluation of aneurysm occlusion, possible parent vessel stenosis and possible procedural adverse events, a brain magnetic resonance (MR) study was performed within 48 h after the procedure. The magnetic resonance imaging (MRI) protocol included a time of flight (TOF) MR angiography and diffusion-weighted sequences (DWI). If a MRI could not be performed due to contraindication for MRI or critical clinical status, a cranial computed tomography (cCT) scan was carried out. The standardized follow-up examination protocol comprised a digital subtraction angiography (DSA) and brain MR study scheduled at six months after treatment, followed by controls one year later and further controls every 2–3 years, depending on the individual findings. If recurrence or progression was suspected on MRI, DSA with possible retreatment was offered.

2.5. Data collection and data analysis

Patient data was collected including age, gender, severity of SAH

using Hunt and Hess (H&H) grade, type of aneurysm (fusiform/dissecting, blister-like or saccular), location of aneurysm, size of aneurysm dome and neck, as well as post-interventional information including clinical outcome using the Glasgow outcome score (GOS), degree of aneurysm occlusion, periprocedural thromboembolic and hemorrhagic complications.

The initial degree of occlusion was graded using the Raymond-Roy classification as 1—complete, 2—residual neck and 3—residual aneurysm [6]. At follow-up, recurrence was stated if an aneurysm that was previously completely occluded showed a partial recurrence of the neck and/or the sac.

Procedural thromboembolic events were defined as complications in cases of visible thrombus formation and/or parenchymal ischemia not related to vasospasm. The detected ischemic complications were considered minor if their size did not exceed 10 mm on DWI sequences in non-eloquent areas. Lesions larger than 10 mm – as well as smaller infarcts located in the brainstem or basal ganglia – were considered major infarcts. Only major infarcts were recorded as stent procedure-related thromboembolic complications since minor DWI lesions are noted after catheterization itself in up to 26% of cases [7].

Hemorrhagic events were categorized into intraprocedural complications due to aneurysm re-rupture, as well as into periprocedural complications as aneurysm re-rupture, intraparenchymal hemorrhage (not ventricular drain-related) and intraparenchymal hemorrhage (ventricular drain-related) as observed during follow-up examinations.

3. Results

3.1. Patient and aneurysm characteristics

A total of 29 patients (18 females, 11 males, mean age 52, range 31–83 years) underwent attempted stent-assisted coiling for ruptured intracranial aneurysm. One patient had two aneurysms mirroring at the proximal basilar stem in which one was responsible for the hemorrhage, whereby both were treated at the same time.

Eleven (37.9%) patients were admitted in a clinically poor grade condition (H&H of IV or V), while six (20.7%) patients presented in moderate clinical condition (HH III) and twelve (41.4%) in a good status (HH I or II). Nine (31%) patients harbored more than one aneurysm, although the site of ruptured aneurysms could be identified. The majority had broad-based (72.4%) saccular aneurysms and six fusiform/dissecting aneurysms as well as two blister-like aneurysm were identified. The mean diameter of the dome of the saccular aneurysms was 7.5 ± 6.3 mm, with a mean neck width of 4.7 ± 3.3 mm. The size of fusiform/dissecting aneurysms was 5.7 ± 1.8 mm, with an average width of 5.2 ± 1.5 mm. Twenty-five (86.2%) aneurysms were localized in the posterior circulation and four (13.8%) aneurysms were situated in the anterior circulation (Table 1).

3.2. Embolization results

In 27 (93.1%) cases, the stent was deployed in the desired position, while in 25 (86.2%) of these cases additional coiling was performed. In one patient the stent was not deployed in the desired position. In another patient, stent placement was not possible due to extreme vessel

Table 1
Location of aneurysms.

Vessel	Abs.	%
ICA	3	10.3
AomA	1	3.4
PcomA	1	3.4
BA tip	11	37.8
BA trunk	5	17.2
VA	8	27.6

Table 2
Technical considerations and aniogr. Results after EVT.

	Abs.	%
Patients treated with stent and coils	25	86.2
Patients treated with stent only	3	10.3
Patients requiring subsequent surgical intervention	1	3.4
Raymond class I occlusion	16	55.2
Raymond class II occlusion	7	24.1
Raymond class III occlusion	4	13.8
No occlusion	2	6.9

elongation, whereby this patient underwent clipping for a para-ophthalmic aneurysm.

Initially sixteen (55.2%) aneurysms were completely occluded (Raymond class I), seven (24.1%) aneurysms showed near complete occlusion (Raymond class II) and four aneurysms (13.8%) had a residual neck (Raymond class III), see Table 2 (Fig. 1a, b).

3.3. Complications

Procedural/periprocedural thromboembolic events were observed during EVT in seven patients (24.1%). Two acute complete and irreversible stent occlusions were observed. Among them, one basilar artery occlusion due to in-stent thrombosis led to death. In one patient with a small blister-like aneurysm, postprocedural ICA occlusion occurred due to in-stent thrombosis, although it remained clinically asymptomatic. This patient was only treated with a stent since after stent deployment thrombosis of the aneurysm started and coiling was not feasible (Fig. 2a–e). Additionally, one incomplete and asymptomatic in-stent stenosis was observed.

In one patient, bilateral cerebellar infarctions in the AICA and PICA territories were revealed by MRI four days after EVT. The concerned vascular supplies were jailed by the stent, although there was no observation of impair arterial supply during the procedure nor on behalf of the follow-up DSA. Clinically, these events remained silent. In all other patients with thromboembolic complications, either recanalization or sufficient collateralization of the occluded vessel was angiographically documented and no infarction was seen (Fig. 3a–d). MRI revealed minor DWI lesions in twelve patients (41.4%) where no thromboembolic arterial occlusions were identified during EVT, all of which were without clinical impairment.

Hemorrhagic events were seen in six patients (20.7%). In two patients, intraprocedural aneurysm perforation occurred, both with very small aneurysms (3 resp. 4 mm). Both patients also had thromboembolic complications and thus are listed above: one patient recovered completely, while the other patient had GOS3. In two patients with a blister-like aneurysm resp. a dissecting aneurysm, postprocedural aneurysm re-rupture occurred and both patients died. One patient experienced fatal massive spontaneous parenchymal hemorrhage (not ventricular drain-related) the day after successful treatment and one patient had fatal parenchymal hemorrhage due to ventricular drain, which was inserted after the treatment (Table 3).

3.4. Clinical outcome

At discharge, eleven patients (37.9%) were in good clinical condition (GOS 4 and GOS 5), eight patients (27.6%) were in moderate clinical condition (GOS 2 and GOS 3) and ten patients (34.5%) died within the first 30 days. The causes of death are detailed in Table 4. Most patients who died had been admitted in poor grade condition. Two patients with good initial clinical status at admission died: one due to postprocedural parenchymal hemorrhage and one due to aneurysm re-rupture of a blister-like aneurysm. Conversely, four patients could be discharged in good clinical condition despite their initial poor grade condition. At clinical follow-up over an average of 42 months, no relevant change of outcome compared to discharge was observed.

4. Discussion

Aneurysms where the use of stent assistance is deemed necessary are usually more complex in morphology than coil-alone aneurysms. With this technique, overall aneurysmal occlusion in the acute phase in our series was satisfactory. Only one failure to deploy the microstent and consequent failure in securing the aneurysm was observed.

The presented sub-group of patients with SAH treated with a microstent in the acute phase demonstrates that although the procedural complication rate is remarkably high – indeed higher than in non-ruptured stent-assisted coiling – the resulting morbidity and mortality rates are much lower than could have been expected. This is mainly due to proper complication management. The complication rates found in this study are in line with those reported in similar studies [8–12].

There are several reasons or conditions that may possibly explain the high rate of hemorrhagic as well as thromboembolic complications observed.
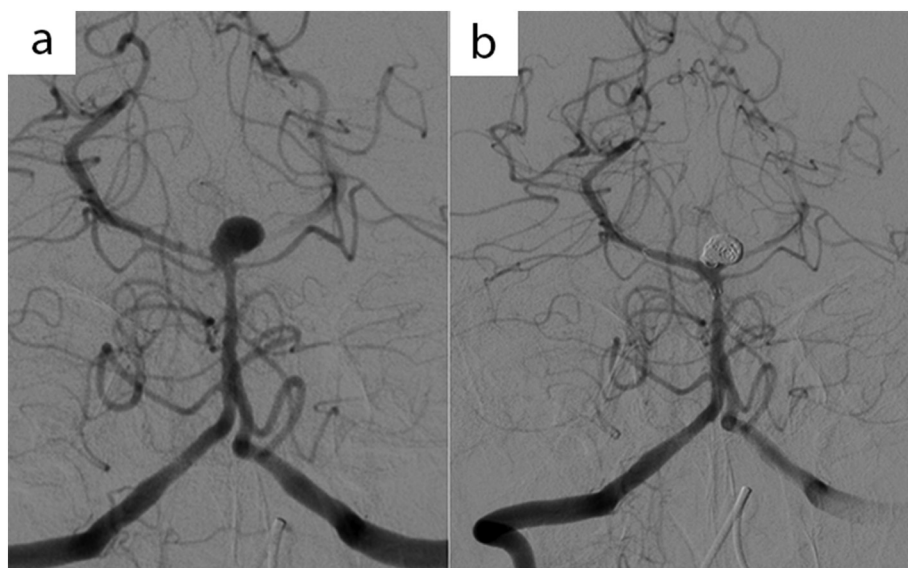

Fig. 1. a, b Ruptured basilar tip aneurysm (a), stent assisted coiling was performed in the acute phase with obvious vasospasm (b). Stent was placed from the right ACP into the basilar artery and complete aneurysm occlusion (Raymond class I) was achieved (b).
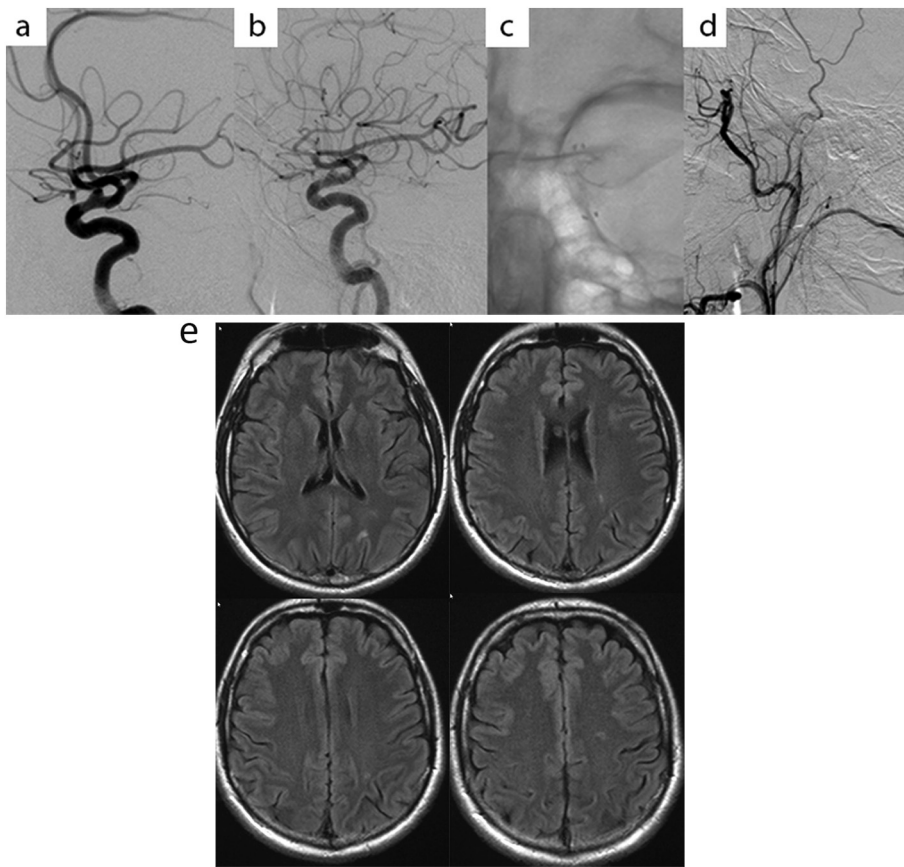
Fig. 2. a–d Blister-like aneurysm of the ICA, after stent placement reduction in aneurysm size did occur and coiling was not feasible (a–c). Control angiogram one week later showed complete occlusion of the ICA, which was asymptomatic (d). e MRI 7 years after EVT: no larger ischemic lesion is visible, the patient is in good clinical condition and got back to work.

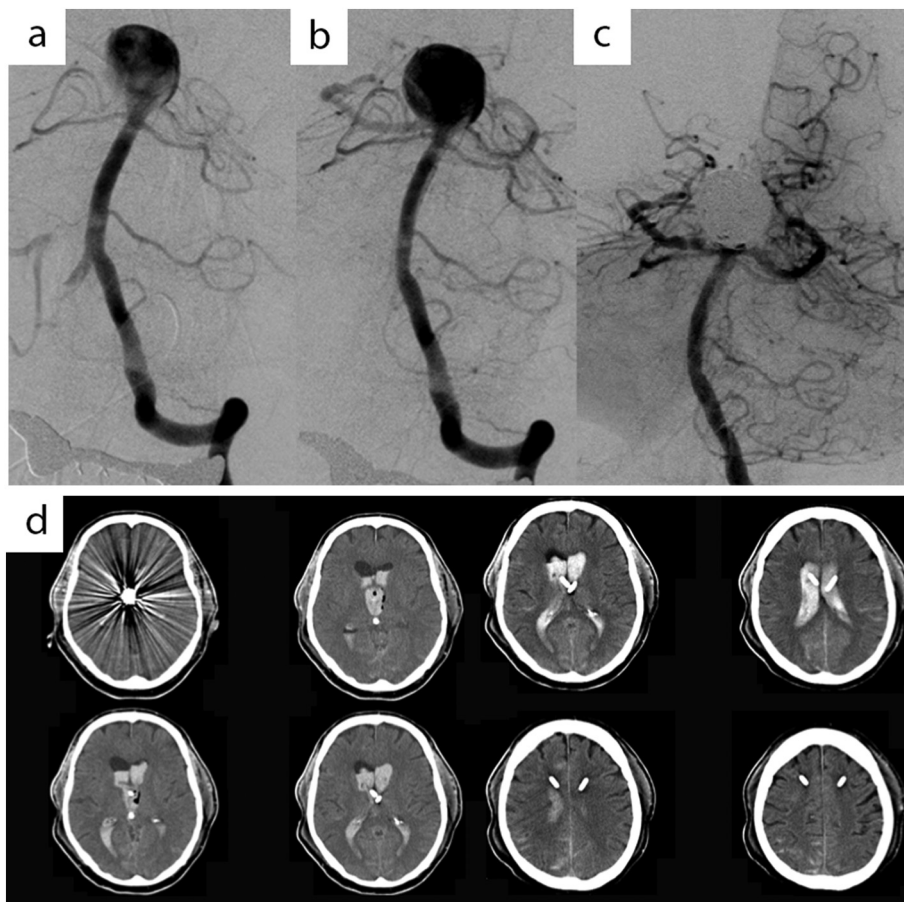**Fig. 3.** a–c Large and broad based, ruptured aneurysm of the basilar tip before (a) and after (b) stent assisted coiling. The stent was placed from the left posterior cerebral to the basilar artery. Control angiogram after the procedure showed flow reduction in the right posterior cerebral artery due to thrombus formation. Abciximab was administered (c). d CT one day after treatment did not show any infarction.

Table 3
Hemorrhagic complications.

Type of complication	Abs.	%
Intraprocedural aneurysm rerupture	2	6.9
Postprocedural rerupture	2	6.9
Postprocedural intraparenchymal hemorrhage (not ventricular drain-related)	1	3.4
Postprocedural intraparenchymal hemorrhage (ventricular drain-related)	1	3.4

Table 4
Mortality.

Cause of death	Abs.	%
Death due to intraprocedural thromboembolic complication of EVT	1	3.4
Death due to postprocedural hemorrhagic complications (< 30 days)	3	10.3
Death due to SAH related complications	6	20.7

5. Hemorrhagic complications

Perforation of the aneurysm during treatment might be promoted by the complexity in navigating through the stent mesh into a small aneurysm. In both patients with intraprocedural aneurysm perforations, the event happened even before stenting, presumably due to the very small aneurysm size. Therefore, we recommend using a compliant microballon assistance before starting coiling to manage this potential complication in a proper way, especially when treating very small aneurysms. Furthermore, spontaneous intracranial hemorrhages not related to the ventricular drainage – as stated in one of this study's patients – have previously been observed [8,13]. This patient in our series suffered from chronic alcohol abuse, which may have been one factor in promoting the spontaneous hemorrhage due to failing coagulation homeostasis in the presence of liver dysfunction and aggravating the dimension of the fatal bleeding. Ventricular drain-related hemorrhagic complications – which were noted in one patient – are normally avoided by preprocedural placement of an EVD. Nonetheless, the replacement or removal of the ventricular drain under dual platelet therapy poses the risk of intraparenchymal bleeding [8].

We observed two patients with a postprocedural aneurysm re-rupture, whereby both patients were successfully treated with sufficient aneurysm occlusion. One lethal re-rupture occurred 30 min after finishing treatment in a patient with a presumably dissecting basilar artery aneurysm. In one lethal case, postprocedural re-rupture occurred 10 days after discharge from hospital in a good clinical condition (GOS 5) after a technically successful occlusion of the ruptured aneurysm (Raymond class I). This patient was diagnosed with a blister-like ICA aneurysm.

Both etiologies of aneurysms are very particular and do not reflect the typical broad-based aneurysms: especially blister-like aneurysms are malignant in nature and nowadays the implantation of a flow diverter would obviously be the more appropriate solution [14,15]. There exists only one case report with a delayed and rapid re-growth of a ruptured blister aneurysm treated by flow diverter [16].

6. Thromboembolic complications

The deployment of a microstent in the intracranial circulation necessitates antiplatelet therapy to reduce the risk of thromboembolic complications. In the setting of acute SAH, the tendency for clotting is aggravated as the bleeding triggers a coagulation cascade. It is known that both coagulative and fibrinolytic activities are altered after the onset of SAH, posing a challenge to the homeostasis of coagulation [17].

Appropriate preprocedural preparation of a patient with antiplatelet therapy in an emergency setting is difficult, in most cases being impossible and potentially insufficient. Therefore, a significant concern remains about the proper medication regimen and its timing. Aspirin is available for i.v. injection and is effective immediately. Clopidogrel must be administered per os (e.g. gastric tube), although the resorption status in an acutely severely diseased patient is unclear, thus rendering dose control difficult. Clopidogrel resistance may be caused by insufficient drug absorption or impaired metabolic activation of the drug, which might be influenced by the dose and other co-medication [18]. In patients with unruptured aneurysms, we nowadays perform testing of response to platelet inhibition, which reduces the rate of thromboembolic complications by either adapting to an appropriate dose or switching to another drug (e.g. prasugrel). If a stent thrombosis occurs during treatment in the acute phase of a ruptured aneurysm, one has to weigh the risk of aggressive medical recanalization against the risk of re-rupture of the aneurysm leading to a devastating problem.

In the literature, there is no consensus between different studies on the timing of antiplatelet administration. In our center, a loading dose of aspirin and clopidogrel was administered shortly before or intraprocedurally. Most other centers give an initial dose of dual antiplatelet medication either pre- or postprocedurally [19]. Intraprocedural hemorrhage was higher for preprocedural antiplatelet administration than for postprocedural antiplatelet administration, whereas postprocedural hemorrhage is more likely to occur in the postprocedural initiation of antiplatelet therapy [19].

7. Aneurysm occlusion grade

While generally achieving comparably good occlusion results with the technique [1–3] – as also supported by the results of our study with 82.8% Raymond class I and II occlusions – the nature of the aneurysm plays an important role in determining immediate stability, as demonstrated in two of our series with a dissecting or blister aneurysm. Dissecting aneurysms are not rare and due to the likelihood of a long segmental injury the concept of treatment with parent vessel occlusion should always be considered. In our patient with an early re-rupture, the aneurysm was located at the basilar artery; therefore, vessel occlusion would not have been an alternative. Blister aneurysms are rare and have a dangerous natural course if untreated or treated by neurosurgical means.

8. Alternative strategies

During the period of observation, on average 68 patients per annum with ruptured aneurysms were treated at our hospital, whereby stent-assisted coiling was only performed in about 3% of all cases. The relatively small number of aneurysms included in this series demonstrates that this treatment concept was only applied in patients from whom alternative strategies would not be considered safe and sufficient. Balloon-assisted coiling as well as other successful methods were either not yet available or considered too risky and insufficient in terms of aneurysm occlusion.

9. Conclusion

Stent-assisted coiling of acutely-ruptured aneurysms achieves good immediate aneurysm occlusion. The rates of intra- and periprocedural adverse events observed in this series were significant, although they did not translate into corresponding morbidity and mortality in all cases. The retrospective analysis did not allow assessing the overall risks of endovascular therapy with stent use in ruptured and complex aneurysm when compared to the overall risks with other alternative options.

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in the 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.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ensci.2018.01.001.

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