Intrasaccular combination of metallic coils and Onyx liquid embolic agent for the endovascular treatment of cerebral aneurysms

H. SARUHAN ÇEKIRGE, M.D., ISİL SAATÇI, M.D., SERDAR GEYIK, M.D., KIVILÇİM YAVUZ, M.D., HALİL ÖZTÜRK, M.D., AND GÜLSÜN PAMUK, M.D.

Departments of Radiology and Anesthesiology, Hacettepe University Hospitals; and Department of Radiology, Sağlık Bakanlığı Ankara Eğitim ve Araştırma Hastanesi, Ankara, Turkey

Object. The aim of this study was to report on a novel technique in which metallic embolization coils were combined with the Onyx liquid embolic agent in the aneurysm sac to achieve a more durable result after endovascular treatment. This therapeutic procedure was performed in selected cases in which, based on the authors’ experiences, either coil embolization or Onyx alone would likely have failed. The authors report long-term clinical and angiographic follow-up results in 20 consecutive intracranial aneurysms treated using this combination for defined indications.

Methods. Twenty aneurysms in 20 patients were treated with a combination of embolic coils and Onyx. Four aneurysms were giant; 13, large; and three, small. This new technique was used when standard Onyx or coil treatment with balloon assistance was determined to involve a higher possibility of recanalization, because either an adjunctive stent insertion could not be performed or the Onyx technique could not be used due to an unsuccessful seal test or intraneurysm balloon prolapse. In one case, an adjunctive stent was placed before coil placement and Onyx deposition to control the material in the sac of the aneurysm, which had a fusiform neck.

All aneurysms were completely occluded after using this technique. No clinical or technical adverse events occurred in any of the cases. Follow-up angiography was performed in all patients: 3-year studies in six patients, 2-year studies in five, and 1-year studies in nine. None of these studies demonstrated aneurysm regrowth or parent artery occlusion.

Conclusions. The combination of the embolic coils and the Onyx liquid embolic agent provides very durable aneurysm occlusion for defined indications.

KEY WORDS • aneurysm • embolic agent • coil embolization • endovascular occlusion
anywhere other than the origin of the anterior choroidal artery. The study consisted of a series of 20 consecutive aneurysms in 20 patients who, after signing informed consent, agreed to receive Onyx treatment and to obey our strict angiographic follow-up protocol. Fourteen patients were female and six were male, with ages ranging from 17 to 54 years. All aneurysms were located in the intradural segment of the ICA; 14 were paraophthalmic and six were located at the posterior wall of the ICA, including lesions of the posterior communicating artery. Four aneurysms were giant (> 25 mm), 13 were large (10–25 mm), and three were small (< 10 mm). All lesions were wide-necked (neck ≥ 4 mm and/or dome-to-neck ratio < 2). One aneurysm had a near-fusiform neck in which an adjunctive stent had been placed before endosaccular coil and Onyx deposition. Seventeen aneurysms were unruptured and three were ruptured; patients with lesions in the latter group had a clinical status of Hunt and Hess Grade I. One patient demonstrated mass effect. Data were collected in all patients before the procedure, at the time of the procedure, at discharge, and at 6 months and 1 year posttreatment. Additional follow-up evaluations at 2 to 3 years posttreatment were performed in some patients. Recorded clinical data included Glasgow Outcome Scale scores, modified Rankin Scale scores, cranial nerve deficits, any adverse events, and any changes in the baseline neurological status.

**Therapeutic Procedure**

The fundamental technique involving the Hyperglide balloon and the Rebar 14 microcatheter (both products of MicroTherapeutics, Inc.) to embolize aneurysms with the Onyx liquid polymer has been previously described. In this paper we describe some technical variations in the use of Onyx, combining it with intrasaccular coils. All patients were treated while in a state of general anesthesia and full systemic anticoagulation with heparin. Use of the coil and Onyx combination was decided during the endovascular operation according to the following criteria.

**Failed Balloon Seal Test.** With the balloon positioned and inflated over the aneurysm neck and the microcatheter placed within the aneurysm, contrast agent is slowly injected to ascertain the extent of aneurysm sealing by the balloon. This so-called seal test must be performed and have a successful outcome to conclude that the Onyx treatment is suitable and depends on two conditions: adequate control of the aneurysm neck by using the inflated balloon and absence of a vessel originating directly from the sac during the seal test. When the vessel is slightly bigger than 4 mm, which is the maximum diameter of the available Onyx-compatible balloon, contrast may leak out, resulting in a failed test (Fig. 1). The seal test can also fail in a parent artery smaller than 4 mm when the aneurysm has a wide neck (Fig. 2). An initial failed seal test was considered a condition predating the coil and Onyx combination for successful endovascular treatment. In such cases, after several 3D coils were placed in the aneurysm with balloon assistance, the seal test was repeated. If the coil mesh controlled flow into the aneurysm sac, subsequent sealing of the aneurysm was achieved. Onyx HD 500 (MicroTherapeutics, Inc.) could then be injected into the aneurysm sac by using standard procedures.

**Substantial Parent Artery Involvement.** As large or giant aneurysms grow, the neck composes an increasing proportion of the parent vessel wall’s circumference. In our experience with Onyx in treating aneurysms, we demonstrated that there was still a considerable rate of aneurysm regrowth, especially when the lesions were large or giant and adjunctive stent placement could not be performed. Thus, in large or giant aneurysms with substantial circumferential parent artery involvement and with necks in which a stent could not be placed, the coil and Onyx combination was utilized, even if the seal test was successful, either to reinforce the intraaneurysm embolic cast or to better control the liquid embolic agent in the sac for more effective reconstruction of the parent artery at the lesion neck (Fig. 3).

**Balloon Prolapse Into the Aneurysm Sac During the Seal Test.** In some cases, the balloon inflated across the aneurysm neck may prolapse into the aneurysm sac, resulting in a successful seal during the test. This complication points to one of the limitations of the balloon sealing technique: the prolapsed balloon may prevent total closure of the aneurysm and reconstruction of the lesion neck, and thus lead to aneurysm regrowth if a stent cannot be placed in the neck. In such cases, multiple 3D coils could be placed in the aneurysm sac to create a coil bridge across its neck, thereby preventing further balloon prolapse and achieving a successful aneurysm seal with less balloon inflation. Subsequently, Onyx could be injected to complete the reconstruction (Fig. 4). Note that the prolapse of the balloon may also cause a failed seal test. The coil and Onyx combination can also be used in that context not only for better reconstruction at the neck, but also for better control of the liquid embolic agent in the aneurysm sac.

In one case in the present study, despite prior placement of a stent, the coil and Onyx combination was used to control the embolic agent in the sac of the aneurysm, which had a fusiform neck. Coils were inserted to create a barrier preventing the Onyx from leaking through the outflow of the aneurysm where the anterior choroidal artery was seen in proximity (Fig. 5).

Immediately after treatment, cranial computed tomography scans were obtained to rule out intracranial hemorrhage in all patients. The anticoagulation regimen was as follows: 1) intravenous heparinization, continued until the day after the procedure; 2) clopidogrel, loading dose of 300 mg administered immediately after embolization and followed by 75 mg daily; and 3) oral acetylsalicylic acid, 300 mg daily for at least 6 months, as previously described. The angiographic follow-up evaluation at 6 months posttreatment, the clopidogrel could be ceased. Follow-up catheter angiography was performed at 6 months and 1 to 3 years posttreatment.

**Results**

All aneurysms in this study were completely occluded after using the featured technique. No clinical or technical adverse event occurred during or after any of the procedures, and all patients were discharged home with no neurological sequelae. No adverse effects were related to the intraarterial dimethyl sulfoxide infusion, as reported previously. Follow-up angiography studies were performed according to a strict protocol in all patients. Results to date include 3-year results in six patients, 2-year results in five, and 1-year re-
results in nine. None of the patients showed aneurysm regrowth. No spontaneous parent artery occlusion was observed on the follow-up angiograms. In one patient who had presented with sixth cranial nerve palsy due to mass effect of the aneurysm, complete recovery was observed at the 4-week posttreatment clinical evaluation.

Discussion

It is still difficult or impossible to treat some patients with complicated, wide-necked large or giant aneurysms by using coil embolization, despite recent advances in the procedure. Gruber and colleagues achieved a 71% rate of complete or subtotal coil occlusion of large and giant aneurysms. However, these authors noted the requirement for multiple endovascular procedures given that the single endovascular treatment success rate was only 12.5% for giant and 31% for large aneurysms. Sluzewski and colleagues reported incomplete occlusion in 69% (20 of 29) of large or giant aneurysms at the follow-up evaluation. In addition, 12 (41%) of 29 aneurysms remained incompletely occluded after repeated endovascular treatment; these lesions then required surgical treatment or parent vessel occlusion. Murayama and associates reported 40 and 26% complete occlusion at the end of the treatment, and recanalization rates of 35 and 59.1% in large and giant aneurysms, respectively.

Stents have been used in association with coils to treat aneurysms that cannot be treated with simple coil insertion or balloon-assisted coil embolization to achieve more stable aneurysm occlusion. Nonetheless, there is still a considerable rate of incomplete occlusion with stent and coil combinations, resulting in recanalization rates of approximately 20% on follow up. The stents used in the aforementioned studies were balloon-expandable coronary stents. Self-expandable nitinol stents dedicated to neurovascular systems have been widely used, and the first clinical results have been reported. Note, however, that there have been no published mid- or long-term results for self-expandable stent–assisted coil occlusion of large or giant aneurysms.

Surface-modified coils have been developed to solve the problem of recanalization and to provide a more durable result. To our knowledge, however, no data on the mid- or long-term results in large or giant aneurysms have demonstrated the effectiveness of this therapeutic alternative.

The Onyx liquid embolic system is intended for full reconstruction of the parent vessel wall and permanent closure of the aneurysm. Its use for cerebral aneurysms, especially those located at the ICA, with and without a stent, has been reported on in the literature. In these studies, authors have shown that Onyx can produce very durable aneurysm occlusion in patients with difficult, wide-necked large or giant intracranial aneurysms in which other endovascular techniques are likely to fail and in which surgery carries substantial morbidity. According to data from the prospective CAMEO study, the clinical results and complication rates of endovascular aneurysm treatment with Onyx appear to be comparable to other endovascular techniques in similar patient populations. However, the final complete occlusion rate of 79% appears to be significantly better than those reported for large and giant aneurysms after coil treatment.

In our recently published study with long-term clinical and angiographic data from the largest single-center experience, the complete occlusion rate was 87.5% at the 3- to 6-month posttreatment evaluation and 93% at the 12-month evaluation including six retreatments. Note, however, that
there is an important difference between this single-center analysis and the CAMEO study. Our study included carotid artery–ophthalmic artery and posterior wall ICA aneurysms that could be embolized with coils and required balloon remodeling for endovascular treatment. In fact, our study had a much greater percentage of these small aneurysm types than did the CAMEO trial, which included 80% large or giant aneurysms (as opposed to the 35% in our study). The net result was a higher overall complete occlusion rate than that in the CAMEO study.

In addition, we reported very durable results, with a 0% recanalization rate in the group of aneurysms that could be embolized with coils and required balloon remodeling for endovascular treatment. In fact, our study had a much greater percentage of these small aneurysm types than did the CAMEO trial, which included 80% large or giant aneurysms (as opposed to the 35% in our study). The net result was a higher overall complete occlusion rate than that in the CAMEO study.

Although excellent long-term results have been published for stent and Onyx combinations in large or giant aneurysms, the availability of stents that can be satisfactorily placed into the intracranial circulation has been limited because of the stiffness of these devices. There have been significant improvements in stent technology in recent years, and new flexible self-expanding stents that can be delivered via a microcatheter are becoming more widely used. An unresolved issue is the fact that these stents have a very low radial force, which may not allow for complete reconstruction of the diseased and missing parent artery wall. Moreover, the technical features of currently available self-expandable stents may interfere with balloon use, which is an inherent part of Onyx treatment. Because these stents are not as stable as the balloon-expandable stents in the vessel wall, given their low radial force, placement of the balloon may easily dislodge the stent immediately.
ately after its activation. Although Onyx aneurysm treatment can be performed after waiting some period of time from the day of stent insertion, we find this solution to be risky given that the patients need to be kept on anticoagulation therapy, despite open aneurysm sacs.

During the evolution of the Onyx technique in complicated, wide-necked large or giant aneurysms in which stents cannot be inserted adjunctively, crescentic reconstruction around the parent artery with the Onyx material was attempted. Note, however, that even after such reconstructions of the parent artery were achieved using Onyx, aneurysm regrowth (69%) necessitating further treatment was still observed. Based on this clinical experience, we concluded that better intrasaccular reinforcement was needed in addition to the Onyx reconstruction of the parent artery at the aneurysm neck.

We determined that a combination of coils and Onyx in the aneurysm sac might address this problem. Note that coils create a scaffold within the aneurysm sac. This scaffold not only reinforces the intraaneurysm coil-and-Onyx cast but also better controls the liquid embolic agent in the lesion sac for more effective reconstruction of the parent artery at the neck.

In more complicated cases in which the balloon prolapses into the aneurysm sac during a seal test inflation, multiple 3D coils can be placed in the aneurysm sac to form a coil bridge across the neck, which requires less balloon inflation to achieve a successful seal and prevents further balloon prolapse during intraaneurysm Onyx injection. In this technique, coils are used as an intraaneurysm reconstruction device at the lesion neck, thus confirming the Onyx liquid embolic system as an alternative to stents (Fig. 4). As demonstrated in one anecdotal case in this study, coils can be combined with the liquid embolic agent in the aneurysm sac even after a stent has been placed across the lesion neck. This strategy provides better control of the liquid embolic agent in the aneurysm sac, especially in critical anatomical locations.

Despite the highly complicated endovascular cases in the present study, no aneurysm has recurred at the 1- to 3-year angiographic follow ups. In fact, it has been very encouraging to have not a single regrowth during the follow-up evaluation of 17 large or giant paraophthalmic and posterior wall ICA aneurysms, which typically have a very high rate of regrowth (Figs. 2 and 3).

In our experience the third indication for the coil and Onyx combination is small, wide-necked carotid artery–ophthalmic artery or posterior wall ICA aneurysms that fail the initial seal test. In these cases the use of intrasaccular coils makes the Onyx treatment possible. In such cases several 3D coils are placed in the aneurysm with balloon assistance, and the seal test is repeated. Because the coil mesh creates flow control in the aneurysm sac, the seal test becomes successful, and the Onyx treatment can be applied (Fig. 1). In this particular group of patients, the Onyx liquid embolic system provides very durable results, as previously reported in another of our studies in which a 0% regrowth rate was documented in 63 such ICA aneurysms with at least 1 year of follow-up angiography data.

**Conclusions**

In summary, the very durable results obtained in this small series of lesions are very encouraging, and thus we have started treating an increasing number of large or giant wide-necked aneurysms by using a combination of intrasac-
Metallic coils and Onyx liquid for treatment of cerebral aneurysms

Fig. 5. Angiograms demonstrating the treatment course for a partially thrombosed, wide-necked caroticoophthalmic artery aneurysm that had caused a subarachnoid hemorrhage. A and B: Note the fusiform dilation of the ICA and the proximity of the aneurysm outflow to the anterior choroidal artery origin (arrowheads in B). C: Successful seal test after stent activation. D: Although the seal test was successful, three 3D coils were placed in the sac to create a barrier at the aneurysm outflow to control the Onyx within the sac. E: Complete occlusion of the aneurysm as well as perfect reconstruction and remodeling of the fusiformly diluted ICA 1 year after treatment with stent, coils, and Onyx.

References

12. Lylyk P, Ferrario A, Pasbon B, Miranda C, Doroszuk G: Buenos Aires experience with the Neuroform self-expanding stent for the


Manuscript received December 14, 2005. Accepted in final form April 20, 2006.

Address reprint requests to: Isil Saatci, M.D., Hacettepe University Hospital, Radiology Department, Sihhiye 06100, Ankara, Turkey. email: cekirgesaatci@superonline.com.