Endovascular Treatment of Intracranial Aneurysms With Flow Diverters
A Meta-Analysis

Waleed Brinjikji, MD; Mohammad H. Murad, MD, MPH; Giuseppe Lanzino, MD; Harry J. Cloft, MD, PhD; David F. Kallmes, MD

Background and Purpose—Flow diverters are important tools in the treatment of intracranial aneurysms. However, their impact on aneurysmal occlusion rates, morbidity, mortality, and complication rates is not fully examined.

Methods—We conducted a systematic review of the literature searching multiple databases for reports on the treatment of intracranial aneurysms with flow-diverter devices. Random effects meta-analysis was used to pool outcomes of aneurysmal occlusion rates at 6 months, and procedure-related morbidity, mortality, and complications across studies.

Results—A total of 29 studies were included in this analysis, including 1451 patients with 1654 aneurysms. Aneurysmal complete occlusion rate was 76% (95% confidence interval [CI], 70%–81%). Procedure-related morbidity and mortality were 5% (95% CI, 4%–7%) and 4% (95% CI, 3%–6%), respectively. The rate of postoperative subarachnoid hemorrhage was 3% (95% CI, 2%–4%). Intraparenchymal hemorrhage rate was 3% (95% CI, 2%–4%). Perforator infarction rate was 3% (95% CI, 1%–5%), with significantly lower odds of perforator infarction among patients with anterior circulation aneurysms compared with those with posterior circulation aneurysms (odds ratio, 0.15; 95% CI, 0.08–0.27; P<0.0001). Ischemic stroke rate was 6% (95% CI, 4%–9%), with significantly lower odds of perforator infarction among patients with anterior circulation aneurysms compared with those with posterior circulation aneurysms (odds ratio, 0.15; 95% CI, 0.08–0.27; P<0.0001).

Conclusions—This meta-analysis suggests that treatment of intracranial aneurysms with flow-diverter devices is feasible and effective with high complete occlusion rates. However, the risk of procedure-related morbidity and mortality is not negligible. Patients with posterior circulation aneurysms are at higher risk of ischemic stroke, particularly perforator infarction. These findings should be considered when considering the best therapeutic option for intracranial aneurysms. (Stroke. 2013;44:442-447.)

Key Words: endovascular treatment ■ interventional neuroradiology ■ intracranial aneurysm ■ subarachnoid hemorrhage

Flow-diverter devices are new, important tools in the treatment of intracranial aneurysms.1 Several single- and multicenter studies have demonstrated acceptable rates of aneurysm occlusion, morbidity, and mortality for patients treated with flow diverters.2–30 These devices are being deployed in greater numbers of patients with more complex aneurysm morphologies and locations.9,12,18,22,25,29 With increasing experience, some of the limitations and unexpected complications of flow diverters have been recognized. These include intraparenchymal hemorrhage (IPH), postprocedural subarachnoid hemorrhage (SAH), as well as ischemic stroke.8

Improved understanding of safety and efficacy profiles associated with flow-diverter treatment of intracranial aneurysms would help guide practitioners in selection and follow-up of patients treated with these devices. We conducted a systematic review and meta-analysis of the literature regarding aneurysmal occlusion rates and procedure-related complication rates for intracranial aneurysms treated with flow diverters.

Methods

A comprehensive review of the literature was performed using the keywords “Intracranial aneurysm”, “divert”, “diversion”, “silk”, “pipeline,” and “pipeline embolization device” to search Pubmed, Ovid Medline, Ovid EMBASE, Scopus, and Web of Science database. Inclusion criteria were the following: English language, >5 patients, studies published between January 2005 and September 2012, and data on postoperative complications and aneurysmal occlusion rates. The exclusion criteria were the following: case reports, in vitro or cadaveric studies, review articles, guidelines, technical notes, and disaster series (series in which all patients were selected because of certain major complication). The electronic search was supplemented by contacting experts in the field and reviewing the bibliographies of included studies for relevant publications. Abstracts, methods, results, figures, and tables were relevant to the search criteria and were retrieved for full-text review. In the case of a lack of relevant publications, the reference lists of selected studies were reviewed for relevant material.

A total of 29 studies were included in this analysis, including 1451 patients with 1654 aneurysms. Aneurysmal complete occlusion rate was 76% (95% confidence interval [CI], 70%–81%). Procedure-related morbidity and mortality were 5% (95% CI, 4%–7%) and 4% (95% CI, 3%–6%), respectively. The rate of postoperative subarachnoid hemorrhage was 3% (95% CI, 2%–4%). Intraparenchymal hemorrhage rate was 3% (95% CI, 2%–4%). Perforator infarction rate was 3% (95% CI, 1%–5%), with significantly lower odds of perforator infarction among patients with anterior circulation aneurysms compared with those with posterior circulation aneurysms (odds ratio, 0.15; 95% CI, 0.08–0.27; P<0.0001). Ischemic stroke rate was 6% (95% CI, 4%–9%), with significantly lower odds of perforator infarction among patients with anterior circulation aneurysms compared with those with posterior circulation aneurysms (odds ratio, 0.15; 95% CI, 0.08–0.27; P<0.0001).
of full text were searched for data on aneurysmal occlusion rates, procedure-related morbidity and mortality, and procedure-related complications.

Aneurysm occlusion was defined as complete occlusion at 6 months. We studied the effect of aneurysm size and aneurysmal occlusion rates, stratifying aneurysms as small (<10 mm), large (10 mm ≤ aneurysm size ≤ 25 mm), or giant (>25 mm).

Procedure-related complications were stratified as total, early (within ≤ 30 days), and late (>30 days). Complications studied included total, early, and late ICH; total, early, and late ischemic stroke; total perforator infarction; and total, early, and late SAH. We examined the association between aneurysm size (small versus large/giant) and aneurysm location (anterior versus posterior) and the total rates of each of the studied complications.

Statistical Analysis
We estimated from each study the cumulative incidence (event rate) and 95% confidence interval (CI) for each outcome. Event rates were pooled across studies using random effects meta-analysis. Subgroup interactions (ANCOVA) were conducted using an interaction test as described by Altman. Heterogeneity across studies was evaluated using the I² statistic.

Results

Study Selection
A total of 505 articles were retrieved, of which 29 met our inclusion criteria (Table 1). Eighteen studies were retrospective case series, and 11 were prospective single-arm studies. Twenty-six studies reported aneurysmal occlusion rates; 29 reported procedure-related morbidity, mortality, and complication rates; and 26 reported both. We included 1451 patients and 1654 treated aneurysms. The mean (±SD) number of patients and treated aneurysms per study were 50.0±59.4 and 57.0±69.9, respectively.

Study Outcomes
Complete occlusion rate was 76% (95% CI, 70%–81%) at 6 months. Complete occlusion rate was 80% (95% CI, 69%–88%) for small aneurysms, 74% (95% CI, 63%–83%) for large aneurysms, and 76% (95% CI, 53%–90.0%) for giant aneurysms (P=0.83).

Procedure-related permanent morbidity rate was 5% (95% CI, 4%–7%), and procedure-related mortality rate was 4% (95% CI, 3%–6%). ICH rate was 3% (95% CI, 2%–4%), with 3% (95% CI, 2%–4%) experiencing early ICH and 2% (95% CI, 1%–3%) experiencing late ICH. Aneurysm size and location were not significantly associated with ICH rate (OR, 0.43; 95% CI, 0.11–1.65; P=0.24 and OR, −1.73; 95% CI, 0.62–4.68, respectively; P=0.35).

SAH rate was 4% (95% CI, 3%–5%), with 3% (95% CI, 2%–5%) experiencing early SAH and 2% (95% CI, 1%–3%) experiencing late SAH. Patients with small aneurysms had a significantly lower rate of postoperative SAH (OR, 0.10; 95% CI, 0.02–0.42; P<0.0001). Aneurysm location was not associated with SAH rate (OR, 1.89; 95% CI, 0.43–8.21; P=0.55).

Total ischemic stroke rate was 6% (95% CI, 4%–9%), with 5% (95% CI, 3%–8%) experiencing early ischemic stroke and 3% (95% CI, 2%–4%) experiencing late ischemic stroke. Patients treated for smaller aneurysms had lower rates of ischemic stroke than their large/giant counterparts (OR, 0.26; 95% CI, 0.07–0.91; P=0.03). Patients treated for anterior circulation aneurysms also had significantly lower ischemic stroke rates than those treated for posterior circulation aneurysms (OR, 0.15; 95% CI, 0.08 to 0.27; P<0.0001). Perforator infarction rate was 3% (95% CI, 1%–5%). Patients with anterior circulation aneurysms had significantly lower perforator infarction rates than their posterior circulation counterparts (OR, 0.01; 95% CI, 0.00–0.08; P<0.0001). Aneurysm size was not associated with perforator infarction risk (OR, 0.33; 95% CI, 0.09–1.25; P=0.13).

An analyses of aneurysm occlusion, total ischemic stroke, and perforator infarction were associated with substantial heterogeneity (I² ≥50%), suggesting unexplained differences in study populations and procedures. The remaining analyses had minimal heterogeneity.

Table 2 summarizes outcomes independent of aneurysm size and location. Table 3 summarizes clinical outcomes by aneurysm size and location.

Discussion
Our meta-analysis demonstrated high occlusion rates for aneurysms treated with flow divers, irrespective of aneurysm size. However, we also demonstrated that the complications associated with flow diverter treatment are not negligible, with morbidity and mortality rates of 5% and 4%, respectively. The safety of flow diversion in small aneurysms was superior to that of large aneurysms, with the latter associated with higher rates of both ischemic infarction and SAH. Higher morbidity in larger aneurysms may relate to the technical challenges as well as the inherent instability of these lesions. We did not find any specific aneurysm type associated with higher rates of IPH but did find an alarmingly high association between perforator infarction and posterior location of intracranial aneurysms. These findings suggest that practitioners must be judicious in selecting candidates for flow-diverter therapy, especially for large or posterior circulation aneurysms.

Published aneurysmal complete occlusion rates are often variable, ranging anywhere from 55% to 95%. In combining aneurysmal occlusion rates from 29 studies, our meta-analysis provides more representative data on aneurysmal occlusion rates than any single study. Furthermore, in studying such a large sample, we had more power to detect differences in aneurysmal occlusion rates by size. This lends greater validity to our finding that aneurysmal occlusion rates were high regardless of size. This finding is extremely important because the current dogma in endovascular intracranial aneurysm treatment is that smaller aneurysms have better occlusion rates than larger aneurysms. The finding that even giant aneurysms have such high occlusion rates provides important implications for those looking to stem the rates of aneurysm recurrence among this population.

Among larger studies, mortality rates have ranged from 0% to 7%, whereas morbidity has ranged from 0% to 12%. Our meta-analysis provides more representative data on morbidity, mortality, and complication rates associated with flow-diverter treatment. Another advantage of this meta-analysis is its increased power to detect differences in complication rates
Table 1. Studies Included in Meta-Analysis

<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Journal</th>
<th>Year</th>
<th>Study Design</th>
<th>No. of Patients</th>
<th>Aneurysms Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barros Faria et al</td>
<td>The role of the pipeline embolization device for the treatment of dissecting intracranial aneurysms</td>
<td>American Journal of Neuroradiology</td>
<td>2011</td>
<td>Retrospective</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Briganti et al</td>
<td>Italian multicenter experience with flow-diverter devices for intracranial unruptured aneurysm treatment with periprocedural complications—a retrospective data analysis</td>
<td>Neuroradiology</td>
<td>2012</td>
<td>Retrospective</td>
<td>273</td>
<td>295</td>
</tr>
<tr>
<td>Byrne et al</td>
<td>Early experience in the treatment of intracranial aneurysms by endovascular flow diversion: a multicentre prospective study</td>
<td>PLoS ONE</td>
<td>2010</td>
<td>Prospective single-arm interventional cohort</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Chan et al</td>
<td>Pipeline embolization device for wide necked internal carotid artery aneurysms in a hospital in Hong Kong: preliminary experience</td>
<td>Hong Kong Medical Journal</td>
<td>2011</td>
<td>Retrospective</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Colby et al</td>
<td>Immediate procedural outcomes in 35 consecutive pipeline embolization cases: a single-center single-user experience</td>
<td>Journal of Neurointerventional Surgery</td>
<td>2012</td>
<td>Retrospective</td>
<td>34</td>
<td>41</td>
</tr>
<tr>
<td>Cruz et al</td>
<td>Delayed ipsilateral parenchymal hemorrhage following flow diversion for the treatment of anterior circulation aneurysms</td>
<td>American Journal of Neuroradiology</td>
<td>2012</td>
<td>Retrospective</td>
<td>47</td>
<td>47</td>
</tr>
<tr>
<td>Deutschmann et al</td>
<td>Long-term follow-up after treatment of intracranial aneurysms with the pipeline embolization device: results from a single center</td>
<td>American Journal of Neuroradiology</td>
<td>2012</td>
<td>Prospective single-arm interventional cohort</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Fischer et al</td>
<td>Pipeline embolization device for neurovascular reconstruction; initial experience in the treatment of 101 intracranial aneurysms and dissections</td>
<td>Neuroradiology</td>
<td>2011</td>
<td>Retrospective</td>
<td>88</td>
<td>101</td>
</tr>
<tr>
<td>Kulcsar et al</td>
<td>High-profile flow-diverter (silk) implantation in the basilar artery: efficacy in the treatment of aneurysms and the role of perforators</td>
<td>Stroke</td>
<td>2010</td>
<td>Retrospective</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Lubicz et al</td>
<td>Flow-diverter stent for the endovascular treatment of intracranial aneurysms: a prospective study in 29 patients with 34 aneurysms</td>
<td>Stroke</td>
<td>2010</td>
<td>Prospective single-arm interventional cohort</td>
<td>29</td>
<td>34</td>
</tr>
<tr>
<td>Lylyk et al</td>
<td>Curative endovascular reconstruction of cerebral aneurysms with the pipeline embolization device: the buenos aires experience</td>
<td>Neurosurgery</td>
<td>2009</td>
<td>Prospective single-arm interventional cohort</td>
<td>53</td>
<td>63</td>
</tr>
<tr>
<td>Maimon et al</td>
<td>Treatment of intracranial aneurysms with the SILK flow diverter: 2 years experience with 28 patients at a single center</td>
<td>Acta Neurochir</td>
<td>2012</td>
<td>Retrospective</td>
<td>28</td>
<td>32</td>
</tr>
</tbody>
</table>
by aneurysm size and location, thus allowing practitioners to risk stratify potential patients.

One of the unanticipated and most feared complications of flow diverters is aneurysm rupture after treatment with these devices. The overall incidence of this complication is unknown, although it is thought to be low and critically related to the complexity of the treated aneurysm. Our meta-analysis suggests that SAH from delayed aneurysm rupture occurs in ≈4% of patients treated with flow diverters, with significantly higher rates among patients with large and giant aneurysms. Aneurysm rupture at ≥1 month postoperative was a relatively rare occurrence (2% of cases). Nonetheless, concerns regarding delayed rupture are so serious that Balt Extrusion issued a medical device alert instructing practitioners not to use the Silk flow diverter without coils owing to the potential for patient death.15 Our study emphasizes that postoperative SAH is a real and significant complication of flow-diverter patients, especially for those with large or giant aneurysms. It is not known at this point whether the practice of using endovascular coils in association with flow diverters in the treatment of larger aneurysms has resulted in a decreased incidence of this devastating complication.

IPH not associated with aneurysm rupture is another dreaded and poorly understood complication of flow-diverter treatment. Previous studies have reported rates ranging from 0% to 10% for this complication.2,4,8,19 We demonstrated a
acute thrombus formation can be mitigated by prompt injec-
tions of antiplatelet therapy. Intraoperatively, stent wall, 
leading to stent occlusion, parent artery occlusion, or 
distal thromboembolic events.35,36 The higher rates of isch-
emic stroke, hemodynamic alteration from flow-diverter 
treatment, and dual antiplatelet therapy are proposed mecha-
nisms.8 In our study, neither aneurysm size nor location was 
associated with IPH rate. All studies included both pre op-
erative and postoperative dual antiplatelet therapy; thus, we 
could not examine any independent role this might play in 
IPH formation. Further studies are needed to determine the 
ultimate cause of IPH.

Ischemic stroke and perforator infarction are well-described 
complications of flow-diverter treatment.15,36 We demonstrated 
an ischemic stroke rate of 6%, with higher rates in posterior 
circulation aneurysms and large/giant aneurysms. Ischemic 
stroke is thought to result from thrombus formation along the 
stent wall, leading to stent occlusion, parent artery occlusion, 
or distal thromboembolic events.15,36 The higher rates of isch-
emic stroke among patients with large/giant aneurysms may be 
related to the fact that, these aneurysms likely required more 
flow-diverter devices to achieve successful occlusion and may 
have been subject to longer operation times. Intraoperatively, 
acute thrombus formation can be mitigated by prompt injec-
tion of Abciximab.27 However, in the long term, it is difficult 
to reduce the risk of thromboembolic events associated with 
flow-diverter treatment.

Perforator infarction in our meta-analysis was not uncom-
mon and often led to devastating consequences. Perforator 
vessels in the posterior circulation are at particularly high 
risk for infarction relative to those in the anterior circulation. 
This is likely because of the delicate perfusion and lack of 
collaterals to brain stem structures. Many case series of pos-
terior circulation aneurysms treated with flow diverters have 
demonstrated this fact.12,21,25 Thus, given the relatively high 
rates of this complication and the devastating consequences 
of brain stem infarction, treatment of posterior circulation aneu-
rysms in which perforator vessels could be involved should 
be performed only when absolutely necessary. When possible, 
deconstructive technique (parent vessel occlusion with flow 
reversal) should be the first consideration for treatment of 
large or giant basilar artery aneurysms.

This study has various limitations. Ecological bias (ie, 
comparisons are made across studies and not within studies), 
presence of publication bias, and statistical heterogeneity are 
limitations that affect all meta-analyses. Our study also has 
limitations because of the methodologic limitations of included 
studies. A majority of the included studies were retrospective 
case series. No prospective studies included were randomized 
or included control groups. Many of the included studies had 
a small sample size and incomplete follow-up data. Because a 
majority of previously published studies did not stratify out-
comes based on important variables, such as patient demo-
graphics, duration of antiplatelet therapy, aneurysm rupture 
status, aneurysm subtype (secular versus fusiform), number 
of devices deployed, use of concomitant coiling, and previ-
ous aneurysm treatment status, we were unable to control for 
these findings in our analysis. Efficacy of flow-diverter treat-
ment in treating compressive symptoms was rarely reported 
in the included studies; thus, we were unable to determine the 
efficacy of flow diverters in treatment of these symptoms. Our 
findings represent a very wide spectrum of aneurysms and 
clinical presentations, and thus our findings cannot be applied 
to determine the risks and complications associated with treat-
ing individual patients or different subgroups of aneurysms 
with flow diverters. Given the heterogeneity of the patients 
and aneurysms in our study, our data cannot be used to com-
pare the efficacy of flow-diverter technology versus treat-
ments, such as coiling and clipping. Therefore, the overall 
quality of evidence (strength of inference) presented in this 
systematic review is considered to be low.

Conclusions

Our study suggests that treatment of intracranial aneurysms 
with flow-diverter devices is feasible and effective with high complete oc-
cclusion rates. The rates of procedure-related morbidity and mortality 
are not negligible. Patients with posterior circulation aneurysms are at 
higher risk of ischemic stroke, particularly perforator infarction, and 
patients with larger aneurysms are at increased risk of ischemic stroke

### Table 2. Outcomes for Endovascular Treatment of Intracranial Aneurysms With Flow Diverters

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate (%)</th>
<th>95% CI</th>
<th>F (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete aneurysmal occlusion ≥6 months</td>
<td>76.0</td>
<td>70.0–81.0</td>
<td>69.0</td>
</tr>
<tr>
<td>Procedure-related morbidity</td>
<td>5.0</td>
<td>4.0–7.0</td>
<td>15.0</td>
</tr>
<tr>
<td>Procedure-related mortality</td>
<td>4.0</td>
<td>3.0–6.0</td>
<td>35.0</td>
</tr>
<tr>
<td>SAH &lt;30 days</td>
<td>3.0</td>
<td>2.0–5.0</td>
<td>0.0</td>
</tr>
<tr>
<td>SAH &gt;30 days</td>
<td>2.0</td>
<td>1.0–3.0</td>
<td>0.0</td>
</tr>
<tr>
<td>SAH total</td>
<td>4.0</td>
<td>3.0–5.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Intraparenchymal hemorrhage ≤30 days</td>
<td>2.0</td>
<td>2.0–4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Intraparenchymal hemorrhage &gt;30 days</td>
<td>2.0</td>
<td>1.0–2.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Intraparenchymal hemorrhage total</td>
<td>2.0</td>
<td>2.0–4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Ischemic stroke ≤30 days</td>
<td>3.0</td>
<td>3.0–8.0</td>
<td>48.0</td>
</tr>
<tr>
<td>Ischemic stroke &gt;30 days</td>
<td>5.0</td>
<td>2.0–4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Perforator infarction</td>
<td>3.0</td>
<td>1.0–5.0</td>
<td>60.0</td>
</tr>
</tbody>
</table>

### Table 3. Outcomes by Aneurysm Size and Location

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneurysm size (small/large vs giant)*</td>
<td>0.26</td>
<td>0.07–0.91</td>
</tr>
<tr>
<td>Aneurysm location (anterior vs posterior)*</td>
<td>0.15</td>
<td>0.08–0.27</td>
</tr>
<tr>
<td>SAH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneurysm size (small/large vs giant)*</td>
<td>0.10</td>
<td>0.02–0.42</td>
</tr>
<tr>
<td>Aneurysm location (anterior vs posterior)</td>
<td>1.89</td>
<td>0.43–8.21</td>
</tr>
<tr>
<td>Perforator infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneurysm size (small/large vs giant)</td>
<td>0.33</td>
<td>0.09–1.25</td>
</tr>
<tr>
<td>Aneurysm location (anterior vs posterior)</td>
<td>0.01</td>
<td>0.00–0.08</td>
</tr>
<tr>
<td>Intraparenchymal hemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneurysm size (small/large vs giant)</td>
<td>0.43</td>
<td>0.11–1.65</td>
</tr>
<tr>
<td>Aneurysm location (anterior vs posterior)</td>
<td>0.48</td>
<td>0.17–1.35</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; and SAH, subarachnoid hemorrhage.

*Denotes statistically significant results. Odds ratio <1.0 favors the characteristic mentioned first.
Disclosures
Dr Cloft was the site PI at enrolling site for SAPPHIRE (Stenting and Angioplasty with Protection in Patients and High Risk for Endarterectomy) registry sponsored by Cordis Endovascular, and Dr Kallmes received a grant, ev3-funding for clinical trials and preclinical research and has pending grants from Penumbra, MicroVention, Micrus, and Cordis. The other authors have no conflicts to report.

References
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Flow Diverter を用いた脳動脈瘤の血管内治療
メタアナリシス

Endovascular Treatment of Intracranial Aneurysms With Flow Diverters
A Meta-Analysis

Waleed Brinjikji, MD2; Mohammad H. Murad, MD, MPH3; Giuseppe Lanzino, MD2,4; Harry J. Cloft, MD, PhD1,2; David F. Kallmes, MD1,2

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背景および目的: Flow diverter は脳動脈瘤の治療において重要な器具である。しかし、動脈瘤閉塞率、罹病率、死亡率、および合併症の発生率に対する影響については完全には解明されていない。

方法: 様々なデータベースで flow diverter を用いた脳動脈瘤の治療に関する論文を検索し、文献を系統的に調べた。ランダム効果メタ解析を用いて、6か月目の動脈瘤閉塞率、手技が原因の罹病率、死亡率、および合併症の発生率をすべての論文から収集した。

結果: 合計 29 篇の論文をこの解析に含めた（患者は 1,654 箇の動脈瘤を有する 1,451 例）。動脈瘤の完全閉塞率は 76%であった [95%CI: 70 ~ 81%]。手技が原因の罹病率は 5% [95%CI: 4 ~ 7%]、死亡率は 4% [95%CI: 3 ~ 6%] であった。術後のくも膜下出血発生率は 3% [95%CI: 2 ~ 5%]、脳実質内出血の発生率は 3% [95%CI: 1 ~ 4%] であった。穿通枝梗塞の発生率は 3% [95%CI: 1 ~ 5%] の中、前方循環動脈瘤患者の穿通枝梗塞のオッズは、後方循環動脈瘤患者（オッズ比 = 0.01; 95%CI: 0.00 〜 0.08; p < 0.0001）と比較して有意に低かった。虚血性脳卒中の発生率は 6% [95%CI: 1 ~ 9%] の中、前方循環動脈瘤患者の穿通枝梗塞のオッズは後方循環動脈瘤患者と比較して有意に低かった（オッズ比 = 0.15; 95%CI: 0.08 〜 0.27; p < 0.0001）。

結論: 今回のメタアナリシスの結果、flow diverter を用いた脳動脈瘤の治療は可能で、かつ効果的であり、高い完全閉塞率を示した。しかし、手技が原因の罹病率や死亡率のリスクは無視することはできない。前方循環動脈瘤患者では虚血性脳卒中のリスクが高く、特に、穿通枝梗塞のリスクが高い。脳動脈瘤の最良の治療オプションを検討する際にはこれらの知見を考慮する必要がある。

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表 2 Flow Diverter を用いた脳動脈瘤の血管内治療の転帰

<table>
<thead>
<tr>
<th>転帰</th>
<th>%</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>動脈瘤による完全閉塞 ≥ 6 ヶ月</td>
<td>76.0</td>
<td>70.0～81.0</td>
<td>69.0</td>
</tr>
<tr>
<td>治療が原因の罹病率</td>
<td>5.0</td>
<td>4.0～7.0</td>
<td>15.0</td>
</tr>
<tr>
<td>治療が原因の死亡率</td>
<td>4.0</td>
<td>3.0～6.0</td>
<td>35.0</td>
</tr>
<tr>
<td>SAH ≤ 30 日</td>
<td>3.0</td>
<td>2.0～5.0</td>
<td>0.0</td>
</tr>
<tr>
<td>SAH &gt; 30 日</td>
<td>2.0</td>
<td>1.0～3.0</td>
<td>0.0</td>
</tr>
<tr>
<td>SAH、合計</td>
<td>4.0</td>
<td>3.0～5.0</td>
<td>4.0</td>
</tr>
<tr>
<td>脳実質内出血 ≤ 30 日</td>
<td>3.0</td>
<td>2.0～4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>脳実質内出血 &gt; 30 日</td>
<td>2.0</td>
<td>1.0～2.0</td>
<td>0.0</td>
</tr>
<tr>
<td>脳実質内出血、合計</td>
<td>3.0</td>
<td>2.0～4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>虚血性脳卒中 ≤ 30 日</td>
<td>5.0</td>
<td>3.0～8.0</td>
<td>48.0</td>
</tr>
<tr>
<td>虚血性脳卒中 &gt; 30 日</td>
<td>3.0</td>
<td>2.0～4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>虚血性脳卒中、合計</td>
<td>6.0</td>
<td>4.0～9.0</td>
<td>56.0</td>
</tr>
<tr>
<td>穿通枝梗塞</td>
<td>3.0</td>
<td>1.0～5.0</td>
<td>60.0</td>
</tr>
</tbody>
</table>

CI: 信頼区間、SAH: くも膜下出血。

表 3 動脈瘤のサイズと位置による転帰

<table>
<thead>
<tr>
<th>転帰</th>
<th>オッズ比</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>虚血性脳卒中</td>
<td></td>
<td></td>
</tr>
<tr>
<td>動脈瘤のサイズ（小/大対巨大）*</td>
<td>0.26</td>
<td>0.07～0.91</td>
</tr>
<tr>
<td>動脈瘤の位置（前方対後方）*</td>
<td>0.15</td>
<td>0.08～0.27</td>
</tr>
<tr>
<td>SAH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>動脈瘤のサイズ（小/大対巨大）*</td>
<td>0.10</td>
<td>0.02～0.42</td>
</tr>
<tr>
<td>動脈瘤の位置（前方対後方）</td>
<td>1.89</td>
<td>0.43～8.21</td>
</tr>
<tr>
<td>穿通枝梗塞</td>
<td></td>
<td></td>
</tr>
<tr>
<td>動脈瘤のサイズ（小/大対巨大）*</td>
<td>0.33</td>
<td>0.09～1.25</td>
</tr>
<tr>
<td>動脈瘤の位置（前方対後方）*</td>
<td>0.01</td>
<td>0.00～0.08</td>
</tr>
<tr>
<td>脳実質内出血</td>
<td></td>
<td></td>
</tr>
<tr>
<td>動脈瘤のサイズ（小/大対巨大）</td>
<td>0.43</td>
<td>0.11～1.65</td>
</tr>
<tr>
<td>動脈瘤の位置（前方対後方）</td>
<td>0.48</td>
<td>0.17～1.35</td>
</tr>
</tbody>
</table>

CI: 信頼区間、SAH: くも膜下出血。
* 統計学的に有意な結果を指す。オッズ比が < 1.0 の場合、( )の前に星を支持する