Analysis of Predictors and Probability of Aneurysm Occlusion in the Internal Carotid Artery After Treatment with Pipeline Embolization Device

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BACKGROUND: **Although the Pipeline Embolization Device (PED) has proved to be an excellent option for internal carotid artery (ICA) aneurysms, the rate of occlusion remains difficult to predict and factors associated with aneurysm occlusion are not well elucidated. This study aimed to investigate predictors and the rate of occlusion for aneurysms along the ICA.**

METHODS: **A total of 117 saccular ICA aneurysms treated with the PED were studied. Occlusion rates were divided among 4 groups: group A [lesions >10 mm in the proximal ICA (petrous to the superior hypophyseal segments)]; group B (lesions <10 mm in the proximal ICA); group C [lesions >10mm in the distal ICA (posterior communicating segment to the ICA bifurcation)]; and group D (lesions <10 mm in the distal ICA). Predictors of aneurysm occlusion were entered into a multivariate Cox regression analysis.**

RESULTS: **The median time to aneurysm occlusion was 8 months in group A (95% confidence interval [CI], 7.0–9.1), 5.2 months in group B (95% CI, 4.5–6.0), 6.9 months in group C (95% CI, 6.5–7.2), and 10.2 months in group D (95% CI, 6.9–13.6) ($P = 0.045$). There was a statistically significant difference between the probability of aneurysm occlusion in group B compared with distal ICA aneurysms ($P = 0.02$). Small proximal ICA aneurysms were more likely to occlude over time compared with other aneurysm groups (hazard ratio, 1.76; 95% CI, 1.07–2.9; $P = 0.02$).**

CONCLUSIONS: **The rate of occlusion after PED is highest for small proximal ICA aneurysms and the probability of occlusion is lower for distal ICA aneurysms.**

INTRODUCTION

Flow diverters have become well-accepted endovascular options for the management of intracranial aneurysms and the Pipeline Embolization Device (PED [ev3/Covidien Vascular, Mansfield, Massachusetts, USA]) is favored in the United States for the treatment of wide neck and complex aneurysms. The PED has been studied in the setting of nonrandomized clinical trials[1-3] and postmarket series,[4,5] which have provided evidence that flow diverters can be safely used for aneurysms with different characteristics than initially approved by the U.S. Food and Drug Administration. Complete aneurysm occlusion is the end point that justifies prophylactic treatment of unruptured aneurysms and the use of PED has changed the expectations after aneurysm treatment from immediate aneurysm occlusion with clipping and coiling to a delayed process that ensues in the months after PED deployment. The theoretic basis for aneurysm occlusion with flow diverters has been described in detail in previous reports,[6,7] but in practice, aneurysm occlusion with flow diversion is not easy to predict and requires serial imaging surveillance. Although PED treatment is an effective tool for aneurysm treatment, there have been cases of persistent aneurysm filling after 12 months.[8] Intuitively, aneurysm size may affect the propensity for aneurysm occlusion because of inherent differences in hemodynamics (turbulent flow, aneurysm transit

Key words
- Aneurysm
- Endovascular
- Flow diverter
- Pipeline Embolization Device

Abbreviations and Acronyms
CI: Confidence interval
HR: Hazard ratio
ICA: Internal carotid artery
mRS: modified Rankin Scale
PComA: Posterior communicating artery
PED: Pipeline Embolization Device

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time, shifts in inflow stream, and intra-aneurysmal pressure), whereas aneurysm location could disfavor aneurysm thrombosis in instances of persistent demand for blood flow from large arterial branches near the aneurysmal segment, poor neck coverage from increased vessel tortuosity, and areas of vessel bifurcation. The fetal posterior communicating artery (PComA), for instance, has been postulated to negatively affect occlusion rates after PED treatment because of persistent aneurysm filling.[9] Other researchers have focused on creating predictive models for aneurysm occlusion after flow diversion with relatively high accuracy (84%).[10] We thus investigated whether aneurysm size and location along the internal carotid artery (ICA) would have an impact on the rate of aneurysm occlusion over time and analyzed potential predictors of aneurysm occlusion.

METHODS

Study Design

Over a 3-year period, patients treated electively with PED were identified from a prospectively maintained database. Subjects included in the study were adult patients harboring saccular aneurysms located in the ICA between the petrous segment and the carotid terminus. Patients were excluded if the index aneurysm had had previous treatment, fusiform or dissecting aneurysms, or extracranial aneurysms, or if they had had previous subarachnoid hemorrhage 30 days before aneurysm treatment. The study protocol was approved by the institutional review board of our institution before data collection. One patient in the data set was treated under compassionate use before Food and Drug Administration approval of the device in April, 2011.

Data collected from each patient included presenting symptoms, aneurysm characteristics (size and location), intraprocedural complications, number of devices deployed, periprocedural events (i.e., events occurring after the PED procedure up to 30 days), and functional clinical assessment based on 30-day follow-ups and latest clinic visits. Functional outcome was determined based on the modified Rankin Scale (mRS). Aneurysm imaging was routinely obtained at 3, 6, and 12 months. Subsequent imaging follow-ups were scheduled on a case-by-case basis according to the degree of aneurysm thrombosis. The initial imaging modality often consisted of computed tomography angiography or magnetic resonance angiography to reduce the patient's exposure to contrast and radiation, followed by digital subtraction angiography at 6 months. The test modality after 6 months was left at the discretion of the operator. The degree of aneurysm occlusion was assessed at each time point according to the scale of Roy et al.,[11] in which the angiographic appearance was divided into complete aneurysm occlusion, residual aneurysm neck, and residual aneurysm sac.

Patient Selection and Antiplatelet Regimen

The indications for PED treatment in the study included small aneurysms (<10 mm) with a wide neck (≥4 mm or neck/dome ratio <2), large and giant aneurysms because of the high likelihood of failure with conventional endovascular techniques, and multiple adjacent aneurysms.

Patients received dual antiplatelet therapy before each PED procedure. In our protocol, patients were started on aspirin (325 mg/day) and a thienopyridine derivative (clopidogrel, 75 mg daily or ticagrelor, 90 mg twice daily) 7 days before the anticipated date of intervention. Patients who failed to meet the schedule received a loading dose of aspirin (650 mg) and clopidogrel (600 mg) on the day before the procedure. Individual responses to antiplatelet regimen were measured using aspirin assay and P2Y12 assay (Accumetrics VerifyNow, San Diego, California, USA). Clopidogrel inhibition levels >30% or <200 platelet reaction units were considered therapeutic. Patients with a subtherapeutic response to clopidogrel were given a loading dose of ticagrelor (180 mg), which is a highly effective antiplatelet agent with rare instances of resistance reported in the literature. Post-PED treatment, the thienopyridine derivative was maintained for at least 6 months (75 mg/day of clopidogrel or 90 mg/twice daily of ticagrelor) and aspirin (75–325 mg/day) was maintained indefinitely, unless there were severe adverse reactions to dual antiplatelet therapy (e.g., gastrointestinal bleeding or subdural hematoma) in which case the antiplatelet regimen was readjusted.

PED Procedure

PED was deployed under general endotracheal anesthesia with the aid of biplane angiography units. Three-dimensional rotational angiography was routinely performed. The size of the device was selected according to the measurements of the inflow vessel.

A 5F short vascular sheath and diagnostic catheter were exchanged for a 6F 90-cm-long sheath and the intermediate catheter (6F 058 Navien [ev3, Irvine, California, USA]) was navigated selectively in the distal ICA under roadmap guidance. A Marksman (Medtronic, Irvine, California, USA) or an XT-27 (Stryker Neurovascular, Fremont, California, USA) microcatheter was advanced distal to the landing zone and the device was deployed across the neck of the aneurysm using a combination of unsheathing of the device and advancement of the insertion wire. When the device seemed inadequately opposed to the vessel wall, the device was manipulated with the catheter/wire and/or balloon angioplasty (Hyperglide or Hyperform [ev3 Neurovascular, Irvine, California, USA]; Scepter, MicroVention, Aliso Viejo, California, USA). Coverage of the dilated vessel segment with 1 device was the primary goal during the procedures to avoid multiple coverage of clinically significant side branches. Contrast stasis inside the aneurysm was at times observed but not pursued. Multiple devices were used when the aneurysm neck could not be covered completely with a single device, and in rare instances, to potentially decrease the risk of delayed aneurysm rupture in patients with rapidly progressive symptoms after previous PED placement.

Study End Points

The primary end point of the study was angiographic evidence of complete aneurysm occlusion. Complete occlusion was defined on vascular imaging as the absence of opacification on digital subtraction angiography, hyperdensity on computed tomography angiography, or hyperintense signal on magnetic resonance angiography of any portion of the original defect of the arterial wall as seen on any single projection. Aneurysm occlusion was recorded as a binary event in each follow-up appointment and was based on the operator's assessment of the level of aneurysm occlusion. Residual neck or dome filling was not considered aneurysm occlusion and the patient was instructed to return for