Flow diversion using the Pipeline embolization device for intracranial and extracranial pseudoaneurysms: a systematic review and meta-analysis of the literature

Elena Greco, MD, Jorge Rios-Zermeño, MD, Abdul Karim Ghaith, MD, Umme Habiba Faisal, MBBS, Anshit Goyal, MBBS, Oluwaseun O. Akinduro, MD, Samir Kashyap, DO, David A. Miller, MD, Stephen P. Graepel, MA, Mohamad Bydon, MD, Erik H. Middlebrooks, MD, Sukhwinder S. Sandhu, MD, and Rabih G. Tawk, MD

Departments of Neurological Surgery and Radiology, Mayo Clinic, Jacksonville, Florida; Department of Neurological Surgery, Instituto Nacional de Neurología y Neurocirugía, Mexico City, Mexico; Mayo Clinic Neuro-Informatics Laboratory, Mayo Clinic, Rochester, Minnesota; Department of Neurological Surgery, Mayo Clinic, Rochester, Minnesota; All India Institute of Medical Sciences, Kalyani, West Bengal, India; and Department of Education, Division of Biomedical and Scientific Visualization, Mayo Foundation for Medical Education and Research, Mayo Clinic, Rochester, Minnesota

OBJECTIVE Pseudoaneurysms (PSAs) are complex vascular lesions. Flow diversion has been proposed as an alternative treatment to parent artery occlusion that preserves laminar flow. The authors of the present study investigated the safety and short-term (< 1 year) and long-term (≥ 1 year) aneurysm occlusion rates following the treatment of intracranial and extracranial PSAs using the Pipeline embolization device (PED).

METHODS An electronic database search for full-text English-language articles in Ovid MEDLINE and Epub Ahead of Print, Ovid Embase, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus was conducted following the PRISMA guidelines. Studies of any design including at least 4 patients with intracranial or extracranial PSAs treated using a PED were included in this analysis. The primary outcome of interest was the rate of peri- and postprocedural complications. Secondly, the authors analyzed the incidence of complete aneurysm occlusion.

RESULTS A total of 90 patients with 96 PSAs across 9 studies were included. The mean age was 38.2 (SD 15.14) years, and 37.8% of the patients were women. The mean PSA size was 4.9 mm. Most PSAs were unruptured, and the most common etiology was trauma (n = 32, 35.5%), followed by spontaneous formation (n = 21, 23.3%) and iatrogenic injury (n = 19, 21.1%). Among the 51 (53.1%) intracranial and 45 (46.9%) extracranial PSAs were 19 (19.8%) dissecting PSAs. Sixty-six (77.6%) PSAs were in the internal carotid artery and 10 (11.8%) in the vertebral artery. Thirty-three (34.4%) PSAs were treated with ≥ 2 devices, and 8 (8.3%) underwent adjunctive coiling. The mean clinical and angiographic follow-up durations were 10.7 and 12.9 months, respectively. The short-term (< 1 year) and long-term (≥ 1 year) complete occlusion rates were 79% (95% CI 66%–88%, p = 0.82) and 84% (95% CI 70%–92%, p = 0.95), respectively. Complication rates were 8% for iatrogenic dissection (95% CI 3%–16%, p = 0.94), 10% for silent thromboembolism (95% CI 5%–21%, p = 0.77), and 12% for symptomatic thromboembolism (95% CI 6%–23%, p = 0.48). No treatment-related hemorrhage was observed. The overall mortality rate at the last follow-up was 14%.

CONCLUSIONS The complete occlusion rate for PSAs treated with the PED was high and increased over time. Although postprocedural complications and mortality were not insignificant, flow diversion represents a reasonably safe option for managing these complex lesions.

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KEYWORDS Pipeline embolization device; flow diversion; pseudoaneurysms; long-term outcomes

ABBREVIATIONS FDA = Food and Drug Administration; ICA = internal carotid artery; ICH = intracranial hemorrhage; PED = Pipeline embolization device; PSA = pseudoaneurysm; SAH = subarachnoid hemorrhage; TIA = transient ischemic attack; VA = vertebral artery.


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Extracranial PSAs are in the cervical segment of the internal carotid artery (ICA) and the preforaminal, foraminal, and atlantic segments of the vertebral artery (VA). Intracranial PSAs are in the intracranial intradural and extradural segments of the ICA, the VA, and their major branches. Extracranial PSAs are usually surgically treated with the failure of medical therapy, that is, in the event of progressive enlargement or persistent neurological symptoms. However, intracranial PSAs often require immediate and definitive treatment. Figure 2 shows an illustration of intracranial and extracranial PSAs of the ICA.

Historically, the preferred treatment option has been parent artery sacrifice with or without revascularization. However, surgical and endovascular treatment in patients experiencing acute hemorrhage and comorbidities can be extremely challenging. Moreover, the morphology of these lesions (wide-based and fusiform or blister-like) makes it challenging to use surgical and endovascular methods.

Flow diverters represent a reconstructive endovascular treatment option that offers a reasonable alternative to parent artery occlusion, with or without bypass. They are considered effective because of their self-expanding design and excellent maneuverability along with the ability to preserve the parent artery while promoting occlusion of the PSA.

The Pipeline embolization device (PED; Medtronic) was approved by the Food and Drug Administration (FDA) in 2011 for the treatment of complex and wide-necked ICA aneurysms located between the petrous and superior hypophyseal segments. Compared to conventional stents, the PED is more flexible and better adapted to vessel curvature. After deployment, it changes the hemodynamics of the aneurysm/PSA, causing thrombosis within the aneurysm and acting as a scaffold to promote neointimal growth. Since its FDA approval, the PED has been increasingly used off-label for treating several vascular lesions, including PSAs of various etiologies and at different locations. Although occlusion rates seem promising, the PED’s safety in treating PSAs remains a concern given the time required for the PSA to reach thrombosis especially in emergency situations. Moreover, the risk of bleeding is high when the pressure gradient is significant. Importantly, the need for dual antiplatelet therapy following PED implantation further complicates the risk of rebleeding, whereas an inadequate antiplatelet
regimen can result in ischemic complications and in-stent thrombosis.8

In this systematic review and meta-analysis, we aimed to summarize the currently available evidence on and analyze the safety and efficacy of PEDs for the treatment of intracerebral and extracerebral PSAs.

Methods

Study Selection and Eligibility Criteria

This systematic review and meta-analysis was performed in compliance with the PRISMA guidelines. A comprehensive search of several databases was performed on August 23, 2022. Results were limited to the English language. The databases searched were Ovid MEDLINE and Epub Ahead of Print, In-Process, and Other Non-Indexed Citations and Daily; Ovid Embase; Ovid Cochrane Central Register of Controlled Trials; Ovid Cochrane Database of Systematic Reviews; and Scopus via Elsevier. Controlled vocabulary supplemented with keywords was used to search for clinical and angiographic outcomes in patients with aneurysms treated with the PED.

Two authors (E.G. and J.R.Z.) independently reviewed the literature, screened the articles yielded by the search strategy, and included all studies reporting angiographic and clinical outcomes in patients who had undergone PED treatment for PSAs.

We used the following keywords: “pseudoaneurysm,” “flow diversion,” “Pipeline,” and “Pipeline embolization device.” We excluded review articles, articles with fewer than 4 patients (case reports and some case series), conference abstracts, and technical notes. We also excluded studies that did not specify the flow diverter type and/or lacked follow-up data. Both intra- and extracranial aneurysms were included.

Outcome Measures

Primary outcomes included short-term (< 1 year) and long-term (≥ 1 year) angiographically complete aneurysm occlusion. Secondary outcomes included long-term (≥ 1 year) complications following PED placement, categorized as dissection, silent or symptomatic thromboembolism (confirmed clinically and angiographically), or death.

Covariates

The main covariates of interest were as follows: total number of patients, number of females, aneurysm location, mean aneurysm size (mm), mean age (years), number of PSAs, etiology (traumatic injury, iatrogenic injury, radiation therapy, or other), number of devices used (1 or ≥ 2), adjunctive coiling, rupture status, previously treated aneurysms, and other characteristics (dissecting and/or association with another aneurysm, carotid-cavernous fistula, or skull base fracture).

Statistical Analysis

Random-effects meta-analysis was performed to obtain the overall estimate of ischemic and hemorrhagic complications across studies. Standard errors and confidence intervals for single proportions were also derived. Subsequently, a meta-analysis of proportions was performed to estimate the pooled rates of short- and long-term complete aneurysm occlusion, long-term symptomatic thromboembolism, aneurysm rupture, and death. A one-arm meta-analysis was performed to determine the incidence of each primary and secondary outcome. The event rate and 95% confidence interval for each outcome were assessed according to the exposure variables. All analyses were implemented in R statistical software (R Foundation for Statistical Computing). A p value < 0.05 was considered statistically significant.

Results

Through multiple electronic database searches, we identified 499 references, from which 9 studies met our inclusion criteria (Fig. 3). A total of 90 patients with 96 PSAs were identified. The mean age was 38.2 (SD 15.14) years, and 34 (37.8%) patients were women. The most frequent PSA etiology was trauma (n = 32, 35.5%), followed by spontaneous formation (n = 21, 23.3%) and iatrogenic injury (n = 19, 21.1%). Twenty-one (23.3%) patients presented with a transient ischemic attack (TIA), 16 (17.8%) with hemorrhage, 12 (13.3%) with headache, and 12 (13.3%) with no symptoms.

The mean PSA diameter was 4.9 (SD 5.05) mm. Nineteen (19.8%) PSAs were dissecting. Five studies (n = 44 patients, 46 PSAs) included exclusively intracranial PSAs, 3 studies (n = 40 patients, 44 PSAs) included exclusively extracranial PSAs, and 1 study included both (n = 6 patients, 6 PSAs). There were 51 (53.1%) intracranial PSAs and 45 (46.9%) extracranial PSAs.

Eight studies (n = 85 PSAs) reported PSA location. Most PSAs (77.6%, 66/85) originated from the ICA: 34.1% (29/85) were in the cervical ICA; 17.6% (15/85) and 14.1% (12/85) were in the petrous and cavernous segments of the ICA, respectively; 4.7% (4/85) were in the paracavernous segment; 2.4% (2/85) were in the suprachiasmal segment; 2.4% (2/85) were in the lacerum segment; and 2.4% (2/85) were at the ICA terminus. Ten (11.8%) PSAs were in the VA.

Among the studies including intracranial PSAs with a specified etiology, there were 44 patients with 46 PSAs. Etiologies included trauma (n = 13, 28.3%), iatrogenic injury (n = 13, 28.3%), radiation therapy (n = 7, 15.2%), and spontaneous formation (n = 4, 8.7%). Among the studies including exclusively extracranial PSAs, there were 40 patients with 44 PSAs. Seventeen (38.6%) PSAs were spontaneous, 16 (36.4%) were traumatic, 4 (9.1%) were caused by arteriosclerosis, and 3 (6.8%) were caused by iatrogenic injury.

Sixty-three PSAs were treated using a single PED, 33 PSAs received 2 or more devices, and coils were added in 8 cases. The mean clinical follow-up was 10.67 months, and the mean angiographic follow-up was 12.9 months.

Patient demographics and clinical characteristics following PED placement for PSAs are shown in Table 1. Characteristics of PSAs in patients treated with the PED are shown in Table 2.

Short- and Long-Term Complete Aneurysm Occlusion

Overall, the short-term complete aneurysm occlusion
FIG. 3. PRISMA flow diagram showing the literature review, search strategy, and study selection process. Data added to the PRISMA template (from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009;6[7]:e1000097) under the terms of the Creative Commons Attribution (CC BY-NC 2.0) License (https://creativecommons.org/licenses/by/2.0).

TABLE 1. Patient demographics and clinical characteristics following PED placement for PSAs

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>Mean Age (yrs)</th>
<th>No. of Females</th>
<th>Etiology (no.)</th>
<th>Presenting Symptom (no.)</th>
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<td>TR</td>
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<td>11</td>
<td>36.4</td>
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<td>Cohen et al., 2016</td>
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<td>27</td>
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<tr>
<td>Cerejo et al., 2017</td>
<td>7</td>
<td>47</td>
<td>5</td>
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<td>Sami et al., 2018</td>
<td>7</td>
<td>37</td>
<td>1</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Chen et al., 2019</td>
<td>19</td>
<td>50</td>
<td>8</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Akinduro et al., 2020</td>
<td>24</td>
<td>51.2</td>
<td>14</td>
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<td>3</td>
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<tr>
<td>Deng &amp; Feng, 2020</td>
<td>4</td>
<td>25.8</td>
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<tr>
<td>Budhoski et al., 2022</td>
<td>6</td>
<td>12</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

ASx = asymptomatic; BLD = blindness; CI = cerebral ischemia; DC = decreased consciousness; HA = headache; Hem = hemorrhage; HS = Horner syndrome; II = iatrogenic injury; NB = epistaxis; NR = neck rigidity; OTH = other; RT = radiation therapy; Spon = spontaneous; TR = trauma; VL = vision loss; — = not available.

* Tinnitus.
† Ear pain.
‡ Ataxia.
§ Tumor invasion.
‖ Atherosclerosis.
Long-Term Complications
The overall rate of long-term silent thromboembolism was 10% (95% CI 5%–21%, p = 0.77; Fig. 5A), and the symptomatic thromboembolism rate was 12% (95% CI 6%–23%, p = 0.48; Fig. 5B). The overall rate of aneurysm dissection was 8% (95% CI 3%–16%, p = 0.94; Fig. 5C). No patients had subarachnoid hemorrhage (SAH) or intracranial hemorrhage (ICH) following treatment at the last follow-up. The death rate was 14% (95% CI 5%–34%, p = 0.02; Fig. 5D). Outcomes following PED placement in patients with a diagnosed PSA are shown in Table 3.

Discussion
PSAs are rare vascular lesions that result from a rupture of the arterial wall. Since extravascular hematomas are contained only by a connective tissue layer, these lesions carry a significant risk of hemorrhage and death.\(^1\)

PSAs remain one of the most difficult vascular lesions to treat, given that surgical and endovascular manipulation in the affected arteries can be challenging and can result in acute and delayed complications.\(^2\)\(^,\)\(^9\) Moreover, the lack of a true wall and true neck makes it challenging to use traditional treatment strategies including parent artery sacrifice. Additional bypass procedures can be performed when needed based on collateral supply with the additional risks inherent to these procedures. However, with current endovascular devices, excluding the PSA

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**TABLE 2. Characteristics of PSAs in patients treated with the PED**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Country</th>
<th>No. of PSAs</th>
<th>Mean PSA Diameter (mm)</th>
<th>Circulation</th>
<th>No. of Devices Used (for PSAs)</th>
<th>No. w/ Adjunctive Coiling</th>
<th>Rupture Status (no.)</th>
<th>No. Previously Treated</th>
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<td>Ant</td>
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<td>6</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Brzazicki et al., 2016(^{17})</td>
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<td>11</td>
<td>—</td>
<td>Ant</td>
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<td>7</td>
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</tr>
<tr>
<td>Cohen et al., 2016(^{11})</td>
<td>Israel</td>
<td>5</td>
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<td>Pst</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>—</td>
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<tr>
<td>Cerejo et al., 2017(^{1})</td>
<td>US</td>
<td>8</td>
<td>6.3</td>
<td>Pst</td>
<td>7</td>
<td>1</td>
<td>3</td>
<td>4</td>
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<tr>
<td>Sami et al., 2018(^{2})</td>
<td>US</td>
<td>8</td>
<td>9</td>
<td>Ant &amp; pst</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Chen et al., 2019(^{11})</td>
<td>US</td>
<td>19</td>
<td>8.8</td>
<td>Ant</td>
<td>12</td>
<td>7</td>
<td>—</td>
<td>8</td>
</tr>
<tr>
<td>Akinduro et al., 2020(^{3})</td>
<td>US</td>
<td>28</td>
<td>17.7</td>
<td>Ant</td>
<td>21</td>
<td>7</td>
<td>3</td>
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</tr>
<tr>
<td>Deng &amp; Feng, 2020(^{18})</td>
<td>China</td>
<td>4</td>
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<tr>
<td>Budohoski et al., 2022(^{15})</td>
<td>US</td>
<td>6</td>
<td>—</td>
<td>Ant</td>
<td>5</td>
<td>1</td>
<td>0</td>
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</table>

ant = anterior; pst = posterior.
FIG. 5. Forest plot showing the long-term silent stroke (A), symptomatic stroke (B), aneurysm dissection (C), and death (D) rates following PED placement in patients with diagnosed PSAs.
PSA wall further increases the risk of rebleeding. As recent SAH or ICH, the high-pressure gradient across the vessels does not provide immediate protection with thrombosis; their predisposition for rebleeding. Moreover, flow diverters may be a promising alternative for these otherwise challenging lesions, making it possible to preserve the parent artery while promoting thrombosis of the PSA and vessel remodeling. Flow diverters may be a promising alternative for these otherwise challenging lesions, making it possible to preserve the parent artery while promoting thrombosis of the PSA and vessel remodeling. The first cases of intracranial PSA treated with the PED were published as case reports. After initial promising results, the off-label use of the PED to treat PSAs of various etiologies and locations has been increasingly reported. However, only a limited number of patients have undergone this application, with inconclusive results.

One concern is the need for dual antiplatelet therapy to prevent thromboembolic complications and in-stent thrombosis, as this therapy carries a high risk of hemorrhage given the significant instability of these lesions and their predisposition for rebleeding. Moreover, flow diverters do not provide immediate protection with thrombosis; therefore, in patients with acute PSAs in the setting of a recent SAH or ICH, the high-pressure gradient across the PSA wall further increases the risk of rebleeding. As a consequence, the role and safety of the PED in treating PSAs is still unclear and requires further investigation. To the best of our knowledge, this is the first meta-analysis and comprehensive review on the safety and efficacy of the PED in treating intracerebral and extracerebral PSAs. Traumatic and iatrogenic injuries were the primary causes of PSAs reported (35.5% and 21.1%, respectively), whereas 23.3% of PSAs were spontaneous. We found high occlusion rates after PSAs had been treated with the PED. The complete occlusion rate was 79% at the short-term follow-up (< 1 year) and 84% at the long-term follow-up (≥ 1 year). However, postprocedural morbidity and mortality were considerable, and the rate of symptomatic strokes was 12%, with a mortality rate at 14%. The overall rate of iatrogenic dissection was 8%, and the overall rate of silent thromboembolism was 10%. Interestingly, no treatment-related hemorrhagic events were observed at the last follow-up.

### Intracranial PSAs

In our meta-analysis, 51 (53.1%) lesions were intracranial PSAs, and 38 (74.5%) were in the ICA. Fifteen (29.4%) were in the petrous ICA, and 12 (23.5%) were in the cavernous ICA. Intracranial PSAs are rare, accounting for 1% of intracranial aneurysms, whereas PSAs of the ICA account for less than 6% of all carotid aneurysms. Endovascular treatment of intracranial ICA PSAs with the PED seems to involve a higher risk of treatment failure and complications than extracranial ICA PSAs. Intracranial vessels are often tortuous, narrow, and distal. Therefore, they are more difficult to access and fragile. The unstable nature of intracranial PSAs increases the risk of rupture with consequent SAH, ICH, and neurological deterioration, with a mortality rate between 31% and 54%.

The clinical course is influenced by various factors, including etiology, anatomical location, vascular collateral reserve, clinical presentation, dimension, and neurological consequences, including hemorrhagic and ischemic events. In our meta-analysis, among the studies reporting intracranial PSAs exclusively, traumatic and iatrogenic injuries were the primary etiologies (28.3% each), whereas 15.2% of PSAs were caused by radiation therapy. Deng and Feng described 4 patients with traumatic intracranial ICA PSAs who had undergone flow diversion with the PED during the chronic phase. After a year, 75% of PSAs were occluded, and the remainder were almost completely occluded. No in-stent stenosis, symptomatic stroke, perforator occlusion, or hemorrhagic complications were observed. These authors recommended using the PED only during the chronic phase of PSAs and covered stents as the preferred method for PSAs in the acute state with recent

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**TABLE 3. Outcomes following PED placement in patients with diagnosed PSAs**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Deaths</th>
<th>No. of PSAs</th>
<th>Complication</th>
<th>Complete Occlusion</th>
<th>Clinical Occlusion</th>
<th>Angio FU</th>
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<td>Tsang et al., 2015</td>
<td>5</td>
<td>2</td>
<td>Silent Stroke, SX, Dissection</td>
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<td>0</td>
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<td>Brzezicki et al., 2016</td>
<td>1</td>
<td>1</td>
<td>Silent Stroke, SX</td>
<td>0</td>
<td>1</td>
<td>9 6 — — —</td>
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<tr>
<td>Cohen et al., 2016</td>
<td>0</td>
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<td>Silent Stroke, SX</td>
<td>0</td>
<td>0</td>
<td>5 5 5 5</td>
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<td>Silent Stroke, SX</td>
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<td>0</td>
<td>3 2</td>
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<td>Sami et al., 2018</td>
<td>3</td>
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<td>Silent Stroke, SX</td>
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<td>1</td>
<td>— —</td>
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<tr>
<td>Chen et al., 2019</td>
<td>1</td>
<td>1</td>
<td>Silent Stroke, SX</td>
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<td>0</td>
<td>18 14</td>
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<td>Budhoski et al., 2022</td>
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<td>Silent Stroke, SX</td>
<td>0</td>
<td>1</td>
<td>6 5</td>
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Angio = angiographic; FU = follow-up; Sx = symptomatic.
hemorrhage and unstable aneurysm capsules. Sami et al. described a series of 7 patients with 8 traumatic intracranial PSAs treated with the PED.\(^8\) At a mean follow-up of 15 months, 83.3% of patients showed complete occlusion, whereas the remaining 16.7% had near-complete occlusion. No patient experienced thromboembolic events, but 1 patient died from a procedure-related complication. One patient developed a carotid-cavernous fistula, which was successfully retreated with a second PED. Chen et al. reported the largest multi-institutional series of intracranial PSAs treated with the PED, consisting of 19 patients with 19 PSAs principally caused by traumatic and iatrogenic lesions.\(^11\) At a mean follow-up of 6 months, 78% of PSAs demonstrated complete occlusion and 11% showed near-complete occlusion. Two (11%) patients had significant PSA enlargement after PED placement, and ICA sacrifice was necessary. No patient experienced neurological events secondary to PED placement. In the studies by Chen et al. and Sami et al., dual antiplatelet therapy with aspirin and clopidogrel was continued for 6 months after the procedure, while aspirin alone was continued indefinitely.\(^8,11\) Both studies showed that the PED is a reasonably safe and effective treatment for traumatic or iatrogenic intracranial PSAs.

Tsang et al. described 7 patients with intracranial extradural ruptured PSAs in the petrous and lacerum segments of the ICA that had developed following radiation therapy for nasopharyngeal cancer.\(^16\) Carotid blowout syndrome caused severe epistaxis in each patient. Endovascular treatment with the PED was effective, and 80% of PSAs were completely occluded at the long-term follow-up. In all patients, the primary goal of hemostasis was achieved. Given the risk of bleeding from PSAs in this cohort, patients received dual antiplatelet therapy (clopidogrel 75 mg daily and aspirin 80 mg daily) for only 1–4 weeks, followed by aspirin for 6 months. Although none of the patients experienced rebleeding events, this conservative antiplatelet regimen led to ischemic risk. One patient experienced multiple cerebral infarctions, whereas 3 patients developed delayed in-stent thrombosis and 1 a symptomatic lacunar infarct. These authors concluded that the high prevalence of thromboembolic complications might be partially attributable to this insufficient antiplatelet regimen. They did not endorse using the PED over covered stents. They did employ multiple PEDs in most patients and used adjuvant coiling in 2 patients with ongoing extravasation or a large PSA sac.\(^16\) Budohoski et al. suggested that a single PED may not be sufficient for treating PSAs that are associated with large vessel-wall defects since, in these cases, a larger area of endothelialization is needed.\(^15\) However, the placement of 2 or more PEDs or PED-assisted coiling increases the risk of branch or perforator occlusion. In contrast to the ICA, the posterior circulation is rich in perforators that can complicate the management of intracranial VA PSAs. Therefore, Cerejo et al. decided to treat 7 patients with 8 intracranial VA dissecting PSAs using the fewest possible devices, with favorable results in terms of safety and efficacy.\(^4\) At a mean follow-up of 14.5 months, 75% of the PSAs were completely occluded. Despite dual antiplatelet therapy for 6–12 months, 2 patients had minor periprocedural strokes with only transient neurological symptoms.

The small caliber of the vessels may explain the risk of thromboembolic events. Some studies have linked the risk of parent artery occlusion after PED therapy to the size of the parent vessel.\(^18,19\) In our meta-analysis, among the 5 studies including intracranial PSAs, 33.3% were treated with 2 or more devices, and 9.8% received assisted coiling.

**Extracranial PSAs**

Our study included 45 (46.9%) extracranial PSAs, and most of these (62.2%) were in the cervical portion of the ICA. Incidental extracranial PSAs often have a benign clinical course and can be treated via medical management (anticoagulation or antiplatelet therapy) with remarkable results. However, surgical or endovascular management is indicated in cases of traumatic etiology, enlarging lesions leading to nerve compression or arteriovenous fistulas, symptoms like TIA and strokes despite medical management, or ischemic symptoms due to flow-limiting stenosis and contralateral occlusion/high-grade stenosis.\(^7,11,17\) Our review included 3 studies with extracranial PSAs, most of which were spontaneous (38.6%) and traumatic (36.4%). Common traumatic injuries included gunshot or stab wounds, whereas iatrogenic causes included primarily spinal surgery, subclavian vein catheterization, and chiropractic maneuvers.\(^11,17,20\) The literature shows that cervical PSAs can lead to recurrent dissections in 3.2% of patients within the 1st month and an additional 1.6% of patients up to 1 year. Dissecting PSAs are a leading cause of stroke in young adults.\(^4,21\)

However, interpretation of the literature on this topic is somewhat unclear since some authors have incorrectly grouped PSAs and dissecting aneurysms together. Although PSAs can be caused by arterial dissection, what differentiates them from dissecting aneurysms is that the latter are limited by the adventitia. Cohen et al. reported 5 patients with 5 cervical VA traumatic dissecting PSAs treated with the PED.\(^22\) At 18 months, all PSAs were completely obliterated, and no periprocedural or delayed clinical complications or deaths were observed, supporting the feasibility and safety of the PED in treating extracranial PSAs.

Brzezicki et al. reported 11 patients with 11 high cervical and skull base PSAs associated with carotid artery dissections, most of which were traumatic.\(^17\) The main indications for intervention were flow-limiting stenosis and/or failed medical management with warfarin. Six PSAs were completely occluded at the first follow-up (1–9 months), and 2 large PSAs had minimal residual filling. No related neurological complication was observed.\(^11\) Finally, Akinduro et al. recently conducted the first multicentric study on the safety and efficacy of the PED for the treatment of extracranial PSAs.\(^5\) In 89% of cases, complete occlusion was achieved, and even in that study, no patient experienced procedure-related complications.\(^11,27\)

In all these studies, patients received aspirin and clopidogrel at least 7 days before treatment in elective cases. Clopidogrel and aspirin were continued for at least 3 and up to 7 months after treatment. Based on the findings of this series, PED treatment is safe and effective for treating cervical ICA and VA PSAs. The tortuosity of the arteries at the skull base and the mobility of the cervical ICA
are potential limitations that can lead to the worsening of acute dissection and device stenosis, occlusion, or migration. Moreover, extracranial arteries are usually larger than intracranial ones, with a mean diameter of 4.6 mm. Considering that its diameter ranges from 2.5 to 5 mm, the PED may not have an adequate diameter to achieve optimal wall apposition. In cases in which the PED is not feasible (e.g., parent vessel diameter too large, active extravasation from the aneurysm), covered stents are a viable option.

Study Limitations

Our study has several limitations. The results specifically for intracranial PSAs could not be obtained; thus, it is important to realize the significant difference in vessels with branches or perforators could affect the probability of a negative outcome. PSAs may also behave differently according to their underlying etiology. We were not able to compare intradural versus extradural or intracranial versus extracranial PSAs because of the low number of papers discussing the use of the PED for PSAs as well as the rarity of these lesions. Newer PED generations are associated with fewer complications and better occlusion rates, but a subanalysis could not be performed. Therefore, thromboembolic and ischemic complications together with occlusive ischemia can result from perforator or branch occlusion, and thromboembolic complications can result from inadequate antplatelet treatment or hypercoagulability. We could not differentiate between anterior and posterior circulation PSAs. This systematic review and meta-analysis is affected by publication bias and statistical heterogeneity. The analysis did not include randomized clinical trials, so we were limited by the retrospective nature of the studies. Although we extensively searched the literature, the number of studies meeting our inclusion criteria was low; therefore, this analysis represents the current best available evidence.

Conclusions

The use of the PED for PSAs is a reasonable option, and the rate of complete occlusion increases over time. The rates of complications and death are considerable, especially in patients with intracranial PSAs, and careful patient selection is essential. The requirement for dual antplatelet therapy remains a limitation of PED treatment, especially in acute cases, in which it is crucial to balance the risks of hemorrhage against thromboembolic complications. Long-term follow-ups to evaluate PSA progression and PED-related events are paramount, given the relatively high rates of morbidity and mortality. Further prospective cohort studies with larger patient populations are needed to better identify the role of the PED in treating PSAs.

References


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Author Contributions

Correspondence
Rabih G. Tawk: Mayo Clinic, Jacksonville, FL. tawk.rabih@mayo.edu.