Pipeline Embolization Device with or without Adjunctive Coil Embolization: Analysis of Complications from the IntrePED Registry


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ABSTRACT

SUMMARY: Flow diversion to treat cerebral aneurysms has revolutionized neurointerventional surgery. Because the addition of coils potentially increases the time and complexity of endovascular procedures, we sought to determine whether adjunctive coil use is associated with an increase in complications. Patients in the International Retrospective Study of Pipeline Embolization Device registry were divided into those treated with the Pipeline Embolization Device alone (n = 689 patients; n = 797 aneurysms; mean aneurysm size, 10.3 ± 7.6 mm) versus those treated with the Pipeline Embolization Device and concurrent coil embolization (n = 104 patients; n = 109 aneurysms; mean aneurysm size, 13.6 ± 7.8 mm). Patient demographics and aneurysm characteristics were examined. Rates of neurologic morbidity and mortality were compared between groups. The Pipeline Embolization Device with versus without coiling required a significantly longer procedure time (335.8 ± 63.9 versus 96.7 ± 46.2 min; P < .0001) and resulted in higher neurological morbidity (12.5% versus 7.8%; P = .13). These data suggest that either strategy represents an acceptable risk profile in the treatment of complex cerebral aneurysms and warrants further investigation.

ABBREVIATIONS: IntrePED = International Retrospective Study of Pipeline Embolization Device; PED = Pipeline Embolization Device

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he recent development of flow diversion for cerebral aneu-
rysms that are difficult to treat has ushered in an exciting time
in the world of neurointerventional surgery.1-17 Reports in the
literature, however, are conflicting concerning the optimal strat-
yegy in using this new device.1,2,4,13,15,16,18-21 The addition of coil
embolization to flow diversion, while prevalent in daily use, has
not been subjected to a large systematic analysis.7-11,16,21-24 The
earliest case report hypothesized that coils within the aneurysm
sac can augment the degree of flow diversion with the goal of
improved occlusion of the aneurysm.3 Others believe that adjunct-
ive coil embolization does little to improve the already high oc-
clusion rates obtained by using the Pipeline Embolization Device
(PED; Covidien, Irvine, California) alone.21 Furthermore, there
have been reports of complications associated with overly dense
coil embolization of aneurysms in this setting.22

We analyzed the International Retrospective Study of Pipeline
Embolization Device (IntrePED [ClinicalTrials.gov identifier: NCT01558102]) data to determine whether there was an increase
in neurologic complications associated with the use of the PED
and adjunctive coil embolization.

MATERIALS AND METHODS

This study is a subanalysis of IntrePED registry data obtained
from a multicenter, observational, international registry of pa-
tients treated with the PED. The primary objective of IntrePED
was to identify any neurologic events following treatment with the
PED. The IntrePED registry includes patients treated with the
PED starting in July 2008 and concluding in July 2013, following
the enrollment of 793 patients. Because the study was conducted
retrospectively, the protocol did not specify the coiling method-
ology, and the decision to use coils with the PED was left to the
discretion of the treating physician. Details regarding the institu-
tional review board and ethics committee approvals, patient pop-
ulation, and protocol requirements are described in the primary
IntrePED article.17

This subanalysis was performed to compare the safety out-
comes of patients treated with the PED alone (PED group) with
those of patients treated with the PED and adjunctive coil embo-
lization (PED/coil group). Data collected for analysis were basic
demographic information, including patient age, sex, and history of aneurysm rupture; aneurysm characteristics, including aneurysm size, neck size, shape, and location; procedural data, including procedure time and devices used; and follow-up data, including any complications. The primary outcomes were neurologic mortality and combined neurologic morbidity and mortality. Neurologic morbidity was predefined as the composite of the following neurologic complications: spontaneous aneurysm rupture, ipsilateral intracranial hemorrhage, ischemic stroke, parent artery stenosis, and cranial neuropathy. These complications were characterized as major or minor, with “major” defined as an ongoing clinical deficit at 7 days after the event. All major adverse events are included in the neurologic morbidity and mortality rates.

The data were analyzed to determine whether there were any significant differences between those patients treated with the PED alone versus those treated with the PED and adjunctive coils. Differences in continuous variables between the 2 groups were tested by using the Wilcoxon rank sum test. Differences in categorical variables between groups were analyzed by using the χ² or Fisher exact test. Data are presented as the number of events and percentage or mean ± SD unless otherwise noted; P values < .05 were statistically significant. Most statistical analyses were performed across patient groups on a per-patient basis. When determining aneurysm size, we categorized patients with multiple aneurysms on the basis of the size of the largest aneurysm. Analysis of aneurysm characteristics was performed across all aneurysms rather than across patients.

RESULTS

The registry included 793 patients with 906 aneurysms: 689 patients with 797 aneurysms were treated with the PED alone, and 104 patients with 109 aneurysms were treated with PED/coil (Table 1). While the patient ages, sex, and length of follow-up were well matched, procedure times were significantly increased for the PED/coil cohort compared with the PED alone group (135.8 ± 63.9 minutes versus 96.7 ± 46.2 minutes, P < .0001).

The mean aneurysm and neck sizes were statistically larger in the PED/coil cohort than in the PED alone group (aneurysm size, 13.6 ± 7.8 mm versus 10.3 ± 7.6 mm, P < .0001; neck size, 6.4 ± 3.0 mm versus 6.2 ± 5.1 mm, P = .017) (Table 2). These larger aneurysms were also more likely to require multiple PEDs during treatment (Table 3). There was also a statistically significant difference in the location of aneurysms treated between the 2 groups (P < .0001). There were significantly fewer internal carotid artery aneurysms treated in the PED/coil cohort compared with the PED alone group (64.2% versus 77%, P = .006). There were significantly more basilar artery aneurysms treated by PED/coil compared with PED alone (14.7% versus 3.5%, P < .0001). There was no statistically significant difference in presentation with subarachnoid hemorrhage between the 2 groups (PED/coil 11.9% versus PED alone 7.9%, P = .155).

Overall, 13 of 104 (12.5%) patients in the PED/coil cohort experienced a major neurologic complication and/or mortality versus 54 of 689 (7.8%) patients in the PED alone cohort (P = .13) (Table 4). Neither the overall nor the individual complication rates reached statistical significance.

DISCUSSION

While the use of adjunctive coil embolization with the PED is not novel, there are questions regarding the efficacy of, and the potential for, increased complications with this strategy compared with PED embolization alone. Certain authors have advocated coil embolization as a method of improving occlusion rates and minimizing the potential for catastrophic aneurysm rupture following the use of flow-diverting stents. Others have argued that the addition of coil embolization to the procedure yields no significant added advantage in regard to treatment efficacy. However, our single-center results, which have been previously presented, did identify a statistically significant increase in the need for retreatment with a strategy of PED alone versus PED/coil.
Additionally, we previously reported our overall (31.7%) and permanent complication (3.2%) rates following use of the PED. However, we did not examine any potential differences in complications between these 2 treatment strategies. In an earlier report on the PED, Siddiqui et al described a patient with a giant middle cerebral artery aneurysm treated with 2 PEDs and dense coil embolization. The patient had an acute thrombosis of the PED following the procedure, which was attributed to the dense coil mass. The authors recommended avoiding dense packing of aneurysms when coil embolization is used as an adjunctive treatment with the PED.

In a recent series published by Lin et al, 75 patients treated with the PED alone were compared with 29 patients treated with the PED and adjunctive coil embolization. There was no statistically significant difference in the complication rates between the 2 groups (10.3% with PED/coil versus 8.0% with PED alone, \( P = .7 \)). Lin et al found, as we did in the IntrePED study, that aneurysms treated with a strategy of PED/coil were statistically larger than aneurysms treated with PED alone (16.3 versus 12.4 mm, \( P = .02 \)). Nossek et al also found similar results in 25 consecutive patients with unruptured aneurysms treated with the PED and adjunctive coiling.

Szikora et al described their series of 19 patients with wide-neck intracranial aneurysms treated with a strategy of both PED/coil and PED alone. Initially, they treated patients with adjunctive coil embolization, maintaining low coil-packing densities; however, they switched to a strategy of overlapping PEDs without coiling in the latter part of their series. Despite the 2 differing strategies, they had similar occlusion rates at the 6-month follow-up interval. Although their overall complication rate (1 permanent nonrestricting morbidity and 1 mortality) was within the rates published in the literature, they did not specify which treatment strategy was associated with these complications.

In the IntrePED registry, there was a statistically significant difference in the aneurysm size between the 2 cohorts we evaluated (\( P < .0001 \)). Aneurysms treated with adjunctive coil embolization were larger in both aneurysm size and aneurysm neck size. These differences are likely related to the individual clinician’s judgment in regard to the efficacy of stand-alone PED placement for this subset of aneurysms. There may have been a stronger desire to have more immediate contrast stasis during the initial treatment of larger aneurysms due to the higher chance of spontaneous rupture with increasing aneurysm size. In this instance, 2 options for increasing stasis would be to add coil embolization or to place multiple PEDs across the aneurysm neck. Potentially, the use of multiple PEDs may also increase the rate of complications during the procedure. However, we did not identify a difference in the percentage of aneurysms treated with multiple PEDs in either cohort. Patients with larger aneurysms, however, were more likely to have multiple PEDs deployed in both groups (PED alone versus PED/coil).

Another interesting finding in our analysis is the statistically significant difference in the location of aneurysms treated by either strategy. Again, this is likely related to clinical judgment in terms of the aneurysm characteristics and their relationship to the parent vessel. Additionally, endovascular surgeons may be more reluctant to use adjunctive coil embolization when using flow diverters in the posterior cerebral artery/posterior circulation, which is currently an off-label indication in some countries.

While one may presuppose a higher intraprocedural rupture rate with a strategy of PED and adjunctive coils, this was not apparent in our findings. Even with manipulation of the aneurysm wall/dome during coil embolization, there was no statistically significant increased rate of ipsilateral intracranial hemorrhage during or following the procedure. While the anatomical differences between the aneurysms in the 2 cohorts may have certainly influenced the practitioner’s judgment as to the optimal treatment strategy, there were no statistically significant differences in the primary or secondary end points for either treatment strategy. Overall, the complication rates reported for the patients in the IntrePED registry for either treatment strategy are in line with those in the published literature for use of flow-diverting stents.

Once the decision is made to use adjunctive coil embolization, the setup and performance of the procedure may be distinctly different from those used in deploying a PED alone. First, one must decide whether to coil the aneurysm before or after placement of the flow-diverting stent. One can choose to proceed first with primary or balloon-assisted coil embolization followed by PED deployment. While this strategy would not significantly affect the deployment of the PED from a guide catheter standpoint, it does add the time required to perform the initial embolization.
to the overall procedure. Once coils are placed within the aneurysm, the microcatheter or balloon microcatheter or both are removed, allowing unencumbered navigation of the catheters for PED deployment. This technique, however, can potentially obscure visualization of the PED during deployment.

Alternatively, one can jail a microcatheter within the aneurysm and initially place the PED followed by aneurysm coiling. This strategy, however, may affect the choice of support catheters. One must ensure that the inner diameter of the guide catheter is sufficiently large enough to support simultaneous navigation of the Marksman catheter (Covidien) and the microcatheter to be used for coil embolization. The use of a second microcatheter for coiling placed through the same guide catheter as the Marksman catheter would likely preclude the use of additional catheters (ie, distal-access catheters) to support PED deployment due to limitations in guide-catheter size. Despite the increase in procedural times and/or case complexity, there was no statistically significant increase in the overall complication rate in terms of neurologic morbidity and mortality in our analysis.

Limitations

Our study is limited by its retrospective nature, with participating sites following their standard practice for treating aneurysms with PEDs. As a result, the decision to use adjunctive coil embolization was left to the discretion of the treating physician and was not standardized across centers. Because the IntrePED study was a retrospective, observational study without preplanned subgroup analysis, no prespecified differences were expected between these 2 cohorts. Additionally, no power analysis was performed. While there are certain inherent limitations with this type of study, we believe that the conclusions may still be clinically relevant.

CONCLUSIONS

Decisions about which strategy to use when faced with a complex cerebral aneurysm are made largely at the discretion of, and with the judgment of, the practitioner. There have been few large series comparing PED alone versus PED with coiling in terms of overall efficacy in aneurysm treatment. While there was a statistically significant difference in aneurysm size and location and procedural times in the IntrePED registry between our 2 cohorts, there was no statistically significant difference in overall complications. These data suggest that either strategy represents an acceptable risk profile in the treatment of complex cerebral aneurysms and warrants further investigation.

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