

Long-term angiographic follow-up of intracranial aneurysms treated with the intracranial neuroform stent reconstruction.

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Abstract

Introduction: The long-term results of intracranial aneurysms treated with a Neuroform stent have been not reported. This study was to investigate the long-term evolution of intracranial aneurysms treated with the Neuroform stent and in-stent stenosis.

Materials and methods: Fifty-one patients with sixty-four intracranial aneurysms underwent Neuroform stent deployment over ten years. Angiographic data were compared before treatment and at each follow-up.

Results: Forty-six aneurysms were treated with stent-assisted coiling while eighteen with stent deployment alone, with a total procedure-related complication rate of 6.7%. Immediate occlusion of the forty-six aneurysms with stent-coiling was complete in thirty-four aneurysms (73.9%), near complete in ten (21.7%) and incomplete in two (0.4%). During follow-up of 89 months (mean 52), twenty-three (71.9%) of 32 aneurysms with initial complete occlusion and follow-up remained completely occluded while nine (28.1%) recurred. Among ten aneurysms with initial near complete occlusion, one remained unchanged, four recurred and were re-treated to complete occlusion, and the other five had progressive thrombosis to complete occlusion. All fifteen aneurysms with stenting alone decreased in size with eight aneurysms completely disappeared. Progressive thrombosis occurred in twenty-two cases (81.5%) and of forty-two aneurysms with complete or near complete occlusion, recurrence occurred in thirteen cases (31%). Mild asymptomatic in-stent stenosis was present in three cases (5.3%).

Conclusion: Stent reconstruction is safe in treating intracranial aneurysms with mild in-stent stenosis rate at long-term follow-up.

Keywords: Intracranial aneurysm, Intracranial stent, Parent artery reconstruction, In-stent stenosis, Long term.

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Introduction

In the therapy of wide-necked intracranial aneurysms, stents have been used to support coil embolization and offer significant advantages, with the applied stents firstly being stiffer coronary stents and later a more flexible, ultrathin, self-expanding Neuroform stent (NF, Stryker Neurovascular, Fremont, CA, USA) [1].

The stent is constructed of nitinol and has diameters ranging from 2.5 mm to 4.5 mm and lengths ranging from 10 mm to 20 mm. The interstices of the deployed stent vary from 2.0 F to 2.5 F, allowing the placement of a micro catheter through the stent into the aneurysm.

The radial force exerted by the stent is minimal at 10 mm Hg which may reduce injury to the vessel wall. In contrast to the previously used coronary balloon-mounted stents, the NF stent

is easier to pass through tortuous cerebral vasculature and has enabled the treatment of aneurysms in previously unreachable vessels [2-5]. Some studies have reported the short and median term results of the NF stent in treating intracranial aneurysms [6-9].

However, little is known about the long-term interaction of the stent with the parent artery wall and the evolution of the coiled aneurysms. It is not clear whether or not the stent will induce neointimal hyperplasia and subsequent luminal loss or stenosis as in coronary interventions while at the same time obliterating the intracranial aneurysms.

This study was to investigate the long-term occlusion results of wide-necked intracranial aneurysms treated the NF stent reconstruction of the parent artery with or without subsequent coiling and the in-stent stenosis.

Materials and Methods

Patient population

In the period between Jun 2004 and Jul 2014, fifty one patients harbouring 64 wide-necked intracranial aneurysms underwent the NF stent reconstruction with or without subsequent coiling in our institution (Table 1). There were 41 females and 10 males, with the age range of 25-83 y (mean 54). The symptoms of these patients were headache in 21, subarachnoid haemorrhage (SAH) in 10, diplopia in 3 and facial pain in 2. The other 15 patients were incidentally found. The aneurysm size ranged 1-22 mm (mean 7) and the location involved the petrous (1), the paraclinoid (19), the cavernous (13) and the ophthalmic (10) segments of the internal carotid artery (ICA), the posterior communicating artery (PCoM, 6), the middle cerebral artery (MCA, 7), the basilar apex (4), the vertebro-basilar junction (2), the posterior inferior cerebellar artery (1) and the superior cerebellar artery (1).

Table 1. Demography and angiographic characteristics of aneurysms.

No. of patients	51
Sex (female/male)	41/10
No. of aneurysms	64
Age (y, mean)	25-83 (54)
Aneurysm size (mm, mean)	1-22 (7)
Aneurysms treated with stent-coiling	3.5-22 (8.7)
Aneurysms treated with stent alone	1-5 (2.5)
Locations of aneurysms	
Internal carotid artery	43
Posterior communicating artery	6
Middle cerebral artery	7
Basilar apex	4
Vertebro-basilar junction	2
Posterior inferior cerebellar artery	1
Superior cerebellar artery	1

NF Stent-assisted coiling and angiographic results and follow-up

The procedure was performed under general anesthesia and an antiplatelet regimen consisting of clopidogrel 75 mg/d and aspirin 325 mg/d was administered at least 3 d before intervention. At the start of the procedure, a weight-based bolus of intravenous heparin (70 U/kg) was administered after bifemoral arterial access had been obtained and before guide-catheter placement for achieving a target activated clotting time of 250 s for the whole duration of the procedure. A 300 cm exchange length 0.014 inch micro wire was used to access the distal cerebral parent vessel and served as the platform to advance the NF stent delivery micro catheter across the target

lesion. The targeted aneurysm was accessed by use of a steam-shaped micro catheter. With the micro catheter in position, coils were deployed into the aneurysm and, after a satisfactory position had been confirmed, detached by use of the electrolytic mechanism according to the manufacturer's recommendations.

Aneurysm occlusion was considered to be complete when the aneurysm sac and neck were packed with no filling of contrast material, near complete when the sac was occluded but a neck remnant was present, and incomplete when there was persistent opacification of a sac remnant. After embolization, patients were followed up both angiographically and clinically at 3-6 months, and based on the angiographic findings; the second follow-up angiography would be performed at 6 months to one year. Follow-up angiography was compared with the immediate postembolization angiography and then assigned to one of three categories: (1) Unchanged when a similar degree of aneurysm occlusion in multiple projections was found; (2) Progressive thrombosis, when the amount of contrast agent in the aneurysm decreased; (3) Recanalization, when an increase of the amount of contrast filling in the aneurysm was observed. An aneurysm was considered to be recurrent if a previously completely occluded aneurysm had a partial or even small recanalization of the neck and if a previously near-completely occluded aneurysm was found to have the neck remnant increased in size or the aneurysm sac filled with contrast agent at follow-up angiography.

Statistics

Differences among different groups were analyzed by use of paired t-tests using the JMP software package, Version 5.0 (SAS Institute, Cary, NC). A P value<0.05 was considered to be statistically significant while a P value<0.01 to be highly significant.

Results

Sixty four intracranial aneurysms in 51 patients were treated with the NF stent reconstruction of the parent artery with (46) or without (18) subsequent coiling, and a total number of 69 stents were deployed. Six patients were managed on both sides of the cerebral vasculature. Four patients were treated with two stents deployed in "Y" configuration to manage a basilar apex aneurysm with the two proximal stent segments in the basilar trunk and distal stent segments in each of the P1 segments of the posterior cerebral artery. In three patients treated with stent-assisted coiling, two stents were deployed in each patient because of a large aneurysm (21 mm) in one, stent navigation needing a second stent deployment in another one, and two stent deployment in the third to induce thrombosis within the recurred aneurysm neck. In two patients, two stents were deployed to cover two small aneurysms (less than 3 mm) on the paraclinoid segment of ICA in one patient and one 3 mm ICA aneurysm in the other patient. In seven patients, a stent was deployed to cover two adjacent aneurysms, with one larger aneurysm (larger than 4 mm) coiled and the other adjacent small aneurysm (less than 3 mm) uncoiled in two patients and

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two adjacent small aneurysms both uncoiled in the other 5 patients.

A highly significant difference ($P=0.0001$) existed in aneurysm size between the aneurysms (size 3.5-22 mm, mean 8.7) treated with the stent-assisted technique and the aneurysms (size 1-5 mm, mean 2.5) treated with stenting alone, with the former aneurysms significantly larger than the latter ones. Stenting and coiling were performed in the same session in 37 cases and in different sessions in 9 cases. During the stenting and coiling procedure, coil herniation into the parent artery occurred in one patient when treating a wide-necked ICA aneurysm and was treated with the deployment of a stent to compress the coil onto the vessel wall. In another patient, the manoeuvre of the microcatheter following stent deployment caused the stent to migrate distally and a second NF stent had to be implanted to cover the aneurysm neck. Stenosis of the parent artery due to coil compression took place in two patients with no severe consequences. The total procedure related complication rate was 6.7%.

Immediately after the embolization procedure, eighteen aneurysms treated with stenting alone had no apparent change in aneurysm size. Among the remaining 46 aneurysms treated with stent-assisted coiling, complete occlusion was achieved in 34 (73.9%) aneurysms, near complete occlusion or neck

remnant in 10 (21.7%), and incomplete occlusion in 2 (0.4%). Two aneurysms with stent-coiling and 3 aneurysms with stenting only had no angiographic follow-up. Forty four aneurysms treated with stent-assisted coiling and 15 aneurysms with stenting alone had the angiographic follow-up from 3-89 months (mean 52) following stenting. All 15 aneurysms with stenting alone decreased in size, with 8 (53.3%) aneurysm disappeared completely and no aneurysms experiencing rupture. For 32 aneurysms with initial complete occlusion, 23 remained completely occluded (71.9%), and 9 (28.1%) recurred with retreatment in 5 (Table 2). For the 10 aneurysms with initial near complete occlusion, one aneurysm had no change, four aneurysms recurred and were re-treated to complete occlusion, and the other 5 aneurysms had progressive thrombosis to complete occlusion. Two aneurysms with initial incomplete occlusion had progressive thrombosis resulting in complete occlusion in one aneurysm and near complete occlusion in the other. Among the 15 aneurysms with stenting alone and 12 aneurysms with near or in-complete occlusion, progressive thrombosis occurred in 22 cases accounting for 81.5%. Among 42 aneurysms with complete or near complete occlusion, recurrence took place in 13 cases (31%). At angiographic follow-up, mild in-stent stenosis was present in three cases (5.3%) with no corresponding clinical symptoms.

Table 2. Results of aneurysms treated with stent-coiling at postembolization (46) and follow-up (44).

Occlusion	Post-embolization (n, %)	Occlusion at follow-up (n, %)			
		Complete	Near complete	Incomplete	Total
Complete	34 (73.9%)	23 (71.9%)	4 (12.5%)	5 (15.6%, retreated)	32 (100%)
Near complete	10 (21.7%)	5	1	4 (retreated)	10
Incomplete	2 (4.4%)	1	1	0	2
Total	46 (100%)	29	6	9	44

Discussion

Since the introduction of the NF stent, the first flexible intracranial stent, to clinical application in assisting coil embolization of intracranial aneurysms, the indications for endovascular treatment of intracranial aneurysms have been greatly expanded, with an increasing number of morphology-unfavourable aneurysms including wide-necked and fusiform aneurysms being treated through stent-assisted coiling with concurrent preservation of the parent artery.

The NF stent can be used to reconstruct the parent artery either with coiling for morphologically-unfavourable aneurysms or alone for small aneurysms whose endovascular therapy is very difficult and may be associated with a higher rate of intra-procedural rupture [10]. The deployment of a stent alone is to induce thrombosis within the aneurysm sac. The mechanism involved in the induction of progressive thrombosis by the deployed stent is the induction of alterations in aneurysmal hemodynamics, wall shear stress and blood flow to the point that spontaneous thrombosis will ensue within the aneurysm

sac [11-14]. The deployment of a stent results in the deviation of blood flow which allows a change in the intra-aneurysmal flow pattern, shifting from a helical to a non-coherent pattern (turbulence), reducing the intrasaccular vortex, producing blood stasis within the aneurysm and leading to aneurysmal thrombosis and permanent occlusion. In this study, eighteen small aneurysms were treated stent reconstruction alone without subsequent coiling. In one case with two adjacent aneurysms (size 1.5 mm and 3 mm, respectively), one NF stent was deployed, and the smaller aneurysm disappeared at 3-month follow-up. A second NF stent was deployed within the first NF stent for further induction of thrombosis within the larger aneurysm sac, and at 6-month angiography, the 3 mm aneurysm decreased to less than 1 mm. All the other aneurysms with stent deployment alone showed decreased size and no rupture at angiographic follow-up. Stent deployment alone was used not only in treating small wide-necked aneurysms but also in recurrent aneurysms initially treated with endovascular coiling.

Stenting alone in treating intracranial aneurysms without subsequent coiling was reported to achieve good results by other researchers [6,15-19]. Unlike the small aneurysms in our series, the aneurysms in the other studies treated with stenting alone ranged from 3-24 mm in the maximum diameter. Zenteno et al. presented an excellent report on 20 patients with complex aneurysms (size 3-24 mm) of the posterior circulation which were treated with a single stent without coil embolization, and the complete occlusion rate at one year following stenting reached 80% [19].

Two stents had been deployed for induction of thrombosis within an aneurysm without subsequent coiling [17,20,21]. Furthermore, two stents could also be deployed within the same parent artery to cover the inflow and outflow region of a large aneurysm followed by coiling in treating large or giant aneurysms. For basilar tip aneurysms, two stents can be deployed in the "Y" configuration followed by coiling [22]. In treating adjacent multiple aneurysms, the stent was very useful because it could cover these aneurysms simultaneously with large aneurysms coiled and small aneurysms left uncoiled. In this study, seven patients had two adjacent aneurysms treated each with a stent deployed to cover these two aneurysms. In two of these patients, the larger aneurysm was coiled while the other smaller one was left uncoiled. In the other five patients, no coiling was performed for these small adjacent aneurysms. At angiographic follow-up, these small uncoiled aneurysms all experienced shrinkage without rupture.

In the majority of reports, stenting was performed before coiling in the same session [2,3,5,6,16,23,24]. Coiling was usually performed with the microcatheter placed in the aneurysm through the mesh of the stent. However, catheterization through the stent mesh may be difficult and may easily displace the stent already deployed across the aneurysm neck because the NF stent does not have a strong radial force to attach to the vessel wall firmly. In this case, the procedure may be interrupted and coiling delayed for 1-3 months. This staged strategy allows for the stent to be endothelialized and incorporated into the vessel wall, enabling safer catheterization of the aneurysm. In our study, apart from 37 cases in which stenting and coiling were performed in the same session, stenting was done first and coiling performed 1-3 months later in a different session in 9 cases for the stent to incorporate into the vessel wall. However, the stenting and coiling can be performed in the same session using the "jailed technique" in which the microcatheter is caged between the vessel wall and the stent to avoid catheterization through the stent struts and to permit stabilization of the microcatheter during coil delivery [2,6,16,23].

In this study, the complete occlusion rate was 73.9% for aneurysms treated with stent-assisted coiling. In their 11 y experience, Murayama et al. reported a complete occlusion rate of 41% or so for either small wide-necked aneurysms or large ones with Guglielmi detachable coils [25]. The 73.9% complete occlusion rate in our study may suggest a better role of the stent in preventing coil herniation as well as in achieving a complete occlusion result. During follow-up of 89 months

(mean 52), all aneurysms treated with stent deployment alone decreased in size with one completely disappeared. Progressive thrombosis took place in 22 cases (81.5%) for the 15 aneurysms with stenting only and 12 aneurysms with near or in-complete occlusion. The progressive thrombosis rate was also higher than in other reports with stent-assisted coiling or stenting alone [16-18]. However, late aneurysm recurrence is common in aneurysms not only with coil embolization alone but also with NF stent-assisted coiling [6,16]. In our study, aneurysm recurrence and neck growth occurred in 9 (28.1%) of 32 aneurysms with initial complete occlusion and in 13 (31%) of 42 aneurysms with complete or near complete occlusion. Chalouhi et al. investigated the outcome of stent-assisted coiling of intracranial aneurysms with both the NF and the Enterprise (Cordis Neurovascular, Miami, FL, USA) stents and reported a lower recurrence rate of 12% [7]. However, their follow-up (mean 26 months) was quite short when compared with ours (mean 52 months).

At angiographic follow-up, mild asymptomatic in-stent stenosis was present in three patients. The three patients with in-stent stenosis had initially stent deployment alone in one patient and stent-assisted coiling in the other two. The deployment of two stents within the same parent artery seemed to have no significant effect on in-stent stenosis, especially when the artery to be deployed is in the normal range of the nominal arterial diameters depicted by this stent product. In this study, one patient had a stent to compress the projecting coil onto the vessel wall and another patient had two stents because the first stent was dislocated. For these patients, follow-up angiography 3 y later revealed complete occlusion of the aneurysm with no in-stent stenosis. Late in-stent stenosis had been noted in NF stent [16,26-28]. Hoit et al. investigated three-dimensional rotational angiographic detection of stenosis in the NF stent in treating wide-necked aneurysms in 14 patients, and a 0.31-0.41 mm reduction in the average diameter of the stented segment of parent artery was found to be significant but causing no clinical symptoms [28]. Stenosis or restenosis is the arterial wall's healing response to mechanical injury [29,30]. The initial consequences immediately following stent deployment are de-endothelialisation, crush of the superficial plaques on the inner membrane and stretch of the arterial segment. Then, platelet aggregation and activation, inflammatory cell infiltration, release of growth factors, medial smooth muscle cell modulation and proliferation, thrombosis invoked by smooth muscle cell proliferation, proteoglycan deposition, and extracellular matrix remodelling were identified as the major milestones in the temporal sequence of this response [29,30]. Negative vascular remodelling is virtually absent after stenting, however, stenting incurs greater neointimal growth compared with balloon angioplasty, with their net benefit being attributable to their larger initial lumen gain and prevention of negative remodelling.

The limitations of this study are the limited number of patients treated with the NF stent reconstruction of the parent artery, non-control, and non-randomization and single center enrolment. In the future, a study with large number of patients

with control, randomization and multiple centre's involved will be performed for further confirmation of the results.

The application of the NF stent has been greatly expanded from the primary use of assisting coil embolization to multiple usages in treating intracranial aneurysms, including stenting alone for both uncoiled aneurysms and coiled but recurred ones, correction of coil herniation and stent dislodgement, expansion of in-stent stenosis, and treatment of multiple adjacent aneurysms. Not only can one stent be implanted in the parent artery, two stents can also be deployed within the same parent artery without aggravating in-stent stenosis. It is certain that in the future better stents will be developed with better qualities facilitating the treatment of intracranial aneurysms with unfavourable morphology.

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