Risk of Hemorrhage in Combined Neuroform Stenting and Coil Embolization of Acutely Ruptured Intracranial Aneurysms

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Summary

Stenting as adjuvant therapy for the coiling of acutely ruptured aneurysms remains controversial due to the necessity of anticoagulation and antiplatelet medications. We report our experience using the Neuroform stent in the management of 41 aneurysms in 40 patients over a period of three years. For aneurysms whose open surgical risk remains excessive with a morphology that would preclude complete embolization, the risks of stenting may be warranted.

Introduction

The Neuroform™ Microdelivery Stent System (Boston Scientific Neurovascular, Fremont, CA) is a microcatheter delivered nitinol device released in the United States in September 2002 under the Humanitarian Device Exemption (HDE) program. The system was originally designed to assist with the endovascular coiling of unruptured intracranial aneurysms. It is also frequently used for the management of ruptured aneurysms with unfavorable fundus to neck ratios or for instances when coils unexpectedly herniate into the parent vessel, thus requiring rescue with a device that can re-constrain the coil within the lesion. While numerous case reports or small case series exist describing short and medium term results in aneurysms treated using the Neuroform device, there are few, albeit growing numbers of published manuscripts involving ruptured aneurysms [1-9].

The Neuroform stent has been utilized at the University of Pittsburgh for the management of ruptured and unruptured intracranial aneurysms that we feel cannot be optimally treated with coils alone. Between March 2004 and February 2007, 130 aneurysms (31%) were treated with the device out of a total of 415 aneurysms treated by endovascular means, including 41 acutely ruptured aneurysms in 40 patients. This paper reports the immediate post-procedure angiographic results and the peri-procedural complication rates associated with our use of Neuroform stents and platinum coils to treat intracranial, intradural aneurysms within 48 hours of subarachnoid hemorrhage (SAH).

Methods

Forty patients with 41 ruptured aneurysms underwent endovascular coil embolization using second and third generation Neuroform stents. Patient information was collected retrospectively via chart review with IRB approval. SAH was diagnosed by non-contrast CT scan or lumbar puncture. All patients were admitted to a neurovascular ICU with strict blood pressure control (SBP cap of 120 mm Hg). Phenytoin (Dilantin; Pfizer, New York, NY) (1000 mg IV load followed by 100 mg IV Q8 hours), nimodipine (Nimotop; Bayer Healthcare Phar-

maceuticals, Wayne, NJ) (60 mg PO Q4 hours), magnesium (12 g IV QD), and H_2 blockers were administered. An external ventriculostomy drain (EVD) was placed in patients with radiographic ventriculomegaly or altered mental status. In general, all patients with H&H grade ≥3 received an EVD. Every attempt was made to diagnose and treat the source of SAH within 24 hours.

During this time period, the algorithm of treatment at our institution involved initial digital subtraction angiography (DSA) for each patient to determine feasibility of endovascular embolization. Approximately 80% of patients were treated via an endovascular approach.

The utilization of a Neuroform stent was based on a case by case basis per the senior author's experience (MH). This primarily entailed an unfavorable fundus:neck ratio (93% had F:N <1) or complex morphology which would not permit maximum packing without coil herniation into the parent vessel. Stents were employed initially >90% of the time as opposed to a salvage procedure at the end of the case. We favored "jailing" the catheter within the aneurysm prior to stent deployment.

Aside from the omission of pre-procedural aspirin and clopidogrel (Plavix; Bristol-Myers Squibb/Sanofi Pharmaceuticals, New York, NY), patients with ruptured aneurysms received the same medical regimen as our elective, unruptured patients. Most patients received intraoperative eptifibatide (Integrilin; Millennium Pharmaceuticals/Schering Corp, Kenilworth, NJ) at the time of stent placement or at the case's conclusion (15 mg IV bolus), intraoperative Heparin (Baxter, Deerfield, IL) (5000 unit IV bolus to maintain ACT greater than 200 seconds), post-procedure clopidogrel (600 mg oral loading dose followed by 75 mg/day for one month) and aspirin (81-325 mg/day for life).

Immediate post-procedure radiographic results were stratified into three categories. *Category 1* was a completely treated lesion which on final angiography demonstrated no contrast within the aneurysm neck or fundal interstices. *Category 2* was defined as having coils packed throughout the aneurysm with some contrast percolating through and filling the interstices of the coil mass. By strict criteria, even stagnant contrast within these interstices late into the venous phase was considered category 2. *Category 3* was defined as a treated aneurysm harboring areas without dense coil packing allowing significant neck or fundal contrast filling. Patient outcome was determined using the Glasgow Outcome Score (GOS) and Modified Rankin Score (MRS).

Table 1 **Hunt and Hess Grade at Presentation.**

Hunt and Hess Score	N	%
1	6	15%
2	3	8%
3	13	32%
4	16	40%
5	2	5%

Table 2 **Aneurysm Size.**

Size (mm)	N	%
1-10 mm	30	73%
11-25 mm	10	24%
>25 mm	1	3%

Results

Patient Demographics and Aneurysm Characteristics

From 2004 to 2007, 41 ruptured aneurysms were treated using stents in 24 women and 16

Table 3 **Aneurysm Location.**

Aneurysm Location	N	%
Basilar Apex	9	22%
Posterior Communicating	9	22%
MCA Bifurcation	4	10%
Vertebral Confluence	4	10%
Posterior Inferior Cerebellar	4	10%
ICA Bifurcation	2	5%
Ophthalmic	2	5%
Anterior Communicating	1	2%
Anterior Cerebral A1	1	2%
Pericallosal-Callosomarginal	1	2%
Anterior Choroidal	1	2%
Superior Cerebellar	1	2%
Basilar Trunk	1	2%
Superior Hypophyseal	1	2%

men ranging in ages from 37–81 years (mean 66). All patients presented with SAH (Table 1) from an intracranial aneurysm measuring 3-32 mm in maximum diameter (mean 9.5 mm) (Table 2,3). Apical irregularities (Murphy's tit) were present in 46% of lesions (19/41).

Ninety-eight percent of patients (39/40) were treated within 24 hours of hemorrhage and 100% were treated within 48 hours. Six patients (15%) harbored multiple aneurysms (three patients with two aneurysms each; two patients with three aneurysms each).

In one of these individuals it was difficult to ascertain the culprit lesion thus requiring embolization and stenting of two lesions (basilar artery and posterior communicating artery aneurysms) during a single procedure. The remaining five patients had a single aneurysm treated during the acute period with the remaining lesions left untreated.

Anticoagulation and Antiplatelet Regimen (Table 4)

Almost all patients (97.5%) received some form of anticoagulation and/or antiplatelet therapy during and/or after the embolization procedure. Heparin was administered intravenously in 97.5% of patients prior to coil and stent placement. Heparin doses ranged from 3000 – 8000 units with a mean and median dose of 5151 units and 5000 units, respectively. Eptifibatide was administered during or immediately after stent/coil embolization in 78% (32/41) of treated aneurysms.

One patient received eptifibatide (120 *u*g/kg/hr) for the first ten hours following the procedure. Intravenous heparin at 500 - 1000 units/hour (median dose 500 units/hour) was administered to 59% of aneurysms (24/41) for the first 12-24 hours following their procedure. Clopidogrel was administered to 54% of aneurysms (22/41) immediately post procedure and throughout the subsequent hospitalization period. Aspirin (median dose 325 mg) was administered following the procedure to 78% (32/41). Both heparin and antiplatelet medications were administered for 88% (35/41) of the treated aneurysms. Post procedure heparin or antiplatelets were typically held if there was concern about procedural perforation or rupture, if there was excessive access site hematoma/oozing, or if immediate post-procedure placement of an EVD was expected.

Intraprocedural Aneurysmal Hemorrhage and Embolic Events

Rebleeding of the index aneurysm occurred during angiography in 5/40 patients (12.5%). However, two of these events occurred during the diagnostic arteriogram prior to the administration of anticoagulants/antiplatelets or placement of intracranial catheters/wires. Intraprocedural rupture/perforation occurred during the treatment of 3/41 aneurysms (7.3%) and following administration of one or more anticoagulants (Heparin and/or Integrilin).

All procedural ruptures refer to iatrogenic induced rebleeding of a presumed previously ruptured aneurysm as none of the seven untreated secondary aneurysms found in five patients hemorrhaged during the procedure or hospitalization. Four radiographic embolic/thrombotic events were identified during the coil/stenting procedure (10%). Three of these cleared uneventfully following eptifibatide administration while one (2.5%) led to a clinically significant stroke (see next section).

Post-Procedure Hemorrhage and Post–Procedure Stroke

Two patients (5%) suffered procedural or post-procedural non-aneurysmal hemorrhages. One patient bled from a distal posterior cerebral artery (PCA) wire perforation that was not visualized during the procedure despite numerous proximal arteriographic runs.

The second patient developed diffuse, multiarterial distribution intraparenchymal hemorrhages that were attributed to intra- and/or post-procedural anticoagulation (Heparin and

Table 4 **Anticoagulation and Antiplatelet Therapy Administered per Procedure.**

Heparin during procedure	Eptifibatide during procedure	Eptifibatide post procedure	Heparin post procedure	Clopidogrel post procedure	Aspirin post procedure	Heparin + Antiplatelet
N = 40	N = 32	N = 1	N = 24	N = 22	N = 32	N = 35
97.5%	78%	2.4%	59%	54%	78%	85%

eptifibatide during the procedure in addition to ASA and clopidogrel after the procedure).

Table 5 shows pertinent information regarding those patients with strokes. In all five patients (12.5%) suffered what we determined were ischemic strokes with or without hemorrhagic conversion. Two (5%) of these patients (#3,#7) suffered post-procedure hemorrhagic strokes while three (7.5%) patients (#2,#4,#6) experienced bland infarcts. One of the five strokes was secondary to an identified procedural embolic event while the remaining four strokes occurred in a delayed manner. Taking into consideration the three additional procedure related hemorrhages from aneurysm perforation/rupture (#8,#9,#10), the distal PCA wire perforation and hemorrhage (#1), and the case of multiple intraparenchymal hemorrhages (#5), the overall intra- and post procedural non-vasospasm related iatrogenic hemorrhage and stroke rate was 7/40 (17.5%). We felt 6/10 cases in Table 5 were related specifically to the use of a stent and/or the requisite anticoagulation regimen used during and/or after the coiling procedure.

Strokes and Relationship to Anticoagulants and Antiplatelet Medications (Table 5)

We evaluated the relationship between stroke and medication use. Two out of five thromboembolic strokes occurred in patients who had not been given eptifibatide during their procedure (#2,#6). Patient #2 did not receive heparin, ASA or clopidogrel, while patient #6 was heparinized (but had the medication reversed at the procedure's conclusion) and received no subsequent anticoagulant/antiplatelet medications. Eight patients received no ASA following

Table 5 **Stroke and Outcome in Relation to Anticoagulation/Antiplatelet Medication.**

Patient	H/H	GOS	MRS	Aneurysm Location	Size mm	Stent Location	Stroke Etiology & Location	Stroke Type	Stent related to or worsened outcome	Anticoagulation Regimen
1	2	1	6	BA	10	BA-L PCA	PCA perforation	Hem	Y	H1, E, H2, C, A
2	4	4	3	R MCA	20	R M1 -M2	Non st M2 occlusion	Ischem/ Bland	N	None
3	1	4	3	L SCA	7	BA-L SCA	Thal/Occ lobe	Ischem/ Hem	Y	H1, E, H2, C, A
4	3	1	6	BA	8	BA-L PCA	B/L PCA	Ischem/ Bland	Y	H1, E, H2, C, A
5	1	3	4	VA trunk	8	R VA	Diffuse hem	Hem	Y	H1, E, C, A
6	5	1	6	ICA Bifurcation	32	R ICA- R MCA	MCA stroke	Ischem/ Bland	Y	H1
7	1	4 (3m)	3 (3m)	BA	10	BA - R PCA & L PCA	L PCA OL	Ischem/ Hem	Y	H1, E, H2, C, A
8	4	1	6	P. comm	7	ICA	Aneurysm Rupture	Hem	N	H1, A
9	4	1	6	Vertebral Confluence	9	Vert-BA	Aneurysm Rupture	Hem	N	H1
10	3	NA	NA	Vert-PICA	7	VA	Aneurysm Rupture	Hem	N	H1, A

H1 - intra-procedural heparin, E - eptifibatide, H2 - post procedure heparin, C - clopidogrel, A - aspirin

their procedure (20%). Two of these individuals (#2,#6) suffered bland strokes.

Three of five ischemic stroke patients received both heparin and antiplatelet medications during and after their procedure. One of these strokes remained bland while two suffered hemorrhagic conversion.

Thirty patients (75%) did not experience ischemic or hemorrhagic complications following treatment. Of these 30 patients, 28 received

Table 6 **Anticoagulation/Antiplatelet Medications in Patients without Strokes.**

Patient	Intra-op Heparin	Intra-op Eptifibatide	Heparin post case	Clopidogrel post case	ASA post case	Eptifibatide post case
1	X	X	X	X	X	
2	X				X	
3	X	X	X	X	X	
4	X	X	X		X	
5	X	X	X	X	X	
6	X	X	X	X		
7	X					
8	X	X	X	X	X	
9	X	X	X		X	
10	X	X			X	
11	X	X			X	
12	X	X	X		X	
13	X		X		X	
14	X	X		X	X	
15	X	X	X		X	
16	X	X	X		X	
17	X	X				
18	X	X	X		X	
19	X	X	X	X	X	
20	X	X	X	X	X	X
21	X	X		X	X	
22	X	X	X	X	X	
23	X	X			X	
24	X	X		X	X	
25	X	X	X		X	
26	X	X	X	X	X	
27	X	X	X	X	X	
28	X	X	X	X	X	
29	X	X	X	X	X	
30					X	

combinations of heparin, eptifibatide, ASA and clopidogrel during and after stent/coiling. Of the remaining two patients, one received Heparin during the procedure and ASA after the procedure and one received only ASA after the procedure.

Table 6 summarizes the medications used in all patients who did not experience an ischemic or hemorrhagic stroke.

Ventriculostomy and Related Complications

EVD placement information related to use and timing is shown in Table 7. Thirty-three new EVDs were placed with two requiring replacement/revision secondary to obstruction and loss of cerebrospinal fluid (CSF) flow. CT scans performed following placement demonstrated an associated hemorrhage in 27% of new EVDs (9/33). Seven patients harbored inconsequential punctate hemorrhages along the catheter tract, while two patients exhibited large intraparenchymal hemorrhages (45 cm^3 and 20 cm^3). Neither case required surgical evacuation. Three percent of virgin EVDs (1/33) resulted in a neurological deficit, with the 45 cm^3 clot producing a mild hemiparesis.

The relationship of hemorrhage to timing of catheter insertion was also analyzed. Thirty-two percent (7/22) of ventriculostomies placed preoperatively had blood along the tract. Twenty percent (2/10) of catheters placed post-coiling had blood along the tract.

Table 7 **External Ventricular Drain Placement and Timing.**

Ventriculostomy	Timing	N
Not placed		7 (17.5%)
Placed		33 (82.5%)
	Placed Pre-Procedure	22 (67%)
	Placed During Procedure	1 (3%)
	Placed Post Procedure	10 (30%)
	Replaced During Procedure	2 (6%)

Table 8 **Hemorrhage associated with External Ventricular Drain Placement.**

Patient	Tract Blood	Hematoma	Clinically Significant	H/H	GOS	MRS	Anticoagulation
1	X		No				H1, E, H2, C, A
2	X		No				H1, E, H2, C, A
3	X		No				H1, E, H2, C
4	X		No				H1, E, H2, A
4	X		No				H1, E
5	X		No				H1, E, C, A
6	X		No				H1, E, H2, C, A
7	X		No				H1, E, H2, C, A
8		45 cc	Yes	2	4	3	H1, E, H2, A
9		20 cc	No	4	1	6	H1, I, A

H1 - intra-procedural heparin, E - eptifibatide, H2 - post-procedure heparin, C - clopidogrel, A - Aspirin

The single catheter placed intra-procedurally had no hemorrhagic complications. Of note, two catheters that were subsequently replaced down the same tract had no hemorrhagic complications. Table 8 provides relevant clinical data regarding each patient with an EVD associated hemorrhage.

Other Hemorrhagic Complications

Four patients (10%) had significant post procedural bleeding at sites other than the head. These included twp significant groin hematomas, twp retroperitoneal hematomas, and twp GI bleeds. Fourteen patients underwent tracheostomy (35%) with only one episode of associated site bleeding that required platelet infusion. Thirteen patients received gastrostomy tubes with no associated bleeding episodes. Table 9 summarizes important data regarding some of these individuals.

Immediate Angiographic Results

Immediate angiographic results with regard to aneurysm obliteration are tabulated in Table 10.

Discussion

Several groups have described their initial experience using first, second and third generation Neuroform stents. Eleven of the largest studies were reviewed [1-11]. These studies describe the treatment of 461 aneurysms in 432 patients when utilizing the Neuroform stent. Unfortunately, the patient population remains heterogenous, with acute SAH comprising 0 - 75% of patients and treatment time windows spanning hours to years after ictus.

No series has focused specifically on the analysis of Neuroform stenting and coil embolization in acutely ruptured, intradural aneurysms primarily treated within 24 hours of ictus. Without such information it is difficult to assess the device's safety in the face of recent intracranial hemorrhage.

This is especially important when one recognizes that stent placement requires additional technical steps, potential increased arterial manipulation, placement of an expandable device across the neck of an acutely ruptured aneurysm, and administration of both anticoagulants and antiplatelet agents. Patient's in the acute period surrounding SAH often require further surgical procedures including ventriculostomies, tracheostomies, gastric feeding tubes, and permanent CSF shunting. Each of these procedures can involve major hemorrhagic complications.

It is generally accepted that the use of a Neuroform stent should be preceded by an antiplatelet regimen of aspirin and clopidogrel. In a 2004 editorial published by Howington et Al, the authors state "we strongly recommend that patients receive dual antiplatelet therapy for several days before stent placement. … Alternatively, if a patient needs urgent treatment and has not received pretreatment with the above regimen, a loading dose of clopidogrel (375-600 mg) is given" [12].

The authors go on to warn against the use of such antiplatelet agents in acutely ruptured aneurysms due to the risk of intra-procedural hemorrhage. While it would be difficult to disagree with this opinion, situations do arise when Neuroform stents facilitate the management of ruptured lesions.

The decision to use a stent in this setting requires an understanding of antiplatelet/anticoagulant medication risk versus sub-total coiling treatment.

Table 9 **Extracranial Bleeding Complications.**

Patient	Groin Hematoma	Retroperitoneal Hematoma	GI Bleeding	Anticoagulation	Stroke	Ventriculostomy Bleeding
1	X	X	X	H1, E, H2, C, A	No	No
2	X			H1, E	No	20cc clot
3		X		H1, E, A	No	No
4			X	H1, E, H2, C, A	No	No

H1 - intra-procedural heparin, E - eptifibatide, H2 - post procedure heparin, C - clopidogrel, A - aspirin

Complications Related to Stenting

Intracranial Hemorrhage

Despite the propensity to use multiple anticoagulant and antiplatelet agents before, during and after stent/coiling (Table 4), the rate of ICH was relatively low and when it did occur, outcomes were not overwhelmingly different from what would have been expected based on either initial presenting examination or aneurysm type. We reported two cases (5% incidence) of ICH unrelated to aneurysmal rupture. One involved a diffuse bleeding pattern that was certainly related to the antiplatelet/anticoagulation regimen. The other involved an occult vessel perforation that went unnoticed during the procedure and caused no SSEP or EEG changes. This PCA perforation (Patient #1, Table 5) with Heparin and eptifibatide already infused was self-limiting and of little clinical significance. The patient's ultimate demise was not felt to be secondary to the hemorrhage itself but rather to sequelae of the initial SAH. The incidence of non-aneurysmal ICH after coiling ranges from 0-4.8% [1-11].

Biondi et Al reported similar findings to ours when they described the development of a subdural hematoma (SDH) and a perforation of the anterior cerebral artery (ACA) when attempting to coil an ophthalmic artery aneurysm [7]. Lee et Al also reported a 4.5% incidence involving a delayed SDH that resulted in mortality [4].

Aneurysm Rupture/Perforation

There were three procedure related iatrogenic aneurysm ruptures/perforations resulting in an incidence of 7.3%. Two of these coil perforations resulted in death that was not clearly related to the bleeding event. Another perforation resulted in a GOS of 3 and MRS of 4. These patients' outcomes were not definitively affected by the use of a Neuroform stent or the need for antiplatelet agents.

A review of the largest studies evaluating outcomes from stent assisted coiling revealed a procedural rupture/perforation rate of 0-6%, although few aneurysms were acutely ruptured and all studies involved <50% ruptured patients [1-11]. Cloft et Al published a meta-analysis of perforations complicating aneurysm coiling [13]. He reported that the risk of intraprocedural perforation was significantly higher in patients with ruptured aneurysms compared with unruptured aneurysms (4.1% vs. 0.5%). When Ng. et Al published their results of coiling in 81 ruptured and 63 unruptured aneurysms, the procedure related rupture rate was 16% vs. 1.3% respectively [14].

When Ross et Al reviewed their three year history of endovascular aneurysm treatment, they noted significant discrepancy between unruptured and ruptured aneurysm complications, with a thromboembolic rate of 2.6% vs. 11.3% and an aneurysm rupture/ perforation rate of zero vs. 12.5% [15]. Thus, a more relevant comparison can be made after reviewing the procedural rupture/perforation rate of treating ruptured aneurysms. A review of 11 selected studies revealed rates of 1.9-16% with an average incidence of 5.7% [14-24]. Of note, there was significant variation in the timing of treatment, which ranged from <24 hours to over one year after SAH. Only one other study treated all aneurysms within 48 hours [22]. It is reasonable to expect a higher procedural rupture rate when treating early (98% of our patients treated within 24 hours) as the incidence of re-rupture during the first 24 hours is 4%, with the maximal risk during the first six hours [25-27]. As cerebral angiography is a known risk factor for SAH, our early treatment paradigm may also explain the two cases of rebleeding during the diagnostic arteriogram which occurred before intracranial access or anticoagulation. We chose not to include these when calculating the incidence of iatrogenic, procedural rupture/perforation.

Vessel and aneurysm perforations were admittedly morbid (Table 5). Three of the four patients died following such complications, however two patients presented as a Hunt and Hess grade 4. The patients did not die immedi-

Table 10 **Immediate angiographic results.**

Immediate Angiographic Results	N	%
Category 1 (no post coiling opacification of aneurysm	11	27
Category 2 (slight opacification within coil mass interstices; dense coil packing in all quadrants)	27	66
Category 3 (residual fundal or neck opacification)	3	7

ately from the procedure and it was unclear the extent to which disease or iatrogenic injury played in the outcome.

Thromboembolic Events

We had a 20% incidence (8/40) of TE events, of which 12.5% were symptomatic. Three patients were successfully treated for radiographic thrombi. For the symptomatic patients, the presence of multiple anticoagulants may have increased morbidity in the setting of acute stroke (Table 5). Of these five iatrogenic incidents, three remained bland whereas two showed some degree of hemorrhagic conversion; none requiring surgical evacuation. Overall outcomes were relatively good with 3/5 ischemic stroke patients having GOSs of 4 and MRSs of 3 at follow-up. While it is true that five ischemic strokes occurred in this series of 41 aneurysms, two of the five patients presented as H&H grade 4 or 5 and four patients presented with either posterior circulation or near giant MCA fusiform aneurysms. Open surgical treatment of these lesions would risk significant morbidity/mortality in the ruptured setting making ultimate GOS and MRS outcomes of 4 and 3 quite acceptable.

For comparison, the incidence of symptomatic thromboembolic (TE) events during stent assisted coiling ranges from 0 - 19% with an average of 7.3%, although the majority of these aneurysms were unruptured and treated electively [1-11,28-30]. Coil embolization of ruptured aneurysms in selected series without stent use yielded a risk of symptomatic TE events ranging from 4.7% - 14.5% with an average of 8.5% [14-24]. Ross et Al also noted significant discrepancy between unruptured and ruptured aneurysm complications, with a TE rate of 2.6% vs. 11.3% respectively [15]. The incidence of total TE events is likely much higher and often not reported or specified. When reported in the stent-coiled group, total TE events increased to an average incidence of 9.9% with a range of 2% - 23.5%.

Ventriculostomy Related Hemorrhage

Eighty-two percent of patients in this study underwent new EVD placement resulting in a 27% incidence (9/33) of catheter associated hemorrhage, of which 3% (1/33) were clinically significant (Table 7). Previously published studies regarding the incidence of ventriculostomy related hemorrhages have shown clinically significant hematomas in 0.5% - 12.5% of patients [31-34]. In the largest such study, Maniker et Al. noted a 33% incidence of catheter related hemorrhages, 2.5% of which were clinically [32] Of note, patients in these patients did not receive anticoagulation or antiplatelets. The incidence rose to 39% when evaluating only those patients receiving an EVD for post-aneurysmal SAH. Ross et Al noted that 3/24 patients (12.5%) suffered a catheter related hemorrhage while receiving heparinoids, while Hoh et al. recorded a 9.2% incidence of catheter related hemorrhages when patients were heparinized after EVD placement, with only 1/119 (0.8%) being symptomatic [31,33]. Our EVD related hemorrhage rate is comparable, even to studies in which no blood thinning agents were utilized.

Extracranial Hemorrhagic Complications

Following SAH, patients often require surgical procedures such as tracheostomies and gastric feeding tube (G-tube) placement. Patients are also at high risk of developing stress related gastric ulcers. In addition, patients undergoing femoral artery catheterization run the risk of developing groin or retroperitoneal hematomas. The use of anticoagulants and antiplatelet agents can potentially increase the risk for each of these procedures or complications. In our series of 40 patients harboring 41 ruptured aneurysms, six extracranial hemorrhages occurred in four patients (Table 9). None of these hemorrhagic complications were life threatening nor required surgical intervention. In addition to the above, only one minor bleeding episode occurred in the 14 patients who underwent G tube and/or tracheostomy insertion. In subsequent surgical cases, all patients had antiplatelet agents reversed with platelets immediately prior to surgery.

Benefit of Antiplatelets/Anticoagulation

A notable finding of this study was the protective effect of anticoagulants and antiplatelet medications against thromboembolic events (Tables 5 and 6). Two patients who developed delayed ischemic complications (#2 and #6 in Table 5) were either on no such medications or were only on Heparin during the procedure

(no antiplatelet medication post-procedure). Only two of the 30 patients that avoided a stroke were treated with mono-drug therapy (patients #7 and #30 in Table 6 receiving only intra-procedural heparin and post-procedural ASA respectively). The remaining 28 patients received at least one anticoagulant and multiple antiplatelet medications during and after their stent/coil procedure.

Immediate Angiographic Outcomes:

We evaluated the immediate angiographic results along with the incidence of subsequent aneurysm re-hemorrhage during the period of maximum anticoagulation. The reason for such evaluation may help determine the utility of stents in this setting. Some endovascular physicians have proposed the acceptance of sub-total coiling for the treatment of complex or wide neck aneurysms that were not amenable to stand alone coiling in the setting of acute SAH. The rationale being that partial flow reduction or protection of the dome might reduce the risk of aneurysmal rupture and avoid the risks of stenting with its concomitant medication regimen. Unfortunately, there is no current evidence to clearly support this hypothesis, and as such, stent coiling to obtain a high degree of aneurysm occlusion may justify the use of such devices. The largest trials evaluating the long term rebleed rate from coiled aneurysms point out the flaw of subtotal coiling, as most late rebleeds occur in aneurysms with residual or regrowth.

The CARAT investigators followed 299 patients with coil treated aneurysms for a mean of 3.7 years [35]. The single case of rebleeding occurred in an aneurysm that showed interval growth on follow up angiography, and it was unclear if 100% occlusion was obtained during the initial treatment. These investigators published a follow up article looking at predictors of rehemorrhage after treatment of ruptured intracranial aneurysms [36]. They noted that the degree of aneurysm occlusion after the initial treatment is a strong predictor of subsequent rupture "which justifies attempts to completely occlude aneurysms".

Moreover, the risk of rupture in aneurysms that were <70% occluded were similar to rerupture rates in prior studies of untreated ruptured aneurysms. In ISAT, 801 patients were followed out to one year [37]. Of the ten patients who bled from the index aneurysm within 30 days who actually underwent placement of coils into the aneurysm, seven were judged to have incomplete aneurysm occlusion. In the follow-up to ISAT, eight patients bled from the target aneurysm over one year after endovascular treatment [38]. Only two of these showed complete occlusion on six month follow-up arteriography, leading the investigators to conclude that patients who have complete aneurysm occlusion can be advised that the risk of rerupture is very low, but the risk of rerupture after subtotal occlusion only seems to be low. Sluzewski et Al reported their incidence of late rebleeding of ruptured aneurysms treated with detachable coils [39]. Four certain and one probable case of late rebleeding occurred after an average of 47 months of follow-up in 393 patients. All patients had subtotal occlusion or evidence of recurrence.

Table 10 delineates our immediate angiographic outcomes, with complete or near complete aneurysm obliteration in 93% of cases. No aneurysm re-rupture occurred during the acute hospitalization period nor has any patient presented with aneurysm rebleeding following discharge. Despite the presence of multiple aneurysms in 15% of patients, no bleeding from untreated lesions occurred during the period of maximum anticoagulation/antiplatelet therapy and no patient has subsequently presented with hemorrhage from an unsecured lesion.

Balloon remodeling

Balloon remodeling remains another option for the treatment of wide neck aneurysms or coil herniation when attempting to avoid the use of a stent. However, balloon remodeling carries its own intrinsic risk. Ross et Al noted a 12.5% risk of aneurysm rupture/perforation, with 8/11 (72%) occurring during the use of a balloon remodeling device [15]. Van Rooij et Al also reported on their treatment of 681 consecutive ruptured aneurysms, reporting that the use of a temporary supporting balloon was the only significant risk factor for procedural complications [17]. Overall, 20% of patients treated with a supportive balloon suffered procedure related death or disability.

The HELPS trial is the first randomized, controlled trial to include a significant number of patients treated with stents (98/499) and bal-

loon remodeling (125/499)[40]. As expected, the investigators noted a trend towards greater procedural adverse events when assist devices were used, however the balloon/other assist-devices conferred the greatest risk; over and above the incidence of adverse events associated with stents.

This also represents one of the few opportunities to evaluate complications from a randomized controlled trial, resulting in a 3.4% perforation/rupture rate and a 10.2% thromboembolic rate. Unfortunately, the incidence with respect to ruptured vs. unruptured aneurysms was not specified. It must also be noted that their complication rates may be slightly skewed towards a better outcome as only half the aneurysms were ruptured, treatment was within 30 days of rupture, and there were few poor grade patients.

Conclusions

The use of Neuroform stents in conjunction with coil embolization of acutely ruptured intracranial aneurysms may have an acceptable risk: benefit ratio.

This is particularly relevant if one believes complete aneurysm obliteration after SAH is the absolute goal, even in the setting of unfavorable aneurysm morphology. Further study is warranted in a multi-center and possibly randomized prospective fashion.

References

1 Fiorella D, Albuquerque FC et Al: Usefulness of the Neuroform stent for the treatment of cerebral aneurysms: results at initial (3-6-mo) follow-up. Neurosurgery 56(6): 1191-1201; discussion 201-202, 2005.
2 Akpek S, Arat A et Al: Self-expandable stent-assisted coiling of wide-necked intracranial aneurysms: a single-center experience. Am J Neuroradiol 26(5): 1223-1231, 2005.
3 Katsaridis V, Papagiannaki C, Violaris C: Embolization of acutely ruptured and unruptured wide-necked cerebral aneurysms using the neuroform2 stent without pretreatment with antiplatelets: a single center experience. Am J Neuroradiol 27(5): 1123-1128, 2006.
4 Lee YJ, Kim DJ et Al: Stent-assisted coil embolization of intracranial wide-necked aneurysms. Neuroradiology 47(9): 680-689, 2005.
5 dos Santos Souza MP, Agid R et Al: Microstent-assisted coiling for wide-necked intracranial aneurysms. Can J Neurol Sci 32(1): 71-81, 2005.
6 Yahia AM, Gordon V et Al: Complications of Neuroform stent in endovascular treatment of intracranial aneurysms. Neurocrit Care 8(1): 19-30, 2008.
7 Biondi A, Janardhan V et Al: Neuroform stent-assisted coil embolization of wide-neck intracranial aneurysms: strategies in stent deployment and midterm follow-up. Neurosurgery 61(3): 460-468; discussion 8-9, 2007.
8 Benitez RP, Silva MT et Al: Endovascular occlusion of wide-necked aneurysms with a new intracranial microstent (Neuroform) and detachable coils. Neurosurgery 54(6): 1359-1367; discussion 68, 2004.
9 Lylyk P, Ferrario A et Al: Buenos Aires experience with the Neuroform self-expanding stent for the treatment of intracranial aneurysms. J Neurosurg 102(2): 235-241, 2005.
10 Jabbour P, Koebbe C et Al: Stent-assisted coil placement for unruptured cerebral aneurysms. Neurosurg Focus 17(5): E10, 2004.
11 Henkes H BA, Felber S et Al: Endovascular Coil Occlusion of Intracranial Aneurysms Assisted by a Novel Self-Expandable Nitinol Microstent (Neuroform). Interventional Neuroradiology 8: 107-119, 2002.
12 Howington JU, Hanel RA et Al: The Neuroform stent, the first microcatheter-delivered stent for use in the intracranial circulation. Neurosurgery 54(1): 2-5, 2004.
13 Cloft HJ, Kallmes DF: Cerebral aneurysm perforations complicating therapy with Guglielmi detachable coils: a meta-analysis. Am J Neuroradiol 23(10):1706-1709, 2002.
14 Ng P, Khangure MS et Al: Endovascular treatment of intracranial aneurysms with Guglielmi detachable coils: analysis of midterm angiographic and clinical outcomes. Stroke 33(1): 210-217, 2002.
15 Ross IB, Dhillon GS: Complications of endovascular treatment of cerebral aneurysms. Surg Neurol 64(1): 12-18; discussion 8-9, 2005.
16 Park HK, Horowitz M et Al: Periprocedural morbidity and mortality associated with endovascular treatment of intracranial aneurysms. Am J Neuroradiol 26(3): 506-514, 2005.
17 van Rooij WJ, Sluzewski M et Al: Procedural complications of coiling of ruptured intracranial aneurysms: incidence and risk factors in a consecutive series of 681 patients. Am J Neuroradiol 27(7): 1498-1501, 2006.
18 Henkes H, Fischer S et Al: Endovascular coil occlusion of 1811 intracranial aneurysms: early angiographic and clinical results. Neurosurgery 54(2): 268-280; discussion 80-85, 2004.
19 Friedman JA, Nichols DA et Al: Guglielmi detachable coil treatment of ruptured saccular cerebral aneurysms: retrospective review of a 10-year single-center experience. Am J Neuroradiol 24(3): 526-533, 2003.
20 Gallas S, Pasco A et Al: A multicenter study of 705 ruptured intracranial aneurysms treated with Guglielmi detachable coils. Am J Neuroradiol 26(7): 1723-1731, 2005.
21 Vinuela F, Duckwiler G, Mawad M: Guglielmi detachable coil embolization of acute intracranial aneurysm: perioperative anatomical and clinical outcome in 403 patients. J Neurosurg 86(3): 475-482, 1997.
22 Tummala RP, Chu RM et Al: Outcomes after aneurysm rupture during endovascular coil embolization. Neurosurgery 49(5): 1059-1066; discussion 66-67, 2001.

23 Ricolfi F, Le Guerinel C et Al: Rupture during treatment of recently ruptured aneurysms with Guglielmi electrodetachable coils. Am J Neuroradiol 19(9): 1653-1658, 1998.
24 Sluzewski M, Bosch JA et Al: Rupture of intracranial aneurysms during treatment with Guglielmi detachable coils: incidence, outcome, and risk factors. J Neurosurg 94(2): 238-240, 2001.
25 Winn HR, Richardson AE, Jane JA: The long-term prognosis in untreated cerebral aneurysms: I. The incidence of late hemorrhage in cerebral aneurysm: a 10-year evaluation of 364 patients. Ann Neurol 1(4): 358-370, 1977.
26 Kassell NF, Drake CG: Review of the management of saccular aneurysms. Neurol Clin 1(1): 73-86, 1983.
27 Jane JA, Winn HR, Richardson AE: The natural history of intracranial aneurysms: rebleeding rates during the acute and long term period and implication for surgical management. Clin Neurosurg 24: 176-184, 1977.
28 Kis B, Weber W et Al: Elective treatment of saccular and broad-necked intracranial aneurysms using a closed-cell nitinol stent (Leo). Neurosurgery 58(3): 443-450; discussion -50, 2006.
29 Weber W, Bendszus M et Al: A new self-expanding nitinol stent (Enterprise) for the treatment of wide-necked intracranial aneurysms: initial clinical and angiographic results in 31 aneurysms. Neuroradiology 49(7): 555-561, 2007.
30 Yavuz K, Geyik S et Al: Immediate and midterm follow-up results of using an electrodetachable, fully retrievable SOLO stent system in the endovascular coil occlusion of wide-necked cerebral aneurysms. J Neurosurg 107(1): 49-55, 2007.
31 Hoh BL, Nogueira RG et Al: Safety of heparinization for cerebral aneurysm coiling soon after external ventriculostomy drain placement. Neurosurgery 57(5): 845-849; discussion -9, 2005.
32 Maniker AH, Vaynman AY et Al: Hemorrhagic complications of external ventricular drainage. Neurosurgery 59(4 Sup2):ONS 419-424; discussion ONS 24-25, 2006.
33 Ross IB, Dhillon GS: Ventriculostomy-related cerebral hemorrhages after endovascular aneurysm treatment. Am J Neuroradiol 24(8): 1528-1531, 2003.
34 Wiesmann M, Mayer TE: Intracranial bleeding rates associated with two methods of external ventricular drainage. J Clin Neurosci 8(2): 126-128, 2001.
35 The CARAT Investigators: Rates of delayed rebleeding from intracranial aneurysms are low after surgical and endovascular treatment. Stroke 37(6): 1437-1442, 2006.
36 Johnston SC, Dowd CF et Al: Predictors of rehemorrhage after treatment of ruptured intracranial aneurysms: the Cerebral Aneurysm Rerupture After Treatment (CARAT) study. Stroke 39(1): 120-125, 2008.
37 Molyneux A, Kerr R et Al: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet 360(9342): 1267-1274. 2002.
38 Molyneux AJ, Kerr RS et Al: International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. Lancet 366(9488): 809-817, 2005.
39 Sluzewski M, van Rooij WJ et Al: Late rebleeding of ruptured intracranial aneurysms treated with detachable coils. Am J Neuroradiol 26(10): 2542-2549, 2005.
40 White PM, Lewis SC et Al: HydroCoil Endovascular Aneurysm Occlusion and Packing Study (HELPS Trial): Procedural Safety and Operator-Assessed Efficacy Results. Am J Neuroradiol 29(2): 217-223, 2008.

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