Single Stage versus Multi-staged Stent-assisted Endovascular Repair of Intracranial Aneurysms

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Abstract

Background: Stent-assisted coiling of intracranial aneurysms is performed either as a single-stage or a multi-staged procedure. The objective of our study is to compare the complications between the in single-stage versus the multi-staged stent-assisted coiling of intracranial aneurysm.

Methods: From January 2003 to January 2010, consecutive patients treated with intracranial stent for aneurysms were prospectively enrolled. Patients' demographics including cerebrovascular risk factors, aneurysms size and locations were collected. Technical and clinical complications as well as outcomes were measured. Data were analyzed retrospectively using SPSS software version 11.5.

Results: 87 patients (87 aneurysms) with a mean of 51.2 ± 13.6 years were treated with 90 intracranial (Neuroform 74, Enterprise 16) stents, single-stage 37 (42.5%) and multi-staged 50 (57.5%). Eight adverse events were observed without any mortality, 6 of which were in the single-stage group-rupture of aneurysm in 2, and thrombo-embolic events in 4. Both rupture occurred in basilar artery bifurcation aneurysms, required ventriculostomy and resuscitations. In single-stage, asymptomatic intra-operative stent thrombosis developed in one, symptomatic stent thrombosis in one on day 14, transient ischemic attack on day 6 and immediate post operative stroke in one. Only two minor strokes were observed in the multi-staged group, one on post-procedure day 7 and other on day 60. Majority of the patients had good outcomes including those with events.

Conclusion: Our study revealed that single-stage stent-coiling technique is associated with a higher rate of complications than multi-staged procedure. Therefore, staging the procedure may be an option whenever possible

Keywords: Wide-necked intracranial aneurysms, fusiform aneurysm, Stent-assisted coiling, thrombo-embolic events, single stage coiling of aneurysm, multiple staged coiling of aneurysm.

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Introduction

The challenges of stent-assisted treatment of intracranial aneurysm (STIA) have been described in previous studies.[1-9, 12] Most of the data[1-9,12] arrived from the experiences of using Neuroform stent (Boston Scientific Target, Fremnt, CA) which has been approved by Food and Drug Administration (FDA) in 2002 under humanitarian device exemption (HDE). The Enterprise stent (Cordis Neurovascular, Miami, FL) is a relatively new intracranial stent that has also been approved by FDA in 2007 under the guideline of HDE for the treatment of wide-necked intracranial aneurysm. The most common clinical complication is transient or permanent thrombo-embolic event related to intracranial stent, the incidence of which varies from 2% to 21%. The second most common clinical complication is intra-operative rupture of aneurysm and hemorrhage that varies from 1.5 % to 15%. Based on the previous literatures, some of the stent-assisted procedures are performed as a single staged procedure and others are performed as staged fashion.[1-9, 12] The single or staged technique in stent-assisted treatment of intracranial aneurysm is chosen by the authors[1-9] based on the clinical circumstances or by their personal preference. In most of the series,[1-8, 10] the complications of STIA are the reflection of mixed group of patients in which some were underwent single and others underwent multi-staged procedure. At present time, it is difficult to understand the technique that may be considered better than other in stent-assisted treatment of intracranial aneurysm. Additionally, it is also not clear that if waiting period for the staged procedure is associated with more risk of interval rupture of aneurysm. Therefore, it is our objective to

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Table 1: Demographics, clinical characteristics and outcome

Number of patients	87
Number of Intracranial stents	90
Neuroform	74
Enterprise	16
Average age (mean ± SD)	51 ± 14 years
Gender (female)	69/87 (80%)
Race	
White	74 (85%)
African American	13 (14%)
Previous History	
Hypertension	50 (57%)
Coronary Artery disease	6 (7%)
Diabetes	8 (9%)
Hyper-lipidaemias	15 (17%)
Stroke	15 (17%)
Active Smoker	37 (43%)
Mean diameter of the aneurysm	10.59 ± 6.2 mm (range 2-30 mm)
Location of aneurysms:	
Internal carotid artery (ICA)	39
ICA bifurcation	5
Cavernous carotid	6
Ophthalmic carotid	19
Supraclinoid carotid	5
Middle cerebral artery (MCA)	9
MCA bifurcation	8
MCA M1	1
Posterior communication artery (PCA)	17
Vertebrobasilar artery junction	3
Basilar artery	19
Basilar bifurcation	17
Basilar trunk	2
Outcome	
GOS 1 or NIHSS 0	83 (95%)
GOS 2 or NIHSS 2	1 (1%)
GOS 3 or NIHSS 4 - 6	3 (3%)

GOS = Glasgow Outcome Scale, NIHSS = National Institute of Health Stroke

compare the rate of complications associated with single versus multi-staged STIA in our series. We would also like to tease out any potential risk of interval rupture of aneurysm associated with staged procedure.

Methods

All patients undergoing placement of an intracranial stent for the treatment of an intracranial wide-necked and fusiform aneurysm were registered in a prospectively maintained database. From this database, consecutive patients who underwent stent-assisted coiling of an intracranial aneurysm were selected for analysis and the data were retrospectively analyzed. Institutional Review Board (IRB) approval was obtained prior to the treatment and retrieval of the data. Similarly, informed consent was obtained from all patients prior to placement of an intracranial stent for the treatment of their aneurysms. A total of 495 patients were screened from which 87 patients were enrolled including 15 ruptured cases for intracranial stent assisted (Neuroform 72, Enterprise 15) treatment of intracranial aneurysm. The decision of microsurgical versus endovascular Neuroform stent-assisted treatment of aneurysm was made upon the agreement between a vascular neurosurgeon and an endovascular neuro-endovascular specialist. Additionally, patient's preference played a significant role in the decision making of the procedure. The outcomes were predefined on the basis of radiographic and clinical criteria. The radiographic outcomes were defined as the rate of immediate occlusion (complete occlusion (100%), partial occlusion (› 95% ‹ 100%) or subtotal occlusion ‹ 95%) after treatment with the Neuroform stent. The clinical outcomes were measured using National Institute of Health Stroke Scale (NIHSS) and Glasgow Outcome Scale (GOS). The outcome was defined as good if the obtained GOS was 2 or less and NIHSS 2 or less within 90 days or at a later follow-up visit.

The procedure was categorized in two groups; a single stage stent coiling versus a multi-staged stent-coiling procedure. In the former, the operators intend to complete the procedure by placement of stent/stents followed by embolization with coils in one setting. The multi-staged stent-assisted coiling for wide-necked aneurysm was defined as a stepwise occlusion, where stent placement with or without partial coiling was performed in the first setting, followed by coiling of aneurysm in the subsequent settings. For the wide-necked ruptured aneurysms, the staging was modified due to the risk of aggressive anti-platelets and anti-coagulation therapy required for the procedure. In these instances, coiling to secure the aneurysm was intended first, followed by stent-assisted coiling in subsequent setting. When ruptured aneurysms were intended to repair with stent-assisted coiling procedure in acute phase, we always repaired them in a single-stage procedure. Selection of patients in single versus multi-staged stent coiling procedure was not randomized.

A thrombo-embolic event was defined as the clinical development of a transient or permanent neurological deficit after the procedure. A peri-procedural thrombo-embolic event was defined as the angiographic partial or complete occlusion of an artery or a perfusion defect in the territory of an arterial supply. Patients with a suspected thrombo-embolic event underwent confirmatory imaging including magnetic resonance imaging (MRI) with diffusion-weighted sequences. Routine imaging to identify a silent event in an asymptomatic patient was not performed in our study.

The architecture of aneurysm was obtained by digital subtraction cerebral angiography and a three-dimensional reconstruction of aneurysm. Wide-necked aneurysms were defined as having dome to neck ratios ‹ 2 or a neck › 4 mm in diameter. An intracranial aneurysm was defined as fusiform if the aneurysm was an out-pouching dilatation of the parent blood vessel affecting at least 270 degrees of circumference of the lumen and possessing no discernible neck. All Neuroform stent treated patients were either treated with both aspirin 325 mg/day and Plavix 75 mg/day at least 5 days prior to their treatment or given loading doses

of both Plavix 300 mg and aspirin 325 mg at least 2 hours prior to the procedure. All patients with ruptured aneurysm who received stent-assisted repair were treated with both a loading dose of aspirin 325 mg and clopidogrel 300 mg at least 2 hours prior to their treatment. Patients were continued on both aspirin and Plavix daily for 4 weeks after the stenting procedure, and thereafter on daily either 325 mg aspirin or 75 mg Plavix alone. We usually continue Plavix for at least for 6 to 9 months if not contra-indicated. For the precaution an extra-ventricular catheter was placed first prior to the endovascular procedure and initiation of anti-thrombotic medications to prevent potential bleeding complication related to ventriculostomy. We also avoided post procedural anti-coagulation in sub-arachnoid hemorrhage patient to prevent unexpected bleeding complications associated with ventriculostomy catheter.

Selection Criteria

All patients with the diagnosis of a wide-necked aneurysm or fusiform aneurysm were enrolled. For the un-ruptured aneurysms, the required size of the aneurysm was at least 7 mm or larger in diameter. Informed consent was obtained from the patient or the patient's legal guardian prior to the procedure. Exclusion criteria include active bleeding diathesis and or a platelet count < 100,000/dl, reluctance to take aspirin and Plavix or to give informed consent, or intolerance to general anesthesia and/or had a history of severe life threatening anaphylactic reactions to contrast materials during angiography. Based on the above exclusion criteria no patient was excluded from the study.

Procedures

Stent-assisted coiling techniques have been previously described by the authors[7, 11] Baseline serum activated coagulation time (ACT) was obtained and intravenous heparin was administered to achieve ACT between 1.5 to 2 times of baseline value. A 6F guiding catheter (Boston Scientific Target, Fremont, CA) which was flushed with continuous heparinized saline was placed in the proximal part of the vessel of interest (internal carotid, vertebral artery) under the direct guidance of fluoroscope and road maps. The aneurysm was crossed with a micro-catheter (SL 10™, Boston Scientific Target, Fremont, CA) and a microwire (Synchro 14™, Boston Scientific Target, Fremont, CA, or Transcend 14™, Cordis, Miami, FL). The micro-catheter was swapped with an exchange length microwire (X-celerator™ 300 cm, eV3, Irvine, CA). The Neuroform stent™ delivery system was prepared and advanced over the exchange length microwire as a unit and subsequently deployed across the neck of the aneurysm. Recently, the authors have begun to use a direct approach in which a 200 cm 0.014 compatible microwire was back-loaded through the stent delivery system, after which the stent-delivery system was advanced as a unit through the guiding catheter. To cover the neck of the aneurysm adequately, the stent was deployed at least 4 mm proximal and 4 mm distal to the neck on the parent artery. The aneurysm was catheterized by direct approach in which the micro-catheter was advanced through the cells of the Neuroform stent™. The angiographic and clinical follow-up was planned for each patient at 3, 12, 18, and 36 months.

Statistical Analysis: A prospective database was created and maintained for all patients treated with Neuroform stent for their intracranial aneurysms in a tertiary-care facility. Consecutive patients who underwent treatment of intracranial wide-necked and fusiform aneurysms using nitinol self-expandable stent from July 2003 to August 2006 were enrolled and the data were analyzed retrospectively. Patients' demographics including age, race, gender, cardiovascular risk factors, locations of the aneurysm, and type of aneurysm were collected. Technical complications including intra-operative rupture, vessel injury, thrombo-embolic events, and access site complications were also included. Additionally, a 90 day clinical outcome was measured using national institution of health stroke scale (NIHSS) and Glasgow Outcome Scale (GOS) scores (including an angiographic outcome) were determined. The data were analyzed using SPSS software version 11.5 for analyzing mean value with standard deviation, frequencies and percentages of different parameters of these patients' populations.

Results

Technical outcome

Stent-assisted treatment of intracranial aneurysm was done in 87 patients, out of which 37 (42.5%) were single stage and 50 (57.5%) were multi-staged procedures. A total of 90 intracranial stents (Neuroform 74, Enterprise 16) were used to repair 87 intracranial aneurysms. The mean age of the patients was 51 ± 14 years, majority of whom were females 69/87 (79%) and whites 59 (82%). For complete demographic history please see table 1. Successful deployment of stent in the target artery was achieved in 85/87 (97%). Stent deployment failed in two cases (one in a middle cerebral artery bifurcation, and one in carotid/ophthalmic artery) due to the extreme tortuous nature of the parent artery. These two patients underwent open craniotomy for the treatment of their aneurysm and their outcomes were continuously monitored. For the Y-shaped reconstruction of the aneurysm neck in four patients (two in each group), each required an additional stent. Immediate complete aneurysm obliteration was observed in 27 (31%), neck remnants in 27 (31%), subtotal occlusion (<95%) in 30 (34.5%).

Clinical Outcome

Eight adverse events were observed, two intra-operative rupture of aneurysm and 6 thrombo-embolic events leading to 4 non disabling strokes. Six events were observed in the single stage group and 2 were in multi-staged group. In single state group, intra-operative rupture of aneurysm was observed in 2 patients (Neuroform stent) with un-ruptured aneurysm, and thrombo-embolic events in 4 patients. None of the patient with ruptured aneurysms that underwent stent-assisted repair had ruptured during or after the procedure. Both ruptures occurred at the final stage of Y-shaped stent-assisted coiling procedures in basilar artery bifurcation aneurysms and required

urgent ventriculostomy and resuscitations. Both aneurysms were secured with subsequent packing of aneurysms with coils achieving complete obliteration of aneurysm. These two patient had no focal neurological deficit in the post procedural period, and recovered completely (GOS 5, NIHSS 0) after a prolonged hospitalization and rehabilitation.

Four thrombo-embolic events were observed in single stage procedures. An intra-operative asymptomatic stent thrombosis (Enterprise stent) developed in ruptured ICA small wide neck aneurysm and resolved spontaneously without any clinical or radiographic consequences. One patient suffered a stroke with NIHSS 8 on post operative day 14 due to a basilar artery stent thrombosis (Neuroform stent) in un-ruptured case and was treated with intravenous integrilin for 24 hours. Another patient had immediate post-operative angio-negative left MCA stroke with NIHSS 4 (Enterprise stent) in an un-ruptured patient. Both of these patients recovered completely and had good outcome (NIHSS 0 and GOS 5). A transient ischemic attack developed on day 6 in a patient with right ICA terminus un-ruptured aneurysm (Neuroform stent).

Only two events were observed in the multi-staged group. One patient had a minor stroke (NIHSS 4) on day 7 after the placement of a second Neuroform stent to create Y-shaped neck reconstruction for a right MCA un-ruptured aneurysm (Neuroform stent). This patient was also treated with intravenous integrilin for 24 hours, and her NIHSS returned to 0 at the time of discharge. The second patient, a 42 years old woman who underwent stent-assisted coiling of the right ICA wide neck un-ruptured aneurysm (Enterprise stent), had a lacunar stroke with NIHSS 1 that developed on day 60 and recovered completely with good outcome.

Off 6 patients with thrombo-embolic events, 3 received loading doses of both Plavix and aspirin and 3 received standard doses of both aspirin and Plavix 5 days prior to the procedure. Therefore, acute loading versus standard dosing of both aspirin and Plavix was not associated with increased thrombo-embolic events in out series.

With regards to the 90 days clinical outcome (Table 1), (GOS 5 or NIHSS 0 was observed in 83/87 (95%) cases. GOS 4 or NIHSS 2 was observed in 1 patient, who had prior disability from a ruptured aneurysm. GOS 3 or NIHSS 4-6 was observed in another 3 patients, two of which were ruptured aneurysms (presented with H&H III and Fisher 4) and the other was a symptomatic unruptured aneurysm (NIHSS 6, GOS 3). The unruptured aneurysm patient presented with a NIHSS 6 from a symptomatic BA trunk giant aneurysm; her symptoms remained unchanged after treatment.

Discussion

This is the first study in our knowledge which compares the complication rate between single stage and multi-staged Neuroform stent assisted coiling of wide neck intracranial aneurysms. Our study revealed that single stage procedures were associated with relatively higher incidence of complications such as intraoperative rupture of aneurysms and post-operative thromboembolic events. However the overall event rates in both groups were very low and were not associated with any mortality or permanent morbidity. Additionally, we have not experienced any interval rupture of aneurysm while waiting for the completing of the multi-staged stent-assisted coiling of the aneurysm.

The clinical complications including thromboembolic events and intracranial hemorrhages associated with stent in the treatment of intracranial aneurysms have been described in previous case series[1-9, 12] and also have been described by authors in a previous study.[7, 12] The most common complications associated with Neuroform stent are thromboembolic events followed by intracranial hemorrhages which are relatively less frequent.

The thromboembolic events associated with intracranial stent varies from 0 – 21%[1-10, 12] and the thromboembolic events have reduced over the years with the acquirement of more experiences with intractanial stent.[5, 7, 9, 12] Most of these events were described in the circumstances when the procedures were intended to be completed in a single setting.[1-9] These thromboembolic events were identified either during or after the procedure was completed. In a previous study,[7, 12] authors have described the thromboembolic events and possible mechanisms.

In our current study, we tried to compare the incidence thromboembolic events between single stage versus multi-staged stent-assisted treatment of intracranial wide neck aneurysm. We observed 6 thromboembolic events, 4 in the single stage group and two in multi-staged group. It is difficult to compare our preset study with other previous studies,[1-9, 12] where the thromboembolic events were not systematically analyzed in relation to a single versus multi-staged procedures. However, when previous studies[1-5] were explored in detail, the higher rate of thromboembolic events were observed in cases where the procedure was completed in a single setting. In one study[9] all 50 stent-assisted coiling of the aneurysm were performed in a single setting and there was no report of thromboembolism. This retrospective study[9] was performed in Greece, where patients were not pre-treated with either aspirin or plavix, and Neuroform stents were placed while patients were on heparin. Anticoagulation was continued with low molecular weight heparin for three days and aspirin and plavix were started on day 2 of the procedure. Therefore, it is not wise to compare this study[9] with the rest of the previous Neuroform stent studies[1-8, 12] where appropriate antiplatelet was utilized to protect the stent.

In our present study, there were two (2.3%) intra-operative rupture of aneurysm which occurred in single stage arm. There was no event of intracranial hemorrhage in the multi-staged arm. Both events developed during the final state of stenting followed by coil packing of unruptured aneurysms. The hemorrhagic complications in the form of intracranial hemorrhage vary from 0% to 10.5 % depending on the published studies.[1-9] In all those studies,[1-9] both single-staged and multi-staged cases were mixed and the results were presented as a group. The higher rates of intracranial hemorrhages were observed in series[1, 6] when the

stent-assisted treatment was completed as a single procedure. In a recent study,[6] the incidence of intracranial hemorrhage was observed in 2/42 patients where most of the procedures were performed as a single stage based on the description of the study. Both hemorrhages in that study[6] occurred in patients where the procedure was completed in a single setting. However in another study,[9] 50 stent assisted coiling procedures were performed in single setting which included 33 ruptured intracranial aneurysms. In that study,[9] there was no incidence of intraoperative rupture of aneurysm or intracranial hemorrhage was reported. In a previous study,[7] authors experienced a single episode of intraoperative rupture of aneurysm when the procedure was completed in a single setting and the mechanism of rupture was thought to be associated with coil.

The mechanisms of low complication rate in multi-staged group are not well understood. However, authors have the following hypotheses which might have contributed in reducing the rate of complications in our study. In multi-staged procedure the stent are placed first followed by placement of coils in the subsequent setting. The time between stenting and coiling might have provided adequate insulation time for the stent to avoid complications. First, the time interval likely allowed the stent to be in a stable position preventing stent movement and subsequent endothelial damage and platelet activation. Second, an endothelial layer might have formed in the interval time which might have further stabilized the stent for a safer microcatheter navigation and manipulation thus preventing thromboembolism. Third, the endothelialization of stent at the inflow zone of the neck of the aneurysm may have positively changed the hemodynamics of the aneurysm by reducing the tension on the wall of the aneurysm and ultimately reducing the chances of intraoperative rupture of aneurysm. Finally, since the operators are not in a rush to complete the procedure in a multi-staged setting, they may have an opportunity to stop when an unexpected event occurs.

Our study has several limitations. The number of cases in each arm may not be sufficient to make any definitive distinction between groups. The number of the events in each arm may not be high enough to find any association between events and patient factors. It is also possible that the observed differences are likely to be a combination of chance and aneurysm characteristics. Finally, due to the retrospective and non-randomized nature of our study, the bias aspect of patient's selection could not be completely excluded.

In conclusion, our study shows that single stage stent-assisted coiling of the wide neck intracranial aneurysm is associated with a higher rate of clinical complications such as intraoperative rupture of aneurysms and thromboembolic events. However, based on our data, there was no difference in 90 days clinical outcome between groups despite the presence of higher rate of complications in the single stage arm in our study. Therefore, staging the procedure may be an option whenever possible.

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