Factors Affecting the Obliteration Rate of Intracranial Aneurysms Treated with a Single Pipeline Embolization Device

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■ OBJECTIVE: **To evaluate the clinical and angiographic outcomes of intracranial aneurysm treatment using a single Pipeline embolization device (PED), and to evaluate the factors affecting aneurysm obliteration rate.**

■ METHODS: **The demographic characteristics and anatomic features of 58 aneurysms in 47 patients treated with a single PED were reviewed retrospectively. All aneurysms treated with a PED at a single center and with follow-up angiograms for at least 6 months were included in this study.**

■ RESULTS: **The overall rate of complete and near-complete occlusion was 84% (49 of 58) after a mean follow-up period of 18.3 months. The rate of complete aneurysm obliteration was lower in aneurysms with an arterial branch arising from the aneurysm neck compared with aneurysms without an arterial branch (13% [1 of 8] vs. 68% [34 of 50]; $P = 0.0075$). The overall rate of complete and near-complete aneurysm occlusion was 90% (45 of 50) in aneurysms without an arterial branch arising from its neck. There were no statistically significant associations between obliteration rate and aneurysm neck width, size, or type, or history of previous coil embolization.**

■ CONCLUSIONS: **Our data suggest that a single PED is sufficient to induce complete or near-complete obliteration of most aneurysms. The presence of a branching artery arising from the aneurysm neck is highly predictive of incomplete occlusion after treatment with a single PED.**

INTRODUCTION

The Pipeline embolization device (PED) has recently been introduced as an alternative endovascular technique for treating intracranial aneurysms. The PED diverts flow from an aneurysm, causing shrinkage and thrombosis of the aneurysm, and promotes reconstruction of the vessel's endoluminal layer.[1] The safety and efficacy of the PED in managing large or giant wide-necked aneurysms have been reported in several studies.[2-7] Small aneurysms (<10 mm) are more prevalent than large and giant aneurysms. Implantation of the PED in small aneurysms has been reported to be safe, with angiographic success as early as 2 months post-treatment.[8-11] In addition, use of the PED to treat recurrent previously coiled aneurysms has been found to be safe and to effectively achieve aneurysm occlusion.[12] In a recent review article, the occlusion rate of aneurysms treated with the PED was reported as 83% at 6 months,[13] with overall morbidity and mortality rates of 1.23% and 1.18%, respectively.[14] To date, few published studies have evaluated the factors influencing aneurysm obliteration rate, and most of the previous reports did not isolate aneurysms treated with a single device from those treated with multiple devices.[13,15]

The goal of the present study was to analyze the outcomes of intracranial aneurysm treatment using a single PED. Specifically, we wanted to evaluate the potential factors influencing aneurysm obliteration rates, such as demographic characteristics, aneurysm characteristics, and the presence of arterial branches arising from the neck of the aneurysm. We also wanted to determine whether a single PED is sufficient to obtain high rates of aneurysmal occlusion.

METHODS

Patients

The demographic characteristics of patients with aneurysms treated with a single PED (Covidien/Medtronic, Irvine, California, USA) at the University of North Carolina Hospitals in Chapel Hill

Key words
- Flow diversion
- Intracranial aneurysm
- Occlusion rate
- Pipeline embolization device

Abbreviations and Acronyms
MRI: Magnetic resonance imaging
PED: Pipeline embolization device
PCA: Posterior cerebral artery
PCOM: Posterior communicating artery

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between March 2012 and May 2016, were reviewed retrospectively. All aneurysms treated with a single PED with follow-up angiograms for at least 6 months were included in this study. The obliteration rate was evaluated on a follow-up angiogram. Aneurysm obliteration rate was defined as complete (100%), near-complete (>90%), or incomplete (<90%). Aneurysm size was defined as small (≤10 mm) or large (>10 mm), and neck width was also classified as small (≤4 mm) or large (>4 mm). One fusiform and 4 dissecting aneurysms were included in our analysis, along with saccular aneurysms. Previously coiled aneurysms with neck remnants were included as well. These aneurysms were included to evaluate them as variables in terms of aneurysm obliteration rate. This study was approved by the Institutional Review Board and Office of Human Research Ethics of the University of North Carolina at Chapel Hill.

Endovascular Procedure

Before the procedure, all patients underwent a clopidogrel response genotyping (CYP2C19) assay. Patients evaluated as normal metabolizers were started on aspirin 325 mg and clopidogrel 75 mg once daily starting 1 week before the procedure. In other genotypes, the antiplatelet therapy was adjusted according to guidelines of the Clinical Pharmacogenetics Implementation Consortium.[16] All procedures were performed under general anesthesia. Intravenous heparin was administered after gaining arterial access. Angiograms were obtained after the PED was deployed to confirm the position of the device and the patency of the parent artery. All patients had a postoperative neurologic examination and were admitted to the neuroscience intensive care unit for at least 24 hours after the procedure.

Follow-Up

All patients underwent magnetic resonance imaging (MRI) and magnetic resonance angiography at 3 months after the procedure to assess the aneurysm and the patency of the parent vessel. A follow-up angiogram was obtained at 6 months after the procedure to evaluate aneurysm obliteration and in-stent stenosis. We report 2 follow-up times: an angiographic follow-up time, based on the most recently performed angiogram, and a total follow-up time, based on the most recent clinic visit and noninvasive imaging. This is an important distinction, given that no additional angiograms were scheduled for completely obliterated aneurysms, although these aneurysms were followed with noninvasive imaging. If residual opacification of the aneurysm was noted at the 6-month follow-up, then the patient was evaluated for repeat treatment or a follow-up angiogram. Nearly completely obliterated aneurysms were followed with repeat angiograms, and incompletely occluded aneurysms were more likely to undergo a second treatment. The total follow-up time ranged from 6 to 51 months, and the angiogram follow-up time ranged from 6 to 28 months.

Statistical Analysis

Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA). The angiographic outcome of aneurysmal occlusion after PED treatment was evaluated in the 3 categories of complete, near-complete, and incomplete obliteration. These outcome categories were analyzed for each characteristic of sex, arterial circulation (anterior or posterior), aneurysm size, aneurysm type, previous coil embolization, aneurysm neck width, and arterial branching from the aneurysm neck.

For the categorical variables, preliminary bivariable analysis was conducted using the Mantel–Haenszel mean score tests with standardized mid-rank scores for the cross-tabulation of categorical variables with the primary outcome. Owing to concerns about the small sample size, exact tests were used to test the null hypothesis of no association of such variables with the primary outcome. Analysis of variance was applied to assess variation in the mean of the continuous variables across the 3 categories of the outcome variable.

A multinomial logistic regression analysis using the proportional odds model for the cumulative logits of an ordinal response was used to assess multivariable relationships of patient factors with aneurysm obliteration status. The method of generalized estimating equations with working independence correlation matrices was used to estimate the model to account for clustering of multiple aneurysms within subjects; empirical sandwich standard errors for regression coefficients were computed.

RESULTS

This retrospective study included 47 patients with a total of 58 aneurysms treated with a single PED. Demographic data and aneurysm characteristics are presented in Table 1. Seventeen patients had an initial presentation of subarachnoid hemorrhage; 14 of these patients underwent PED treatment of

Table 1. Patient and Aneurysm Characteristics

Characteristic	Value
Patient age (years), mean ± SD	52.8 ± 11.9
Female sex, *n* (%)	42 (89)
Presenting with subarachnoid hemorrhage, *n* (%)	17 (29)
Multiple aneurysms, *n* (%)	11 (23)
Angiography follow-up (months), mean	8.1
All imaging follow-up (months), mean	18.3
Decreased clopidogrel responders, *n* (%)	2 (4)
Anterior circulation aneurysms, *n* (%)	44 (93)
Cavernous segment aneurysms, *n* (%)	9 (15)
Ophthalmic segment aneurysms, *n* (%)	25 (43)
Supraclinoid segment aneurysms, *n* (%)	14 (24)
Basilar apex aneurysms, *n* (%)	2 (3)
Vertebral segment aneurysm, *n* (%)	2 (3)
Dissecting aneurysms, *n* (%)	4 (6)
Aneurysm size (mm), mean ± SD	10.15 ± 7.2
Large aneurysms (>10 mm), *n* (%)	9 (15)
Small aneurysms (<10 mm), *n* (%)	39 (67)
Previously coiled aneurysms, *n* (%)	17 (29)
Size of neck remnant in previously coiled aneurysms (mm), mean ± SD	9.0 ± 6.4