Peri-Procedural Morbidity and Mortality Associated with Stent-Assisted Coiling for Intracranial Aneurysms

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Key words: broad-based aneurysm, intracranial aneurysms, stent-assisted coiling, stents

Summary

Despite experience and technological improvements, stent-assisted coiling for intracranial aneurysms still has inherent risks. We evaluated peri-procedural morbidity and mortality associated with stent-assisted coiling for intracranial aneurysms.

Patients with cerebral aneurysms that were broad-based (>4 mm) or had unfavorable dome/neck ratios (<1.5) were enrolled in this study between February and November 2011 at our center. Aneurysms were treated with the self-expanding neurovascular stents with adjunctive coil embolization.

Seventy-two consecutive patients (27 men and 45 women; 22-78 years of age; mean age, 52.8 years) underwent 13 procedures for 13 ruptured aneurysms and 64 procedures for 73 unruptured aneurysms. Nine [11.7%, 95%CI(4.5%-18.9%)] procedure-related complications occurred: one and eight with initial embolization of ruptured and unruptured aneurysms, respectively. Complications included six acute in-stent thromboses, one spontaneous stent migration, one post-procedural aneurysm rupture, and one perforator occlusion. Three complications had no neurologic consequences. Two caused transient neurologic morbidity, two persistent neurologic morbidity, and two death. Procedure-related neurologic morbidity and mortality rates, respectively, were as follows: overall, 5.2% (95%CI, 0.2%-10.2%) and 2.6% (95%CI, 0%-6.2%); ruptured aneurysms, 7.7% (95%CI, 0%-36%) and 0% (95%CI, 0%-25%); unruptured aneurysms, 4.7% (95%CI,

0%-9.9%) and 3.1% (95%CI, 0%-7.3%). Combined procedure-related morbidity and mortality rates for ruptured and unruptured aneurysms were 7.7% (95%CI, 1.7%-13.7%) and 7.8% (95%CI, 1.8%-13.8%), respectively.

Stent-assisted coiling is an attractive option for intracranial aneurysms. However, stent-assisted coiling for unruptured aneurysms is controversial for its comparable risk to natural history.

The use of self-expanding neurovascular stents for the treatment of cerebral aneurysms continues to evolve¹. This technical evolution has allowed for previously uncoilable aneurysms to be successfully treated. This "reconstructive" technique is suggested to alter the intra-aneurysmal flow dynamics and lead to thrombus formation within the aneurysm². Stenting alone is best applied to smaller aneurysms³. Using this technique, a single stent is first positioned inside the parent artery bridging the aneurysm. Multiple stents can also be overlapped in a telescopic fashion to form a larger structure. Detachable coils are then delivered into the aneurysm through the stent cells. The stent serves as a scaffold and prevents coil herniation into the parent vessel. Another commonly used method involves the initial placement of the microcatheter for coil delivery into the aneurysm and jailing of the catheter against the vessel wall by stenting. Despite increasing clinical experience and technological improvements, stent-assisted coiling still has inherent risks of morbidity and mortality⁴⁻⁷. The

purpose of this study was to retrospectively review our experience with peri-procedural complications associated with stent-assisted coiling of broad-based cerebral aneurysms and to provide detailed data on the types and frequency of complications observed. This information is useful for advising patients about the general risks of stent-assisted coiling.

Materials and Methods

Patient Selection

Patients with cerebral aneurysms that were broad-based (>4 mm) or had unfavorable dome/neck ratios (<1.5) were enrolled in this study between February and November 2011 at our center. Aneurysms were treated with the self-expanding neurovascular stents with adjunctive coil embolization. Endovascular treatment was performed when it was considered the most appropriate treatment option after individualized evaluation by the vascular neurosurgeon and interventional neuroradiologist, taking into account the lesion's broad-based nature, aneurysm location and surgical accessibility, and patient preferences. Stent-assisted coiling was performed for all broad-based cerebral aneurysms. Presenting clinical symptoms, angiographic features, MR studies if available, peri-procedural studies, and clinical course as well as angiographic and clinical follow-up were prospectively reviewed.

Aneurysm Treatment

Patients were treated under general anesthesia using endovascular stent-assisted coiling techniques as previously described^{5,6}. In all cases, a stent was positioned into the lumen of the parent vessel bridging the aneurysm. The stents available were the self-expanding neurovascular stents. Subsequently, the aneurysm was coiled as described previously with platinum coils. Immediate post-procedure angiograms were obtained and reviewed in 3D views, including standard lateral and anteroposterior projections. All patients were treated in a single session.

The procedure was performed under therapeutic heparinization with activated clotting time of approximately 300 seconds. The patients were kept on heparin for 24 hours. Patients were preloaded with the dual antiplatelet agents, 75 mg clopidogrel daily and 100 mg as-

pirin daily for three to five days before treatment. Post-procedure, the patients were kept on a dual antiplatelet regimen for one month and then 100 mg aspirin for six months.

Clinical and Angiographic Outcome Measures

Clinical data were obtained from examinations conducted by stroke neurologists or neurosurgeons before and after the procedure. Patients were re-evaluated generally within two weeks after the intervention. Technical success was defined by correct placement of the stent and successful positioning of the coils into the body of the aneurysm without compromising the parent vessel. Immediate post-procedure angiography measured aneurysm occlusion using a modification of the Raymond classification scale, which primarily was developed for berry-shaped aneurysms⁷.

Results

There were 27 men and 45 women with an average age of 52.8 years (range, 22 to 78 years). Twelve patients had two separate and one had three separate broad-based aneurysms, which were all treated with 77 procedures. Two aneurysms were covered with one stent in ten patients. Thirteen patients had a 15-day to ten-year history of aneurysm rupture. The most common clinical presentation of unruptured aneurysms was CNIII or CNVI deficits (eight aneurysms [11.1%]). Other symptoms included hemiparesis, hemiplegia, stroke, facial spasm, swallowing disorders, and dizziness or gait disturbance. Six aneurysms (8.3%) were located in the posterior circulation. Mean aneurysm size was 9.0 ± 8.2 mm, and mean neck size was 6.2 ± 4.6 mm. All aneurysms were treated with stents and coils.

Aneurysm Location

Table 1 summarizes the locations of aneurysms treated with stent-assisted coiling. Seventy-nine (91.9%) aneurysms were in the anterior circulation, and seven (8.1%) in the posterior circulation. The most common location was the ophthalmic segment of ICA (39.5%), followed by the posterior communicating artery (20.9%) and cavernous segment of ICA (19.8%). Aneurysms were measured according to their greatest diameter, 60 were small (≤ 10 mm), 18 were large (11–24 mm), and eight were giant (≥ 25 mm).

Table 1 Location and mean maximum diameter of aneurysms treated with stent-assisted coiling.

	Total (n=)	Mean dimension (mm)
ICA cavernous segment	17	11.7
ICA ophthalmic segment	34	5.7
ICA supraclinoid segment	4	8.6
MCA	3	9.7
Acoma	2	3.3
Pcoma	18	6.57
A1	1	1.6
P1	1	2.5
Basilar apex	3	4.7
BA-SCA	1	9
Vertebrobasilar junction	2	27.8
Total (n =)	86	9.0

Abbreviations: n, number of aneurysms; mm, millimeters; ICA, internal carotid artery; MCA, middle cerebral artery; Acoma, anterior communicating artery; Pcoma, posterior communicating artery; BA, basilar artery; SCA, superior cerebellar artery.

Table 2 Clinically significant complications in 77 total procedures performed in 72 patients.

Clinically significant complications	Complications	Mortality
Hemorrhage	1	1
Acute in-stent thromboses	6	1
Perforator occlusion	1	0
Spontaneous stent migration	1	0
Total	9	2

Immediate Angiographic and Clinical Outcome

On immediate post-procedural angiogram, 62 of 86 (72.1%) aneurysms treated with stent-assisted coiling were occluded without a remnant. Twenty-four aneurysms showed subtotal occlusion. Of these 24 aneurysms with subtotal occlusion after treatment, 11 had residual dome filling (Raymond Class 3), whereas the other 13 had filling of a residual base (Raymond Class 2).

Peri-Procedural Complications

Excellent clinical and technical results were achieved in 63 of 72 patients (87.5%) without any peri-procedural complications. Nine [11.7%, 95%CI(4.5%-18.9%)] procedure-related complications occurred: one and eight with initial embolization of ruptured and un-

ruptured aneurysms, respectively (Table 2). Complications included six acute in-stent thromboses, one spontaneous stent migration, one post-procedural aneurysm rupture, and one perforator occlusion. An acute in-stent thrombosis occurred in six patients leading to two cases of major permanent morbidity (two of 72 [2.8%, 95%CI, 0%-6.6%]), and two mortality (2 of 72 [2.8%, 95%CI, 0%-6.6%]) were caused by re-hemorrhage at six hours and five days after treatment. In total, 68 patients (94.4%) retained no permanent deficits and returned to their baseline neurological examination. The two cases of resolved complication were one patient with a transient paralysis and one with transient loss of consciousness, which resolved to baseline at follow-up visit. An acute in-stent thrombosis observed during stenting in three patients did not have any clinical sequelae. There were 13 patients

(18.1%) who initially presented with SAH, one of whom experienced an acute in-stent thrombosis.

The two cases of major permanent morbidity both involved infarctions. After placement of stents into the ICA, one patient had a minor stroke as documented by diffusion-weighted MRI and retained permanent paralysis. An additional patient sustained a middle cerebral artery stroke after the procedure due to acute in-stent thrombosis even though the thrombosis was treated with urokinase, the patient retained some improving neurological deficit, including right paralysis and partial expressive aphasia.

One patient died six hours after urokinase treatment of the acute in-stent thrombosis. Another patient died five days after treatment. The initial attempted endovascular treatment was successful with SILK flow diverter placed from vertebral artery to basilar artery for the 30-mm giant and saccular symptomatic vertebrobasilar junction aneurysm. CT scanning suggested that the death was a result of hemorrhage of the aneurysm (not shown).

Discussion

Several groups have reported procedural complication rates related to stent-assisted coiling. Gao et al.¹ reported a 14.7% procedural complication rate in 232 patients, with procedure-related morbidity and mortality rates of 4.2% and 1.4% respectively. Pötter et al.⁸ observed a 7.4% morbidity and 4.6% mortality in 216 patients treated with stents. In the series by Mocco et al.⁹ of 141 patients with 142 intracranial aneurysms underwent 143 stent deployments led to 5% technical complications. Procedure-related morbidity and mortality rates were 8.8% and 2%, respectively. In the ruptured group, procedure-related mortality was 12%; in the unruptured group, rate was 0.8%. Liang et al.¹⁰ reported the results of endovascular treatment of 110 intracranial aneurysms in 107 patients. The procedure-related morbidity and mortality rates were 5.6% and 0.9%, respectively. Our overall complication rate for all patients was 11.7%, and the overall procedural morbidity and mortality rates were 5.5% and 2.8% respectively. The cause of morbidity was thromboembolism and the cause of mortality was aneurysmal rupture. Overall procedure-related complication rates of embolization for ruptured and unruptured aneurysms were 7.7%

and 7.8%, respectively. In ruptured aneurysms, the procedure-related neurologic morbidity rate was 7.7%, and the mortality rate was 0%. Two main causes of procedural morbidity in this group was thromboembolism. In unruptured aneurysms, procedure-related neurologic morbidity and mortality rates were 4.7% and 3.1% respectively. Thromboembolism was the main cause of procedural morbidity and aneurysmal rupture was the main cause of procedural mortality in this group. For the series, the procedural morbidity rate was higher in the ruptured group and lower in the unruptured group. The procedural mortality rate was higher in the unruptured group than in the ruptured group. These results may be caused by ruptured aneurysms were treated at a delayed SAH stage.

Acute in-Stent Thrombosis

Stent-assisted coiling of intracranial aneurysms is associated with a risk of acute in-stent thrombosis and ischemic complications. Despite routine use of antiplatelet agents and heparin in conjunction with this procedure, complications that related to thromboembolic events occurred in 2.1%-20% of patients treated^{1,2,5,11-17}. In our study, acute in-stent thrombosis complications were observed in six (8.3%) of 72 patients; one (7.7%) of 13 ruptured aneurysms and five (8.5%) of 59 unruptured aneurysms. Acute in-stent thrombosis complications accounted for 66.7% of all complications. All acute in-stent thrombosis complications observed occurred during stent deployment.

Acute in-stent thrombosis can be treated with selective intra-arterial administration of thrombolytic agents (urokinase or tPA). In view of the modest results and limitations of thrombolytic therapy, several authors^{11,15} have proposed the use of abciximab — a chimeric monoclonal antibody fragment against the platelet glycoprotein IIb/IIIa receptor complex — to manage acute in-stent thrombosis during stent placement. This drug, or others like it, may be more effective and logical for intraprocedural acute in-stent thrombosis because most patients have already received full heparinization, making it unlikely that a fibrin clot is present. Six acute in-stent thrombosis complications in our series were treated by using superselective intra-arterial urokinase. We observed complete recanalization in three and partial recanalization in the other three. Three

cases with complete recanalization had no neurologic consequence, and two had persistent neurologic deficit. One of three partially recanalized cases experienced hemorrhage and resulted in death. Overall morbidity and mortality rates from acute in-stent thrombosis complications were 2.8% (two of 72) and 1.4% (one of 72), respectively.

Perforator Occlusion

Self-expanding intracranial stents such as the Enterprise (Codman, Miami Lakes, FL, USA) or the Neuroform (BSC, Natick, MA, USA) have low radial force and are less traumatic. The potential risk of a stroke associated with perforating arteries being covered by stent struts is a consideration¹⁸. We had observed only one case of symptomatic perforator occlusion leading to a small pontine stroke by a Neuroform stent placement before this study. In one patient, an Enterprise stent was implanted for a basilar tip aneurysm and the patient experienced a transient loss of consciousness. Acute CT scanning demonstrated no hemorrhage and acute DSA was performed for this patient showed no in-stent thrombosis, the patient completely recovered without any neurological deficits 30 minutes later. It may be hypothesized that if the pressure gradient across the perforators is maintained and the perforator is covered less than 50% by stent struts, the arteries will remain patent and remodel around struts or coils thereby preserving flow.

Delayed Hemorrhage after Treatment

There was one case of delayed hemorrhage. The patient had a giant saccular vertebrobasilar junction aneurysm as previously discussed. Newer stent-like devices are being developed for intracranial aneurysms to serve as flow diverters within the parent artery to reduce blood flow in the aneurysm sac to the point of stagnation, gradual thrombosis, and neointimal remodeling to maintain outflow in the side branches and perforators. The current two commercially available flow diverters included the Pipeline Embolization Device and the SILK flow diverter. The rates of severe hemorrhagic complications have been reported to be 2% for the Pipeline Embolization Device and 0.8% for the SILK flow diverter, with 5% to 10% of patients experiencing permanent major morbidity and mortality¹⁹.

Spontaneous Stent Migration

The delayed migration of a self-expanding intracranial stent used for the embolization of an intracranial aneurysm has been reported. Spontaneous migration of the stent occurred some time between the control angiogram performed at the conclusion of the procedure and the five-month follow-up. Neuroform stents have been used since 2003, and we have never observed a case of delayed spontaneous stent migration. In addition, no cases of spontaneous Neuroform migration have been reported in the literature. The closed-cell Enterprise (Codman) stent is structurally different from Neuroform, which has an open-cell design. As such, forces exerted on one segment of the Enterprise are transmitted directly to the entire device. In our present case, the differential sizes of the MCA and ICA caused the distal aspect of the stent to be constrained to a greater degree than the proximal portion. We hypothesize that this differential constraint may have transferred a constant retrograde force to the stent, which ultimately caused it to move backwards into the ICA. Placement of the distal aspect of this stent into an artery measuring slightly less than 2 mm may have contributed to the proximal migration of this device.

Reconsideration

Maldonado et al.¹⁴ reported a procedure-related morbidity-mortality rate of 2.9% in Neuroform stent-assisted coiling of unruptured intracranial aneurysms in 68 patients. A series of 216 patients with aneurysms (181 unruptured and 35 ruptured) were treated with stent-assisted coiling⁸. Piotin et al.⁸ reported a procedure-related mortality of 4.6% (10 of 216) and procedure-related permanent neurological deficit (mortality excluded) of 2.8% (6/216). And in our patients, this rate was 7.8%. This is a higher rate of serious complications compare to the natural history of unruptured aneurysms, in the study by Wiebers et al.²⁰ five-year cumulative rupture rates for patients who did not have a history of subarachnoid hemorrhage with aneurysms located in internal carotid artery, anterior communicating or anterior cerebral artery, or middle cerebral artery were 0%, 2.6%, 14.5%, and 40% for aneurysms less than 7 mm, 7-12 mm, 13-24 mm, and >25 mm, respectively, compared with rates of 2.5%, 14.5%, 18.4%, and 50%, respectively, for

the same size categories involving posterior circulation and posterior communicating artery aneurysms. Van Rooij et al. suggested that an unruptured aneurysm with a cumulative risk that outweighs this high complication rate²¹. It could be difficult to conceive that future patients with incidentally found unruptured aneurysms will consent to a proposed therapy with an almost one in eight chance of death or permanent deficit²¹. In our view the only conclusion from this poor study (and that of others such as Piotins study⁸) is that stenting

should be avoided when possible. There are good alternatives such as balloon-assisted coiling or parent vessel occlusion.

Conclusion

Stent-assisted coiling is an attractive option for broad-based cerebral aneurysms. However, stent-assisted coiling for unruptured aneurysms may be controversial for its comparable risk to the natural history.

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