



Original Article

Periprocedural management of ruptured blister aneurysms treated with pipeline flow diversion

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ABSTRACT

Background: Blister aneurysms are high-risk intracranial vascular lesions. Definitive treatment of these lesions has been challenging. Severe disability or mortality rates are as high as 55% when these lesions are treated with open surgery. Recent data show that flow diversion is a safe and effective alternative treatment for blister aneurysms. Rupture of the functionally unsecured lesion remains a concern as flow diversion does not immediately exclude the aneurysm from the circulation.

Methods: A retrospective review was performed of any patients with ruptured blister aneurysms treated with a pipeline embolization device between 2010 and 2020 at the University of Colorado.

Results: In this paper, we present the results of the intensive care management of ruptured intracranial blister aneurysms after flow-diverting stent placement.

Conclusion: Despite the need for dual antiplatelet therapy and the delayed occlusion of blister aneurysms treated with flow diversion, we did not find an increase in periprocedural complications.

Keywords: Blister aneurysm, Flow diversion, Pipeline

INTRODUCTION

Blister aneurysms are classically defined as half-dome-shaped lesions of the supraclinoid internal carotid artery (ICA).^[1,19] Traditional treatment of these lesions with open microsurgery is dangerous, with intraoperative rupture rates as high as 57%.^[1,18,22,27] The option of clip-wrapping these lesions presented a safer treatment option but did not show any decrease in aneurysm growth on follow-up and resulted in severe disability or death rates as high as 55%.^[1,15,18] Thromboembolism occurs in up to one-third of cases treated with traditional endovascular stents and coils.^[23,29] Overall, endovascular treatment produces a higher percentage of favorable outcomes with modified Rankin scale (mRS) 0–2 when compared to microsurgical intervention due to lower perioperative morbidity and mortality.^[17,22,24] The main disadvantage of endovascular treatment is a lower immediate occlusion rate.^[23,28] Most lesions will require more than one stent

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to potentiate aneurysm occlusion and often require extended time to achieve occlusion, as long as 13.6 months.^[5,24]

Recent studies provide evidence for flow-diverting stent placement as a promising option for blister aneurysms that are not safe for immediate obliteration through microsurgery or coil embolization.^[6,13,22,24] Although the initial occlusion rate with flow diversion is lower than stent-assisted coil embolization, early studies show an increased long-term rate of occlusion with a similar periprocedural risk profile with the additional benefit of maintaining the patency of the carotid artery.^[3,15,24] There are no randomized controlled trials for this rare subset of aneurysms, but early data continue to support the efficacy and safety of flow diversion for the definitive treatment of these lesions.

The hospital management of patients with aneurysmal subarachnoid hemorrhage (aSAH) is complicated by placing a flow-diverting stent. Patients often require external ventricular drain (EVD) placement and other invasive procedures after aSAH. Patients on dual antiplatelet therapy (DAPT) are at higher risk of hemorrhagic complications during these procedures.^[9,10,25] In addition, delayed cerebral ischemia (DCI) due to vasospasm is a common sequela of subarachnoid hemorrhage (SAH).^[7,30] An essential treatment for preventing injury due to DCI includes hypertensive therapy.^[2,4] However, hypertension (HTN) leads to a higher risk of bleeding in unsecured aneurysms,^[11,12,21] which may apply to incompletely-occluded lesions after treatment with flow diversion.^[20] Our data show that delayed obliteration seen in flow diversion does not increase risk in the periprocedural setting. This manuscript aims to show the safety of DAPT and hypertensive therapy following flow diversion for ruptured ICA blister aneurysms.

MATERIALS AND METHODS

Patient data

We conducted an IRB-approved retrospective review of patients who presented to the University of Colorado Hospital (UCH) between 2010 and 2020. This review included all patients with SAH from a ruptured blister aneurysm treated with a pipeline embolization device (PED; Medtronic, Minneapolis, Minnesota). All PEDs used were the flex model except one case of retreatment with a Pipeline Classic Embolization Device (Medtronic, Minneapolis, Minnesota). We defined ruptured blister aneurysms as sessile aneurysms arising from non-branching points of the supraclinoid ICA with SAH. Aneurysm data collected through chart review included initial patient demographics, Hunt and Hess (HH) grade, aneurysm characteristics, and aneurysm treatment. Chart review also included intensive care unit (ICU) course and medications, subsequent procedures, complications, mRS at discharge, and follow-up imaging.

RESULTS

Demographics and aneurysm characteristics

Forty-three patients presented to UCH with possible blister aneurysms based on any imaging modality. We excluded patients if there was no treatment at UCH if digital subtraction angiography (DSA) failed to identify a blister aneurysm, or if there was no rupture event. Seventeen patients had a confirmed ruptured supra clinoid ICA blister aneurysm treated at our hospital. Of these, microsurgery was performed in two: one patient had balloon-assisted coiling, one patient had multiple stents placed, and stent-assisted coiling was performed in one patient. Twelve patients (eight females and four males) were treated with a PED and included in this series.

The average age at presentation for patients treated with PED was 49.8 years old (range 28–74), with an average HH score of 2.9 [Table 1]. There were five patients with low HH scores (1–2) and seven with high HH scores at presentation (3–5). The average modified Fischer Grade at presentation was 3.4 (range 2–4). Two patients had multiple aneurysms at presentation. There were seven right ICA and five left ICA aneurysms. One patient had a family history of a brain aneurysm. Five patients had a history of tobacco smoking. Four patients had a history of HTN.

Aneurysm treatment

Microsurgery

Two patients had blister aneurysms treated with open surgery. One underwent a clip wrap of a right ICA blister aneurysm. The second patient underwent clip-trapping of a left ICA blister aneurysm. Both patients suffered large territory strokes and developed malignant intracranial HTN requiring decompressive craniectomy. Discharge modified Rankin score (mRS) was 5 in both patients.

Traditional endovascular therapy

Three patients had ruptured blister aneurysms treated with stents and/or coils. One patient had balloon-assisted coiling

Table 1: Overall ruptured internal carotid artery blister aneurysm demographics ($n=12$).

Males/females	8 (66.7%)/4 (33.3%)
Mean age in years (Range)	49.8 (28–74)
Mean HH grade (Range)	2.9 (1–5)
Mean Fischer grade (Range)	3.4 (2–4)
Positive smoking history	5 (41.7%)
Positive family history of aneurysm	1 (8.3%)
Pre-existing diagnosis of HTN	4 (33.3%)
Multiple aneurysms	2 (16.7%)
mRS at discharge	2.92 (1–6)

mRS: Modified Rankin scale, HH: Hunt and Hess, HTN: Hypertension

with intraprocedural left M3 thrombus, leading to stroke and edema requiring decompressive hemicraniectomy. This patient also had an aneurysm recurrence, which was re-treated with pipeline coiling. Per the patient's goal of care to be independent, the patient's family decided to withdraw care after a lack of improvement in their exam. One patient had two Enterprise stents (Codman, Raynham, Massachusetts) placed initially. On follow-up, DSA growth of the blister aneurysm was noted. Retreatment with coiling led to intraprocedural aneurysmal rupture followed by successful occlusion of the aneurysm. This patient was discharged with mRS of 3. Stent-assisted coiling was performed in one patient who had growth of the aneurysm requiring further treatment with coils. This patient was discharged with mRS of 4. The two surviving patients did not have any residual aneurysmal filling.

PED therapy

Twelve patients had blister aneurysms treated with PED placement. All 12 patients had successful initial PED placement. Two of these patients had two PEDs placed during the initial treatment. The remaining ten patients had a single PED placed at initial treatment. One patient required retreatment after the initial pipeline placement. There were no intraprocedural deaths or intraprocedural hemorrhagic events.

There were two deaths following treatment with PED (mortality rate: 16.7%) [Table 2]. One patient had delayed catastrophic intraparenchymal hemorrhage (IPH) with presumed cortical venous thrombosis. The other patient had a concurrent left middle cerebral artery (MCA) thrombus seen at the time of aneurysm treatment. The operator performed a successful thrombectomy during the procedure. However, the patient had a complete left MCA stroke. In both cases, the patient's family elected for comfort care secondary to a poor neurologic prognosis.

One patient was re-treated after the initial PED Flex placement. The operator attempted to use Pipeline Classic for the second treatment. This treatment followed DSA on

postprocedure day 4, which documented continued growth of the aneurysm. At the time of the second treatment, there was limited availability of a compatible microcatheter system for the Pipeline Flex. During this procedure, the Pipeline Classic stent failed to open. This event led to the fracture of the stent support wire and retention of the unexpanded embolization device in the MCA and subsequent right MCA infarction. Follow-up DSA showed no residual aneurysm filling. The patient experienced left-sided neglect but no other clinical symptoms.

One patient had intraluminal non-occlusive stent thrombosis on follow-up angiography. This thrombosis was treated with heparin therapy, which led to the resolution of the thrombus. There was no clinical or imaging evidence of infarct throughout this patient's hospital course.

One patient had increased technical complexity of PED placement as the PED did not fully deploy and required contralateral femoral puncture and retrograde access from the contralateral ICA to achieve patency. No thrombosis or infarcts occurred from this procedure. This patient had a pre-existing dissection of the bilateral cervical ICA, intraprocedural dissection of the ipsilateral cervical ICA, and pseudoaneurysm of the contralateral cervical ICA, neither of which required further procedural intervention.

No patients treated with flow diversion in this series suffered a re-rupture of the aneurysm.

Radiographic and clinical outcomes

After the initial treatment, all 12 aneurysms were rated a three on the Raymond–Roy Occlusion scale (Class 1: Complete obliteration, Class 2: Residual neck filling, Class 3: Residual aneurysm filling)^[14] [Table 3]. All surviving patients except for two have had follow-up imaging at our institution. One patient lost insurance coverage and has not returned for follow-up. The other was discharged with severe disability and has not returned for follow-up.

Follow-up imaging consists of a DSA except in one patient, followed by magnetic resonance angiography (MRA) due to difficult access and a history of cervical carotid

Table 2: Periprocedural intensive care complication rates in ruptured internal carotid blister aneurysms treated with the pipeline device ($n=12$ except where noted).

Delayed intraparenchymal hemorrhage	1 (8.3%)
Rerupture	0 (0%)
Periprocedural intraluminal thrombus formation	1 (8.3%)
Periprocedural dissection	1 (8.3%)
EVD-associated hemorrhage ($n=9$)	3 (33.3%)
Device malfunction	1 (8.3%)
Mortality	2 (16.7%)

EVD: External ventricular drain

Table 3: Aneurysm characteristics and treatment results in surviving patients with at least three months of follow-up imaging ($n=9$).

Initial RR grade 3	12 (100%)
Initial RR grade 2	0 (0%)
Initial RR grade 1	0 (0%)
Best RR grade 3	0 (0%)
Best RR grade 2	1 (11.1%)
Best RR grade 1	8 (88.9%)
Overall retreatment rate	1 (8.3%)

RR: Raymond–Roy occlusion grade

pseudoaneurysm. Raymond–Roy Occlusion rates of surviving patients with at least three months of follow-up imaging are as follows: eight patients were rated grade 1, and one patient was rated grade 2. No patients remained in grade 3. The occlusion rate was 88.9%. The follow-up period averaged 11.6 months (range: 3–20). One patient required retreatment with another PED for a retreatment rate of 8.3%.

We collected mRS outcomes at the time of discharge from the hospital. Five patients had an mRS of one. Three patients had an mRS of three. One patient had an mRS of four. One patient had an mRS of five. Two patients died. The five patients who presented with a low HH score had an average mRS of 1.4. Patients who presented with a high HH score had an average mRS of 4.

Critical care results

All patients were monitored in the ICU for at least 21 days following hemorrhage. All 12 patients treated with PED had a goal systolic blood pressure (SBP) of 140 mmHg or less until PED placement. One patient transitioned to comfort care due to a concurrent left MCA stroke. Ten of the 11 surviving patients had radiographic evidence of vasospasm. Computed tomography angiogram diagnosed vasospasm in all ten of these patients. DSA confirmed this diagnosis. We treated vasospasm with the administration of intra-arterial verapamil. Six of these patients required repeat treatment over several days. Three patients had symptomatic vasospasm measured by examination changes of new-onset weakness, numbness, or mental status deterioration.

During the vasospasm window, the average maximum SBP goal was 162 mmHg (range 140–220 mmHg). We kept the SBP goal at 140 mmHg in four patients due to a presumed higher risk of rupture based on angiography. The remaining eight patients had a maximum blood pressure (BP) goal of at least 150 mmHg. The average maximum SBP reached was 189 mmHg (Range 157–241 mmHg). The average amount of days spent in permissive HTN was 11.75. Four patients were treated with vasopressors to augment their BP during the vasospasm window. There were no re-rupture events.

We loaded all 12 patients with DAPT before PED placement. All 12 patients received aspirin after PED placement. The second antiplatelet agent used in all cases was clopidogrel, except for one patient maintained on ticagrelor. Nine patients had EVDs present at some point in their ICU stay.

Three patients had evidence of EVD-associated hemorrhage while on DAPT. One patient had an EVD tract bleed before any dual antiplatelet administration, which enlarged after PED placement and initiation of DAPT. One patient had an EVD tract hemorrhage develop at the time of PED placement. One patient had a tract hemorrhage after the removal of the EVD. There was an overall rate of 33% for any EVD tract

hemorrhage or increase in existing tract hemorrhage. None of the EVD tract hemorrhages were clinically relevant or required surgical intervention. A single patient had a lumbar drain placed for CSF diversion. There was no evidence of complication or bleeding in this patient.

DISCUSSION

In this study, we describe our 10-year experience with PED placement to treat ruptured blister aneurysms. Our overall mortality rate of 16% is a marked improvement over the historical mortality rate for the microsurgical treatment of these lesions. The poor outcomes in open surgical intervention for blister lesions led to a search for effective endovascular intervention. Definitive treatment with stents, coils, or both have a high risk of morbidity and intraprocedural rupture.^[23,29] This case series contributes to recent evidence supporting the safe use of flow-diverting stents as a practical option for these delicate lesions.^[6,13,22,24]

One complicating factor for ICU patients with PED placement is the increased risk of bleeding secondary to necessary DAPT. The 33% rate of EVD tract hemorrhage in this study is consistent with rates found in other critical care studies showing EVD hemorrhage in the setting of DAPT.^[25,26] Reported rates of any hemorrhage associated with EVD placement are as high as 41%.^[16] EVD procedures performed in the setting of antiplatelet medications are suspected of having an even higher risk of hemorrhage than those performed without antiplatelet therapy.^[9,25] In our series, the rate of symptomatic EVD hemorrhage on dual antiplatelet agents (25%) was lower than the rates found in the current literature.^[8,9,25]

The second issue arising from PED placement is the lack of immediate occlusion of the ruptured aneurysm.^[20,22] The presence of a ruptured, functionally unsecured aneurysm presents a theoretical risk of hemorrhage, especially in the setting of HTN required to prevent ischemia from vasospasm.^[2,4] Nearly all of our patients had cerebral vasospasm, and we treated them with either induced or permissive HTN. Increased BP is a standard treatment modality to prevent DCI following aSAH.^[2,4] Importantly, all lesions in this study were Raymond–Roy grade 3 at the time of initial PED placement, indicating continued blood flow to the lesion. In this study, there were no re-rupture events despite the need for increased SBP to prevent DCI. As more practitioners utilize PEDs for challenging blister lesions, the advantages and disadvantages will become more apparent.

CONCLUSION

To the best of our knowledge, this is the first paper to discuss the implications of pipeline placement in the periprocedural

ICU setting. Despite the need for DAPT and the delayed occlusion of blister aneurysms treated with flow diversion, we did not find an increase in ICU complications.

Ethical approval

The research/study approved by the Institutional Review Board at the University of Colorado, number 18-1770, dated 3/25/2022.

Declaration of patient consent

Patients' consent not required as patients' identities were not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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