Stent-Assisted Coiling in Endovascular Treatment of 500 Consecutive Cerebral Aneurysms with Long-Term Follow-Up

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ABSTRACT

BACKGROUND AND PURPOSE: Stent-assisted coil embolization has become one of the most preferred techniques in the treatment of wide-neck intracranial aneurysms; however, long-term patency and safety of the self-expanding neurostents and their role in durability of the endovascular treatment has remained ambiguous. We sought to retrospectively examine the long-term results of self-expanding stent usage in conjunction with coil embolization in treatment of wide-neck cerebral aneurysms.

MATERIALS AND METHODS: We coiled 500 wide-neck cerebral aneurysms with different types of self-expanding neurostent assistance in 468 patients. Patient and aneurysm characteristics, pharmacologic therapy protocol, complications, and initial occlusion grades were analyzed. Patients underwent angiographic follow-up at 6 months to 7 years after treatment. DSA or MRA images of all patients were analyzed to assess the occlusion rate of aneurysms and patency of the parent artery.

RESULTS: Enterprise (n = 340), Solitaire (n = 98), Wingspan (n = 41), LEO (n = 16), and Neuroform (n = 5) stent systems were used in this series. Stent-related thromboembolic events occurred in 21 patients and intraoperative rupture occurred in 4 patients. Initially, complete occlusion was achieved in 42.2% of the aneurysms, and, according to the last follow-up data, the rate had progressed to 90.8%. Recanalization rate at 6 months was 8%, whereas the late recanalization rate was 2%.

CONCLUSIONS: The use of stents in endovascular treatment provides high rates of complete occlusion and low rates of recurrence at a long-term follow-up study.

The use of self-expanding neurostents has ensured a significant advance in the endovascular treatment of wide-neck or fusiform aneurysms. However, one of the most important concerns about their use has been the lack of long-term follow-up data to show the long-term safety and durability.

To date, clinical experiences with midterm follow-up results of different self-expandable stents have been reported1-5; however, few reports exist in the literature publishing long-term data in regard to durability and long-term safety of these devices with or without comparison to other endovascular treatment techniques without the use of adjunctive stent placement.6-13 In all these previous reports, the authors concur that stents have been associated with a significant decrease in angiographic recurrences.

However, procedural and late complications caused by stent use remain controversial.

This study reports on our 500 consecutive aneurysms treated with a single stent–assisted coiling technique by use of a variety of stents including Enterprise (Codman & Shurtleff, Raynham, Massachusetts), Solo/Solitaire (ev3, Irvine, California), Wingspan (Boston Scientific, Natick, Massachusetts), LEO (Balt, Montmorency, France), and Neuroform (Stryker Neurovascular, Fremont, California) with emphasis on the long-term results.

MATERIALS AND METHODS

Patient and Aneurysm Characteristics

All patients whose intracranial aneurysms were treated in Hacettepe University and in private practice by the senior author (H.S.C.) by use of a single self-expanding stent (regardless of the stent type) and detachable platinum coils between May 2004 (the initiation of our data base records) and December 2010 have been reviewed based on the data base, medical records and image archive. All procedures were performed with the provision of written informed consent.

Aneurysm sizes were classified as small (<1 cm), large (≥1 cm and ≤2.5 cm), and giant (>2.5 cm). The aneurysms are referred...
to as wide-neck when the dome/neck ratio is <2.0 and/or neck length was ≥4 mm.

**Pharmacologic Therapy Protocol and Endovascular Procedures**

Patients with unruptured aneurysms were premedicated with 300 mg of aspirin and a loading dose of 300–600 mg of clopidogrel 1 week before the procedure, followed by 75 mg daily. On the other hand, patients with ruptured aneurysms, which were to be treated at least 14 days after SAH, premedicated with the same loading dose, started 2–3 days before the procedure. This was considered sufficient to test for clopidogrel responsiveness. Thromboocyte inhibition levels were confirmed by use of whole-blood impedance platelet aggregation (Multiplate; Dynabyte Medical, Munich, Germany) and, since February 2006, the rapid platelet function assay VerifyNow P2Y12 (Accumetrics, San Diego, California). Patients with inhibition value >30% were treated, low responders (<30%) without resistance to clopidogrel were loaded again, and patients with clopidogrel resistance were medicated with ticlopidine 2 × 250 mg. All patients received heparin to maintain an activated clotting time level elevated to 2–3 times of the baseline value during the procedure.

For the stents used without premedication, 500 mg ticlopidine or 600 mg clopidogrel and 300 mg aspirin was administered by naso/orogastric tube combined with low-molecular-weight heparin. These patients also received 1–2 mg of IV tirofiban (a glycoprotein IIb/IIIa inhibitor) during the procedure, as soon as the stent was deployed. Tirofiban infusion (IV and/or intra-arterial) was performed in the case of thrombus formation during the procedure, as well.

After the control angiogram was obtained at 6 months, clopidogrel was discontinued and aspirin was to be taken life-long.

Endosaccular coiling was performed immediately after the stent deployment through the microcatheter, which was either advanced through the stent struts after stent deployment or had been placed inside the aneurysm sac before the stent deployment and jailed between the stent and the vessel wall.

**Follow-Up**

Angiographic results were classified as complete, near complete (>95% occlusion but minimal residual filling with coils at the neck), and incomplete occlusion (<95% occlusion). Any further filling of the aneurysm neck or sac over time was referred to as “recanalization,” whereas a decrease in filling was referred to as “further occlusion.”

Thromboembolic complications were classified as minor if transient or if the mRS was <2 and major if the mRS was ≥2.

Patients underwent angiographic follow-up at 6 months after treatment (midterm) with DSA or gadolinium-enhanced MRA. When there was no in-stent stenosis or recanalization, the subsequent angiographic evaluation was performed 18 months after treatment (long-term). In the case of recanalization, we either scheduled a retreatment or an earlier angiographic follow-up after cessation of clopidogrel/ticlopidine with continuation of aspirin alone. A last DSA follow-up of longer term was planned ≥5 years after the initial treatment.

| Table 1: Patient profile |
|-------------------------|
| Total No. of patients treated | 468 |
| Age, y | Range 10–96 | Mean 50.1 |
| Sex | Female 302 (64.5%) | Male 166 (35.5%) |
| Presenting symptom | SAH 70 (15%) |
| Location | Anterior circulation 445 (89%) |
| Size | Small 304 (60.8%) |
| Location | Extradural 14 (2.8%) |
| Location | Intradural 226 (45.2%) |
| Location | ACA (A1) 5 (1%) |
| Location | AcomA 93 (18.6%) |
| Location | Distal ACA 11 (2.2%) |
| Location | MCA bifurcation 82 (16.4%) |
| Location | Distal MCA 5 (1%) |
| Location | Posterior circulation 55 (11%) |
| Location | VA intradural 7 (1.4%) |
| Location | PICA 7 (1.4%) |
| Location | Vertebrobasilar junction 3 (0.6%) |
| Location | Basilar artery 22 (4.4%) |
| Location | SCA 3 (0.6%) |
| Location | PCA (P1) 12 (2.4%) |
| Location | Distal PCA 10 (2.4%) |
| Previous treatment | Balloon-assisted coiling 27 |
| Previous treatment | Primary coiling 7 |
| Previous treatment | Onyx embolization 2 |
| Previous treatment | Onyx + coil embolization 1 |

**Table 2: Aneurysm characteristics**

| Total No. of aneurysms treated | 500 |
| Size | Small 304 (60.8%) |
| Location | Large 176 (35.2%) |
| Location | Giant 20 (4%) |
| Location | Location | Anterior circulation 445 (89%) |
| Location | Extradural 14 (2.8%) |
| Location | Intradural 226 (45.2%) |
| Location | ACA (A1) 5 (1%) |
| Location | AcomA 93 (18.6%) |
| Location | Distal ACA 11 (2.2%) |
| Location | MCA bifurcation 82 (16.4%) |
| Location | Distal MCA 5 (1%) |
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| Previous treatment | Balloon-assisted coiling 27 |
| Previous treatment | Primary coiling 7 |
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| Previous treatment | Onyx + coil embolization 1 |

**RESULTS**

The patient characteristics and the aneurysm features are given in Tables 1 and 2. This series included 468 patients (302 female and 166 male), with a mean age of 50.1 years (range, 10–96), harboring 500 aneurysms treated with single stent–assisted coil embolization.

Of the 500 aneurysms, 445 were located in the anterior circulation and 55 were located in the posterior; 304 aneurysms were small (60.8%), 176 were large (35.2%), and 20 (4%) aneurysms were giant.

The presenting symptoms of the aneurysms and the previous treatments of the retreatment cases are given in Tables 1 and 2, respectively. Forty of 70 aneurysms that were ruptured were treated at the acute phase of subarachnoid hemorrhage within 14
Close the aneurysm with stent placement during stent-assisted coil embolization. The stent prolapsed into the aneurysm sac in 2 cases, distally mis-
effect on brain stem aggravated after treatment in 1 patient. Disease-related mortality was caused by severe vasospasm in 2 patients. The overall mortality rate was 1.9% (9/468), including procedure-related mortality rate of 0.8% (4/468) and disease-related mortality of 0.4% (2/468) (Table 5).

Immediate and Long-Term Angiographic Results

Angiographic follow-up was available in 440 patients with 467 aneurysms, with a follow-up rate of 94% of patients and 93.4% of aneurysms. Follow-up data were collected for the aneurysms until April 2012, with a range of 6 months to 7 years (mean, 19.2 months). Thirty-three aneurysms of 28 patients did not have a follow-up because of death (n = 9), loss of communication, or patient refusal. Of the 467 aneurysms, 6-month angiographic follow-up was performed with DSA for 459 aneurysms (98%), and with MRA (2%) for 8 aneurysms. For 409 aneurysms, at least 1 year, and for 190 aneurysms, at least 2 years of follow-up results were obtained.

On the basis of postembolization angiography studies, complete occlusion was achieved in 211 of 500 aneurysms (42.2%). In the remaining 289 aneurysms, there was near complete occlusion in 257 (51.4%) and incomplete occlusion in 32 (6.4%). For the 467 aneurysms that had follow-up examinations, the initial angiographic results were as follows: complete occlusion in 194 aneurysms (41.6%), near complete occlusion in 242 aneurysms (51.8%), and incomplete occlusion in 31 aneurysms (6.6%) (Table 6).

Six-month follow-up angiograms of 467 aneurysms showed complete occlusion in 380 (81.3%), near complete occlusion in 238 (51.4%), incomplete occlusion in 90 (18.9%), stabile occlusion in 14 (3.0%), and recanalization in 38 aneurysms (8.2%) (Table 6). Of the recanalized aneurysms, 5 were giant, 28 were large, and 5 were small.

Of the 38 aneurysms that were recanalized at 6 months, 23 that also showed evident coil compaction were retreated: once in 19 aneurysms, twice in 3 aneurysms, and 3 times in 1 aneurysm.

In the remaining 15 patients with recanalized aneurysms showing no apparent coil compaction (with incomplete occlusion in 11 patients and near complete in 4 patients) at 6 months, clopidogrel was discontinued and 1-year control DSA was scheduled. Further occlusion did not occur in these aneurysms; therefore 11 aneurysms with an occlusion grade of class 3 were retreated. At 2-year control angiography, all these retreated aneurysms showed complete occlusion. Overall, the total number of retreated aneurysms after stent-assisted coiling was 34, and 5 aneurysms had retreatments of >1.

Late recanalization (>6 months) was observed in 8 aneurysms (8/409) (2%) (1–5 years; mean, 2 years). Six-month follow-up of all these aneurysms showed stable occlusion. Of these 8 belatedly recanalized aneurysms, 5 were recanalized in the first year, 2 in the third year, and the remaining 1 in the fifth year. Five of these aneurysms were retreated, and 3 are being followed. Overall, recanalization was observed in 46 aneurysms (9.9%), and mean recanalization time was 9.1 months.

According to the last follow-up data, overall occlusion rates were complete in 424 aneurysms (90.8%), near complete in 35 aneurysms (7.5%), and incomplete in 8 aneurysms (1.7%).

All but 7 stents were shown to be patent during follow-up. Asymptomatic parent artery occlusion was observed in 6 patients (6/467, 1.2%). All 6 of these patients were taking clopidogrel and aspirin as the antiplatelet therapy; 1 patient discontinued his drugs by himself and in 1 patient, another physician discontinued clopidogrel and continued with aspirin alone. One of these patients had significant in-stent stenosis resulting parent artery occlusion with no clinical consequence discovered in the follow-up, despite continued dual antiplatelet therapy. In the remaining patient, parent artery occlusion was due to the procedural thromboembolic complication. Asymptomatic intimal hyperplasia or in-stent stenosis was observed in 4 stents (4/467, 0.8%). Clopidogrel and aspirin were continued in these patients. Two remained stable, 1 improved and 1 occluded during follow-up.

DISCUSSION

Having been reported to be safe and effective in the preliminary experiences and midterm follow-up results, stent-assisted coil embolization has become one of the most preferred techniques. Technological advancements resolved the previously reported
limitations of the first-generation stents; however, long-term patency and safety of neurostents and their durability remains ambiguous.

Recanalization has been one of the leading issues regarding endovascular treatment of intracranial aneurysms. Several studies on comparison of coiling without stent use versus stent-assisted coiling have demonstrated significant superiority of stent-assisted groups in terms of avoiding recanalization and even providing further occlusion. On the contrary, in their series, including 216 consecutive aneurysms with long-term follow-up (mean, 14 months), Piotin et al claimed that stent use is associated with higher mortality and morbidity rates because of increased procedure-related complications. However, their results are controversial because of inclusion of balloon-expandable stents in the study group, which are more traumatic for the arterial wall during navigation and delivery.

In our series, we included only the self-expanding stents. These self-expanding stents can be easily delivered and deployed wherever a microcatheter can be navigated.

Deployment is not a traumatic process. This may explain our lower overall mortality rate of 1.9% (compared with 6% mortality rate in the Piotin et al study), with a rate of procedure-related mortality of 0.8% (versus their rate of 4.6%). Our results are comparable with the series with long-term follow-up in which self-expanding stents were used. Because of the ease of delivery and deployment, the Wingspan stent was used in endovascular treatment of aneurysms instead of Neuroform 3 and when the Solo and Enterprise stent systems were not available in our department.

In our series, the overall stent-related thromboembolic complication rate was 4.2% (major = 1.4%, minor = 2.8%), comparable with 2 large series with long-term follow-up, and favorably lower than those in the large series of Piotin et al and Fiorella et al. Piotin et al reported that thromboembolic complications were also more frequent in the stented patients in their comparative study of coiling versus stent-assisted coiling. However, they found that these complications were higher in the patients treated before antiplatelet activity assessment and diminished when the patients who did not respond to antiplatelet drugs were identified. We think that stent use does not increase the thromboembolic event rate if the dual antiplatelet regimen is used and the response in thrombocyte aggregation level is evaluated rigorously. On the contrary, stents may act as a “lifesaver” in the case of thromboembolic events caused by coil protrusion into the parent artery during endovascular treatment of wide-neck aneurysms. In this series, we used stents in 7 patients to restore the normal patency of the parent artery after a thromboembolic event occurred during a coiling procedure without a stent. All these patients were discharged without neurologic deficits. We did not have a control group of coiling without stent assistance in this study; however, previous comparative studies have shown no increase in the frequency of thromboembolic events with the adjunctive use of these devices.

Recently, long-term safety and durability of stent-assisted coiling with Neuroform and Enterprise stents have been investigated. We previously reported our preliminary experience with Solo and Wingspan stents, including the immediate and midterm follow-ups. In this present series, we aimed at extension of the follow-up durations with the addition of newly enrolled patients treated with a variety of stents and evaluation of the overall long-term angiographic outcomes of endovascular treatment by use of the stent-assisted coiling technique; therefore, we included all self-expanding stent types that we have been using (but not a specific brand) because all these stents are neuro-defined and have had their particular series in the literature.

In our study, 440 patients with 467 aneurysms had follow-up imaging with a follow-up rate of 94%. In our study, initial complete occlusion rate was 42.2% (211/500) overall, and that in the aneurysms with follow-up (n = 467) was 41.6%, which is comparable with previously reported studies of Piotin et al (46.3%) and Santillan et al (42.3%).

In 6-month angiographic follow-up, complete occlusion rate increased to 81.3%; stable and further occlusion rates were 48% and 44%, respectively. The recanalization rate was 8%, which occurred mainly in large and giant aneurysms (87%, 33/38) when compared with small ones (13%, 5/38). All recanalized aneurysms with an incomplete occlusion were retreated immediately or after a second 6-month follow-up. We observed recanalization in the latter controls in only a few aneurysms (1.9%, 8/409).

Overall complete occlusion rate according to the latest follow-up reached the rate of 90.8%, comparable to the Santillan et al series and even favorable to other previous series that give the complete occlusion rates at the latest follow-up. Eventually, incomplete occlusion remained only in 1.7% of all aneurysms. No early or late rebleeds occurred.

On the basis of these findings, we may argue that 1) stent use provides better scaffolding for coils at the aneurysm neck so that better packing may be performed without concern of protrusion into the parent artery; 2) with the help of hemodynamic and biologic mechanisms, stents ensure further aneurysmal thrombosis, resulting in improved occlusion rates; 3) complete and nearly complete initial aneurysm occlusion is associated with high final stable and complete occlusion rates; and 4) most recanalizations occur within 6 months after treatment; therefore, 6-month follow-up is essential to probe the early recanalizations.

The survey of stent patency is another important focus of this study. Asymptomatic parent artery occlusion was observed in 6 patients (1.2%). In 2 of these patients, cessation of dual antiplatelet therapy probably resulted in parent artery occlusion. On the other hand, in-stent stenosis was recorded in 4 (0.8%), a rate comparable to that of Santillan et al (1.3%) but lower than those of Fargen et al and Fiorella et al, with rates of 3.4% and 5.6%, respectively. These patients continued taking clopidogrel and aspirin and they remained asymptomatic. Whereas 2 of 4 patients remained stable, angiographic study revealed spontaneous partial resolution in 1 and total occlusion in the other. Spontaneous resolution of delayed in-stent stenosis was first described by Fiorella et al with the use of Neuroform stents and was postulated to be an event unique to the deployment of a low radial force stent within the cerebrovasculature. However, our patient with spontaneous partial resolution was treated by use of a Wingspan stent, designed to exert active, controlled, outward radial force in ath- erosclerotic lesions; therefore, this cannot be explained solely by low radial force. Nevertheless, being aware of this phenomenon is...
important to follow the patients clinically and angiographically with prolonged dual antiplatelet use and to prevent unnecessary interventions.2,22

CONCLUSIONS
Stent-assisted coiling is a safe, effective, and durable treatment of wide-neck intracranial aneurysms. The use of stents in endovascular treatment provides high rates of complete occlusion and low rates of recurrence at long-term follow-up. Proper dual antiplatelet regimen and antiplatelet activity assessment are the key points in preventing procedure-related thromboembolic complications. Six-month follow-up appears to be crucial in detecting recurrence and in-stent stenosis.

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