Initial Experience of Coil Embolization for Unruptured Intracranial Aneurysm Combined with Neuroform Atlas and Undersized Flexible Coils

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Objective: Intraprocedural rupture (IPR) is a rare complication that can occur during endovascular treatment (EVT) of unruptured intracranial aneurysms (UIAs). However, it leads to high morbidity and mortality rates. Others have showed that coil flexibility is a risk factor for IPR. Neuroform Atlas (NA) stents can be deployed with 0.0165-inch microcatheters to enable stent assisted coiling (SAC) with a high likelihood. Undersized flexible coils can be inserted initially during SAC. This study aimed to determine whether SAC using NA and highly flexible coils for UIAs can be conducted without IPR.

Methods: We retrospectively analyzed nine consecutive patients (mean age, 73.2 years; female, n = 6) who underwent SAC for UIAs combined with NA stents and undersized flexible coils between January 2017 and December 2019. Two aneurysms were located at the internal carotid artery (ICA), and one each was located at the ICA-posterior communicating, anterior communicating, middle cerebral, vertebral, vertebra-posterior inferior cerebral and basilar arteries. The mean size of the aneurysms was 4.6 (range, 3.1–8.6) mm. SAC proceeded using the jailing technique. All coils were selected from among the most flexible coils available. We retrospectively assessed technical success rates, aneurysm occlusion at final digital subtraction angiography (DSA), volume embolization ratios (VERs), rates of IPR and symptomatic stroke within 30 days, angiographic findings of aneurysm occlusion at 3 months post-procedure and late adverse events (frequency of aneurysmal rupture, ipsilateral ischemic stroke, and retreated targeted aneurysms).

Results: The technical success rate was 100%. Complete occlusion (CO) was immediate in 8 (89%) patients and a neck remnant persisted in 1 (11%). No IPR or symptomatic stroke developed within 30 days. During a mean follow-up period of 11.8 months, CO persisted in 8 (89%) patients. No late adverse events occurred.

Conclusion: The early clinical and angiographic findings of SAC for UIAs combined with an NA stent and undersized flexible coils were favorable for this series.

Keywords ▶ unruptured intracranial aneurysm, Neuroform Atlas, coil embolization

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Received: March 26, 2020; Accepted: July 20, 2020

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Introduction

Intraprocedural rupture (IPR) is a rare complication that can occur during endovascular treatment (EVT) of unruptured intracranial aneurysms (UIAs). However, it leads to high morbidity and mortality rates.¹⁾ The rates of IPR for UIAs in the Japanese Registry of Neuroendovascular Therapy (JR-NET) and JR-NET2 during 2007 and 2010 using any adjunctive technique except a Flow Diverter, was 1.4% per aneurysm and procedure.²⁾ Lamano et al.³⁾ also reported that the force on the aneurysm wall associated with coil insertion is typically associated with coil flexibility. This could indicate that coil flexibility, the first in particular, is a risk factor for IPR. According to Murayama et al.,⁴⁾ aneurysm perforation is more likely to be fatal when it occurs during the early

Table 1 The characteristics of the patients and aneurysms

	Age	Gender	Aneurysm size (mm)	Neck width (mm)	Dome-to-neck ratio	Aneurysmal location
Case 1	83	Male	8.2	6.1	1.34	MCA
Case 2	77	Female	7.7	7.7	1.0	ICA
Case 3	81	Female	3.2	3.5	0.62	A-com
Case 4	79	Female	3.1	2.1	1.38	VA-PICA
Case 5	78	Female	4.6	3.3	0.85	BA
Case 6	39	Female	6.1	5.0	1.22	ICA
Case 7	76	Female	4	2	2.0	VA-PICA
Case 8	76	Male	4.9	4.1	1.2	VA
Case 9	76	Male	3.1	2.9	0.9	ICA-Pcom

Aneurysmal Location: A-com: anterior communicating artery; BA: basilar artery; ICA: internal carotid artery; ICA-Pcom: ICA-posterior communicating artery; MCA: middle cerebral artery; VA: vertebral artery; VA-PICA: vertebral artery-posterior inferior cerebral artery

phase of EVT. Thus, IPR with the first coil must be avoided as it universally leads to life-threatening outcomes.⁵⁾

The Neuroform Atlas (NA) stent (Stryker, Kalamazoo, MI, USA) was approved in Japan during 2017. This is the first low-profile open-cell stent with a hybrid design. It has closed cells at the proximal ends to improve stability within the vessel and facilitate micro catheter re-crossing, and a central open-cell design to improve wall apposition and flexibility. Because the NA stent can be delivered through a 0.0165-inch microcatheter and has good wall apposition and stability, complex UIAs with a parent vessel that is difficult to access due to tortuosity or a small diameter can be treated by stent-assisted coiling (SAC). Thus, a stiff framing coil is not necessarily required for SAC as the stent covers the aneurysmal neck to avoid coil protrusion into the parent artery. Highly flexible coils can be inserted during SAC as the first coil. The safety and outcomes of EVT of UIAs combined with NA and undersized flexible coils have yet to be assessed. The present study aimed to determine whether SAC using NA and undersized flexible coils to treat UIAs could avoid IPR and result in favorable occlusion outcomes.

Materials and Methods

Patient population

Among 34 patients with a total of 34 unruptured aneurysms that were treated by coil embolization at our hospital between January 2017 and December 2019, we retrospectively analyzed data from nine consecutive patients who had aneurysms (mean age, 73.2 years; range, 39–81; female, $n = 6$) that were embolized using NA stents and undersized flexible coils. All patients were assessed by diagnostic digital subtraction angiography (DSA) before the procedure to

evaluate the morphovolumetric characteristics of the aneurysms. Treatment of UIAs in our center is performed after careful assessment of perceived risk factors for rupture. Neurosurgeons and neuro-radiologists discuss the decision of coiling or clipping. Inclusion criteria for SAC were as follows: (1) wide-necked saccular aneurysm, defined as an aneurysm with a neck dimension ≥ 4 mm or a dome-to-neck ratio < 2 ; (2) parent vessel diameter ≥ 2 mm; and (3) morphology or size of the aneurysm considered to indicate difficulty of treatment using balloon remodeling techniques. The mean aneurysmal size and dome-to-neck ratios calculated from DSA findings were 5.0 ± 1.8 (range, 3.1–8.2) mm and 1.19 ± 0.40 (range, 0.6–2.0). Two aneurysms were located in the internal carotid artery (ICA) and one each was located in the ICA-posterior communicating, anterior communicating, middle cerebral, vertebral, vertebral-posterior inferior cerebral (VA-PICA) and basilar arteries. **Table 1** shows the list for the baseline characteristics of the patients and aneurysms. Ethical approval was obtained from the institutional review board at our hospital (Approval No. 1003) and written informed consent was obtained from all patients before undergoing the procedures.

Antiplatelet therapy

All patients underwent dual-antiplatelet therapy (DAPT) for 14 days before the endovascular procedure with a loading dose of acetylsalicylic acid (ASA) 300 mg and clopidogrel (CLP) 300 mg on day 1 followed by ASA 100 mg and CLP 75 mg from day 2. We tested platelet function using the Verify Now assay system (Accumetrics, San Diego, CA, USA) to ensure a good response to ASA and CLP at 7 days before the procedure. A good response was defined as ≤ 550 aspirin reaction units (ARU) and ≤ 200 P2Y₁₂ reaction units (PRU). Hypo-responders (PRU ≥ 200) to CLP were switched

from CLP to prasugrel (20 mg) on day 1 and maintained on 3.75 mg/day or cilostazol 200 mg/day. The patients were continued on DAPT for 1 month post-procedure and single-antiplatelet therapy was continued for at least two months until follow-up assessment by DSA as described.⁶⁾

Endovascular procedures

All procedures were conducted under general anesthesia. The femoral artery was accessed through an 8Fr long sheath. Systemic heparinization (100 IU/kg) was initiated immediately after a femoral introducer sheath was inserted and activated clotting time (ACT) was maintained at 250–300 s. An 8Fr or a 6Fr guide catheter was placed proximally into the internal carotid or vertebral artery. A 6F distal access catheter was navigated to the petrous or cavernous sinus portion of the ICA if anterior circulation was found. A microcatheter was placed into the aneurysmal sac, then a 0.014 neurovascular microguidewire was crossed over the aneurysmal neck using an Excelsior SL-10 microcatheter (Stryker). An NA stent was deployed across the aneurysmal neck with a jailed intra-aneurysm microcatheter. The stent size was selected based on the size of the parent artery determined by diagnostic DSA. The aneurysm was coiled with a flexible coil via the jailed microcatheter in the same series. All coils were selected from one of the most flexible coil series (HyperSoft) produced by one manufacturer (MicroVention, Aliso Viejo, CA, USA) and Axiom Prime Extra Soft (Medtronic, Dublin, Ireland). How to choose the size and length of coils was as follows: when the maximum diameter of the aneurysm was larger than 5 mm, we chose as the first coil at least 2 mm smaller coil diameter than the maximum diameter and the longest coil among the same diameter coils we had chosen. When the maximum diameter of aneurysm was smaller than 4 mm, basically we chose 2 mm × 4 cm or 3 cm coil. Then, the aneurysm was coiled with 2 mm × 2 cm as much as possible until the jailed microcatheter dropped out of the aneurysmal neck or just before coils protruded into the parent artery. When it was difficult to be coiled with 2 mm × 2 cm, we chose 1.5 mm × 2 cm or 1 mm × 2 cm. Our strategy of coil selection was similar to the so-called piecemeal technique.⁷⁾

Endpoints and definitions

The primary endpoints were periprocedural outcomes within 30 days. We also assessed technical success rates, aneurysm occlusion using the Raymond–Roy Occlusion Classification (RROC) at final DSA, volume embolization

ratios (VERs) and complication rates (frequency of IPR and ipsilateral symptomatic stroke). Technical success was defined as successful placement of NA for targeted aneurysmal neck and placement of coils into the aneurysmal sac. Aneurysm occlusion was classified according to RROC as complete occlusion (CO), residual neck (NR), and residual aneurysm (RA). An expert neuroradiologist who was not involved in the procedures retrospectively assessed the RROC data. The VER was calculated using: $V_{\text{coil}}/V_{\text{aneurysm}} \times 100(\%)$ [$V_{\text{coil}} = \pi \times (p/2)^2 \times L$ and $V_{\text{aneurysm}} = 4/3\pi \times \text{length}/2 \times \text{width}/2 \times \text{height}/2$, where p is the primary diameter of the coil and L is the coil length as described⁸⁾]. Symptomatic stroke was defined as a neurological deficit that persisted for >24 hours. Secondary endpoints were late outcomes from 30 days after the procedure (follow-up). We assessed aneurysm occlusion classified by the RROC using DSA 3 months after the procedure and the rate of adverse events (frequency of aneurysmal rupture, ipsilateral stroke, and re-treated targeted aneurysms).

Results

Table 2 shows the list of the procedure characteristics and periprocedural outcome. The technical success rate was 100% (**Fig. 1C–1F**). The NA stents were appropriately deployed except one patient whose aneurysm was located at VA-PICA. In this case, the first stent was migrated to proximal neck of the aneurysm, then additional stent was placed appropriately. Coils were placed in all aneurysms. Axiom Prime Extra Soft and HyperSoft coils were placed in two and seven aneurysms, respectively. The jailing technique was applied during all procedures. The sizes of the deployed NA stents were 3.0 × 21 (n = 2), 4.0 × 21 (n = 6), and 4.5 × 21 (n = 1) mm, respectively.

CO was immediate in eight (89%) patients (**Fig. 1G**), and an NR remained in one (11%). No RA, IPR or symptomatic stroke occurred and the VER was 55.8% ± 13.9%.

During a mean follow-up period of 11.8 (range, 4–30) months, CO was achieved in eight patients (**Fig. 1H**), with NR remaining in a patient at the time of follow-up DSA to assess aneurysm occlusion. No major adverse events developed.

Discussion

Outcome and follow-up data for treatment of intracranial aneurysms using NA stents in the present and several other

Table 2 The characteristics of the procedure and periprocedural outcome

	Coil series	NA stent dimensions (mm)	Technical success	RROC	IPR	VER (%)
Case 1	AP	3.0 × 21	Yes	NR	No	32
Case 2	AP	4.0 × 21	Yes	CO	No	57.6
Case 3	HS	3.0 × 21	Yes	CO	No	40.7
Case 4	HS	4.0 × 21	Yes	CO	No	49.7
Case 5	HS	4.0 × 21	Yes	CO	No	77
Case 6	HS	4.0 × 21	Yes	CO	No	54
Case 7	HS	4.0 × 21	Yes	CO	No	57.6
Case 8	HS	4.0 × 21	Yes	CO	No	56.1
Case 9	HS	4.5 × 21	Yes	CO	No	76.7

Coil series: AP: Axiom Prime Extra Soft (Medtronic); HS: Hyper Soft (Terumo); NA: Neuroform Atlas; RROC: Raymond—Roy Occlusion Classification; CO: complete occlusion; NR: residual neck; RA: residual aneurysm; IPR: intraprocedural rupture; VER: volume embolization ratio

Fig. 1 Representative coil embolization with jailing technique combined with NA stent and flexible coil. The patient was 39-year-old female and was incidentally pointed out right ICA aneurysm with magnetic resonance imaging. **(A)** Diagnostic three-dimensional DSA shows the length of the aneurysm was 6.1 mm (large white double-headed arrow), that was the maximum diameter. The width of the aneurysm is 2.7 mm (small white double-headed arrow). **(B)** Diagnostic three-dimensional DSA shows the height of the aneurysm was 3.0 mm (white double-headed arrow). **(C)** Pretreatment right carotid angiography for unruptured right ICA aneurysm. **(D)** Unsubtracted image. Right carotid angiography shows neuroform atlas stent (black arrowhead) covering aneurysm neck appropriately jailed with microcatheter (white arrow head) for emboliza-

tion. **(E)** Unsubtracted image. Right carotid angiography shows that first HyperSoft® coil (4.0 mm × 8 cm) is selected. First coil is placed without coil protrusion into parent artery (black arrow). **(F)** Right carotid angiogram demonstrates CO with tight packing (white arrow) using 9 coils (4.0 mm × 8 cm [n = 1], 3.0 mm × 4 cm [n = 1], 2.5 mm × 4 cm [n = 1], 2.0 mm × 4 cm [n = 4], 1.5 mm × 2 cm [n = 1], and 1.0 × 2 cm [n = 1] mm, respectively). The measurement of volume embolization ratios is 54%. The postoperative course was uneventful. The patient discharged a week after treatment without any complication. **(G)** Follow-up DSA at 3 months post-procedure demonstrates that occlusion remains complete without any symptoms (white arrow). CO: complete occlusion; DSA: digital subtraction angiography; ICA: internal carotid artery; NA: Neuroform Atlas

studies are summarized in **Table 3**. Although long-term occlusion and a need for retreatment are important outcomes of EVT for UIAs, avoiding IPR that leads to life-threatening

outcomes is most important.⁵⁾ Focusing on IPR, A wide spectrum of IPR rates have been reported, and it is currently estimated to be between 1% and 5%.^{9,10)} Pierot et al.⁹⁾

Table 3 Summary of follow-up and outcome data for treatment of intracranial aneurysms using Neuroform Atlas stents

Authors, year	Number of aneurysm*	Technical success†	Peri-Procedure Outcome			Follow Up Outcome‡		
			Occlusion classification	Complications	Ischemic stroke	Occlusion classification	Retreatment	
			RROC1	RROC2	IPR	RROC2		
Goertz et al., 2019 ⁽²⁾	37	100% (37/37)	84% (31/37)	16% (6/37)	0% (0)	81% (21/26)	12% (3/26)	8% (2/26)
Caralano et al., 2019 ⁽³⁾	113	100% (113/113)	88% (99/113)	9% (10/113)	0% (0/113)	82% (93/113)	13% (14/113)	0% (0/113)
Present series	9	100% (9/9)	89% (8/9)	11% (1/9)	0% (0/9)	89% (8/9)	11% (1/9)	0% (0/9)

*Includes unruptured and ruptured aneurysms. †Technical success is defined as successful placement of Neuroform Atlas stent for targeted aneurysmal neck and placement of coils into aneurysm sac. ‡Different follow-up durations. Ulfelt C et al., 6 months; Jankowitz BT et al., 12 months; present series, 3 months. IPR: intraprocedural rupture; RROC: Roy-Raymond Occlusion Classification

reported in the prospective multicenter study the rate of IPR at SAC was 1.7% (1/57). In addition, a retrospective analysis of 1312 patients with an UIA by Li et al. found a lower risk of IPR with, than without stent deployment,⁽¹¹⁾ indicating that SAC would be as a regarding adjunctive technique from the perspective view of preventing IPR.

In *in vitro* experiments, Lamano et al.⁽³⁾ showed that framing coil deployment could potentially increase the force acting on the aneurysmal wall. This indicated that IPR is associated with coil flexibility, particularly with that of framing coils that tend to be stiff. Firm framing coils are not necessarily required under a neck bridge stent. Although flexible first coils can be used to avoid IPR, the outcomes of SAC with flexible coils have not been assessed as far as we can ascertain. Therefore, this present study was conducted and showed no IPR occurred in all cases.

The present and several other studies have found that NA stents were correctly deployed with 100% technical success.^(12,13) Aydin et al.⁽¹⁴⁾ reported a 97.5% technical success rate of using Leo Baby stents for SAC, Poncyłjusz et al.⁽¹⁵⁾ had a 91% technical success rate with LVIS/LVIS Jr. stents, and Mocco et al.⁽¹⁶⁾ described correct deployment of an Enterprise stent in 95% of patients. The rates of technical success for other low-profile or microstent series were similar, but not 100%. SAC with flexible coils is inevitable for stent placement. NA was suitable stent for SAC with flexible coils. Then, stent design might be one cause of these differences. The NA stent has an open- and closed-cell design, which is supposed to offer the advantages of both cell types, unlike previous stents. Cay et al.⁽¹⁷⁾ reported that open-cell stents should be characterized by relatively low radial force, good wall coverage, and low bending stiffness. A cell stent with a closed design provides stable adherence to the vessel wall. Furthermore, foreshortening is negligible for laser-cut stents, which allows for accurate placement. On the other hand, braided stents have the disadvantages of foreshortening and the possibility of an hourglass configuration during deployment, which results in incomplete neck bridging. However, stent migration occurred in one case of right VA-PICA aneurysm which stent placement was attempted from the right PICA to the right VA to spare PICA. In this case, the angle between the right PICA and the right VA was <80°, and the difference of diameter between right PICA and the right VA was about five times. The cause of stent migration may be associated with these factors. Furthermore, the NA is compatible with good accessibility, allowing deployment with conventional coiling with 0.0165-inch microcatheters. These advantages might result

in excellent outcomes of even higher technical success rates. Although none of the coils unraveled in our patients, coils can unravel during stent-assisted procedures.¹⁸⁾ Because coils can become trapped in intracranial-stent struts regardless of stent design, physicians should consider the possibility of coil unraveling during embolization.

Goertz et al.¹²⁾ and Caragliano et al.¹³⁾ achieved immediate CO in 84% and 88% of aneurysmal occlusions, respectively, using NA, and 81% and 82% occlusion rates at 6 and 12 months of follow-up, respectively. We achieved immediate CO in 89% of aneurysmal occlusions (**Table 3**). These results were favorable compared with those for braided stents. A recent study achieved immediate CO in 85% of 78 patients treated with LVIS stents and 82% CO at 6 months of angiographic follow-up. Our CO at 3 months of angiographic follow-up was 89%. Retreatment rates in the two series of patients who were treated with NA^{12,13)} were 2 (7.7%) of 26 and 0 (0%) of 112, respectively. The RROC status was intraoperative aneurysm remnant in two patients, and secondary SAC achieved CO. None of the patients treated with NA in the one series¹²⁾ who had a neck remnant required retreatment. None of our patients had an aneurysm remnant, which might be associated with the 0% retreatment rate. We assume that the long-term outcomes for our patients would be favorable compared with previous findings.

The rates of ischemic stroke complications were 2.7%–6.2% among the series of patients treated with an NA.^{12,13,19)} None of our patients were complicated with ischemic stroke, perhaps because of how we managed antiplatelet therapy. The rates of morbidity and mortality including subarachnoid hemorrhage (SAH) in other NA series were 0%–3.3% and 0%–2.65%,^{12,13,19,20)} and were both 0% in one NA series with UIA.¹⁹⁾ Morbidity was associated with peri-interventional thromboembolic events, in which in-stent occlusion did not occur due to rupture. Mortality was mainly associated with the severity of SAH. No intraprocedural hemorrhage was reported. Among patients with UIA, permanent neurological deficits did not arise due to the interventions, and neurological death did not occur. The morbidity and mortality rates were 3.0% and 1.0% for the LVIS Jr stents, respectively,²¹⁾ and 1.4% and 0% for LVIS stents, respectively.²²⁾ The SAC using NA and the most flexible coils seems less complicated as morbidity and mortality did not arise in the present study.

Yagi et al.²³⁾ significantly associated a high VER with low recurrence of coil embolization. This study found that the recanalization rate of 57 aneurysms at 6 months after coil embolization was significantly lower in a group with a high

(≥25%) than a low (<25%) VER (2 [8%] of 25 vs. 21 [66%] of 32). The VER in the present study was 55.8%, which was twice as high as the reported optimal VER cutoff to reduce recanalization of 20%–25%.^{24,25)} None of our patients required recanalization, but they were assessed by DSA at only 3 months after the procedure. The higher VER in the present study might be associated with long-term stability.

In conclusion, the initial experience of SAC combined with an NA stent and undersized flexible coils to treat UIA resulted in complete technical success, no complications, high rates of complete periprocedural occlusion, and follow-up compliance. However, larger samples and longer-term follow-up should be needed to determine durability and the need for retreatment.

Limitations of the Study

This retrospective study included a small patient cohort and a short follow-up period. Late rebleeding and repeated treatment should be assessed during a longer follow-up period.

Conclusion

SAC for UIA using an NA stent and undersized flexible coils was associated with favorable early clinical outcomes and angiographic results.

Ethical Approval

All study patients signed a written authorization allowing access to their medical records for research purposes, and our institutional review board approved the research protocol (No. 1003).

Informed Consent

Written informed consent was obtained from all patients who participated in the study.

Disclosure Statement

The authors have no conflicts of interest to declare.

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