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ABSTRACT

BACKGROUND: The safety and efficacy of reconstructive and deconstructive endovascular treatments of very large/giant intracranial aneurysms are not completely clear.

PURPOSE: Our aim was to compare treatment-related outcomes between these 2 techniques.

DATA SOURCES: A systematic search of 3 data bases was performed for studies published from 1990 to 2017.

STUDY SELECTION: We selected series of reconstructive and deconstructive treatments with >10 patients.

DATA ANALYSIS: Random-effects meta-analysis was used to analyze occlusion rates, complications, and neurologic outcomes.

DATA SYNTHESIS: Thirty-nine studies evaluating 894 very large/giant aneurysms were included. Long-term occlusion of unruptured aneurysms was 71% and 93% after reconstructive and deconstructive treatments, respectively ($P = .003$). Among unruptured aneurysms, complications were lower after parent artery occlusion (16% versus 30%, $P = .05$), whereas among ruptured lesions, complications were lower after reconstructive techniques (34% versus 38%). Parent artery occlusion in the posterior circulation had higher complications compared with in the anterior circulation (36% versus 15%, $P = .001$). Overall, coiling yielded lower complication and occlusion rates compared with flow diverters and stent-assisted coiling. Complication rates of flow diversion were lower in the anterior circulation (17% versus 41%, $P < .01$). Among unruptured lesions, early aneurysm rupture (within 30 days) was slightly higher after reconstructive treatment (5% versus 0%, $P = .08$) and after flow diversion alone compared with flow diversion plus coiling (7% versus 0%).

LIMITATIONS: Limitations were selection and publication biases.

CONCLUSIONS: Parent artery occlusion allowed high rates of occlusion with an acceptable rate of complications for unruptured, anterior circulation aneurysms. Coiling should be preferred for posterior circulation and ruptured lesions, whereas flow diversion is relatively safe and effective for unruptured anterior circulation aneurysms.

ABBREVIATIONS: BAC = balloon-assisted coiling; PAO = parent artery occlusion; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SAC = stent-assisted coiling

Very large (diameter of ≥2 cm) and giant (diameter of ≥2.5 cm) intracranial aneurysms remain challenging lesions to treat by both surgical and endovascular approaches. Because of their size, intraluminal thrombosis, neck dimension, and involvement of neural structures, giant aneurysms are often associated with high rates of recurrence and treatment-related morbidity and mortality.[1,2] Treatment should result in the following[3-5]: 1) protection against aneurysm rupture, 2) prevention of thromboembolic complications, 3) improvement of mass effect, and 4) prevention of aneurysm growth. The endovascular strategies can be divided into 2 groups: 1) selective aneurysm treatment with coiling, balloon-assisted coiling (BAC), stent-assisted coiling (SAC), and flow diversion (reconstructive techniques); and 2) parent artery occlusion (PAO) (deconstructive technique). Both techniques have limitations: selective aneurysm embolization is

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usually associated with high recurrence rates, with important differences in the various available techniques, while, PAO is potentially associated with long-term complications related to vessel sacrifice.[4,6,7] We performed a meta-analysis of all published series examining endovascular treatments of very large and giant aneurysms with the aim of clarifying the following: 1) occlusion rate, 2) treatment-related complications, and 3) clinical outcome of reconstructive and deconstructive techniques.

MATERIALS AND METHODS

Literature Search

A comprehensive literature search of PubMed, Ovid MEDLINE, and Ovid EMBASE was conducted for studies published from 1990 to September 2017. Guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[8] were followed. The detailed search strategy is reported in On-line Table 1. The inclusion criteria were the following: studies reporting very large (diameter of ≥2 cm) and giant (diameter of ≥2.5 cm) aneurysms treated endovascularly[2] (coiling/BAC, SAC, flow diversion, and PAO). Exclusion criteria were the following: 1) studies with <10 patients, 2) review articles, 3) studies published in languages other than English, and 4) treatment with Onyx (Covidien, Irvine, California) or covered stents. In cases of overlapping patient populations, only the series with the largest number of patients or most detailed data were included. Two reviewers independently selected the included studies, and a third author solved discrepancies.

Data Collection

From each study, we extracted the following: 1) treatment-related outcomes, 2) long-term occlusion rates, 3) incidence of early (within 30 days) and late (after 30 days) ruptures after treatment, 4) rate of recurrence, 5) mean and median times between treatment and recurrence, and 6) rate of retreatment. Treatment-related outcomes were dichotomized into 2 groups: reconstructive techniques (coiling/BAC, SAC, flow diversion alone, and flow diversion plus coiling) and deconstructive techniques. In addition, the influence of 4 parameters (age, aneurysm size, location, and shape) on the occlusion and complication rates was analyzed. Finally, good outcome was defined as a modified Rankin Scale score of 0–2 or a Glasgow Outcome Score of 4–5, or it was assumed if the study used terms such as "no morbidity," "good recovery," or "no symptoms."

Outcomes

The primary objectives of this meta-analysis were to compare reconstructive and deconstructive techniques for the following outcomes: 1) aneurysm occlusion rate, 2) treatment-related complications, and 3) clinical outcome. Among the reconstructive group, complications and angiographic outcomes were compared between coiling and flow diversion.

Quality Scoring

The Newcastle-Ottawa Scale[9] was used to assess the quality of the included studies (On-line Table 2). "High-quality" studies were defined on the basis of the following: 1) the presence of a study and imaging protocol, 2) defined inclusion and exclusion criteria, 3) detailed information about treatment-related outcomes, and 4) adequate length of follow-up. Adequate length of follow-up was considered approximately 12 months because most of the reported outcomes (treatment-related complications and angiographic outcomes) occurred within this time. The quality assessment was performed by 2 authors independently, and a third author solved discrepancies. Studies receiving ≥6 stars are considered "high-quality" (score range from 0 to 9).

Statistical Analysis

We estimated, from each cohort, the cumulative prevalence and 95% confidence interval for each outcome. Event rates were pooled across studies with a random-effects meta-analysis. Heterogeneity across studies was evaluated using the I^2 statistic: An I^2 value of >50% suggests substantial heterogeneity. We also extracted a 2 × 2 table to calculate *P* values for the comparisons among the results. Meta-regression was not used in this study. Statistical analysis was performed using OpenMeta[Analyst] (http://www.cebm.brown.edu/openmeta/).

RESULTS

Literature Review

Studies included in our meta-analysis are summarized in On-line Table 2. The search flow diagram is shown in the On-line Figure. A total of 39 studies and 894 giant and very large intracranial aneurysms were included in our review. Mean radiologic and clinical follow-ups were 26 months (range, 6–66 months; median, 21 months) and 34 months (range, 6–20 months; median, 28 months).

Quality of Studies

Overall, 20 studies were rated "high quality." All the high-quality articles reported detailed information about aneurysm occlusion rates, treatment-related complications, factors related to occlusion and complications, and adequate length of follow-up. Three articles were prospective studies, 6 series were obtained from a prospectively maintained data base, and 30 articles were retrospective.

Patient Population and Treatment Characteristics

Detailed information about patient populations is reported in On-line Table 3.

Overall, 75% (95% CI, 72%–78%) and 25% (95% CI, 22%–27%) of aneurysms were treated with reconstructive and deconstructive techniques, respectively. About 70% of unruptured aneurysms were treated with reconstructive techniques. Among these patients, coiling/BAC was performed in 40% of cases; SAC, in about 16% of cases; and flow diversion, in 42% of patients. A deconstructive approach was performed in about 30% of unruptured aneurysms. Ruptured aneurysms were treated with coiling and PAO in 75% and 25% of cases, respectively. No acutely ruptured large and giant aneurysms were treated by flow diversion.

Balloon test occlusion was performed in about 86% of patients before PAO. In about 4% of patients, the occluded vessel was a nondominant vertebral artery and balloon test occlusion was not necessary. In 10% of cases (2 articles), there was not enough information about balloon test occlusion (On-line Table 2). About

Table 1: Angiographic outcomes for unruptured and ruptured very large/giant intracranial aneurysms—comparison between reconstructive and deconstructive treatments

Variables	Unruptured Group (Results of Meta-Analysis)	No. of Articles	P Value	Ruptured Group (Results of Meta-Analysis)	No. of Articles	P Value
Angiographic outcomes						
Long-term aneurysm occlusion (complete/near-complete)	122/175 = 71%	14		23/31 = 72%	5	
Reconstructive	(60–81) (I^2 = 69%)			(57–87) (I^2 = 0%)		
vs			.003[a]			.5
Deconstructive	147/158 = 93%			13/15 = 80%	4	
	(89–98) (I^2 = 4%)	8		(60–97) (I^2 = 42%)		
Recanalization after reconstructive treatment	45/110 = 40%	9		15/31 = 47%	4	
	(13–60) (I^2 = 95%)			(30–64) (I^2 = 0%)		
vs			.001[a]			.1
Recanalization after deconstructive treatment	3/66 = 5%			1/8 = 22%		
	(1–10) (I^2 = 0%)	6		(7–52) (I^2 = 49%)	3	
Time between treatment and recanalization						
Reconstructive	Median, 5 mo; mean, 8.7 mo; IQR, 4–13.5					
vs	vs					
Deconstructive	Median 6 mo; mean 13 mo; IQR, 5–21					
Retreatment after reconstructive treatment	34/105 = 32%	8		14/29 = 48%	3	
	(10–55) (I^2 = 90%)			(30–66) (I^2 = 0%)		
vs			.001[a]			.007[a]
Retreatment after deconstructive treatment	1/66 = 4%			1/8 = 22%		
	(1–8) (I^2 = 0%)	6		(7–52) (I^2 = 49%)	3	
Early aneurysm rupture after reconstructive treatment	8/165 = 5%	14		3/37 = 8%	6	
vs	(1.7–8) (I^2 = 0%)		.08	(2–22) (I^2 = 5%)		.2
Early aneurysm rupture after deconstructive treatment	0/86	8		0/36	5	
Late aneurysm rupture after reconstructive treatment	3/148 = 3%	12		0/36	5	
vs	(0.6–6.2) (I^2 = 0%)		.4			.4
Late aneurysm rupture after deconstructive treatment	0/86	8		0/10	4	

Note:—vs indicates versus; IQR, interquartile range.
[a] Significant.

70% of deconstructive treatments in the posterior circulation were performed in the basilar artery/posterior cerebral artery, whereas 30% were performed in the vertebral artery.

Angiographic Outcomes

Unruptured Aneurysms. The rate of long-term complete/near-complete occlusion was 71% (95% CI, 60%–81%) and 93% (95% CI, 89%–98%) after reconstructive and deconstructive treatments, respectively ($P = .003$) (Table 1). The rate of recanalization was higher after reconstructive treatment (40%) compared with the deconstructive technique (5%) ($P = .001$). Similarly, the rate of retreatment was significantly higher among the reconstructive group (32% versus 4%) ($P = .001$). Early and late aneurysm ruptures after reconstructive techniques were 5% and 3%, respectively. No cases of rupture were described after PAO.

Ruptured Aneurysms. There were comparable rates of complete/near-complete occlusion (72% versus 80% after reconstructive and deconstructive treatments, respectively) ($P = .5$). Aneurysm recanalization was 47% after reconstructive and 22% after deconstructive techniques ($P = .1$). There was a significantly higher rate of retreatment after reconstructive compared with deconstructive treatments (48% versus 22%) ($P = .007$). The rate of early aneurysm rupture after coiling was 8%, whereas no cases were described after deconstructive treatment.

Treatment-Related Complications and Clinical Outcomes

Unruptured Aneurysms. Overall, treatment-related complications were 30% (95% CI, 22%–37%) and 16% (95% CI, 7%–25%) after reconstructive and deconstructive treatments ($P = .05$) (On-line Table 4). Similarly, permanent complications were higher among the reconstructive group (15% versus 8.6%, $P = .01$). Most complications were related to ischemic events (15% and 11% among reconstructive and deconstructive groups, respectively). Worsening of mass effect was comparable between reconstructive and deconstructive treatments (1.7% versus 3.5%). Finally, the rate of hemorrhagic complications was higher after reconstructive techniques (6%) compared with PAO (2%) ($P = .03$). There was no significant difference in mortality rates between the 2 groups (9% versus 6%, $P = .35$).

The rates of good neurologic outcome were 80% and 89% after reconstructive and deconstructive treatments, respectively ($P = .1$). During follow-up, mass effect symptoms were improved in about 48% of patients after reconstructive treatments and in 77% of patients after PAO ($P = .02$).

Ruptured Aneurysms. The overall rates of complications and permanent complications were slightly higher after PAO (38% and 29%) compared with coiling (34% and 20%). The incidence of ischemic events was slightly higher after deconstructive compared with reconstructive treatments (33% versus 18.8%, $P = .3$), as was worsening of mass effect (14% versus 7%, $P = .2$). Hemorrhagic complications were higher after coiling compared with PAO (17% versus 9%, $P = .5$). The rate of good neurologic outcome was close to 60% for both types of treatment. Improvement of compressive symptoms was reported in 24% of reconstructive cases, whereas no data were available among the deconstructive group.

Factors Related to Occlusion and Complication Rates after Treatment

Reconstructive Group. Differences in occlusion rates were not statistically significant in relation to aneurysm size (less or more than 3 cm), anterior-versus-posterior circulation, and saccular-versus-fusiform aneurysms. However, there was a slightly higher incidence of occlusion among younger patients (younger than 60 years) compared with elderly patients (older than 60 years) (82% versus 71%) (P = .09, OR = 1.97). The incidence of complications was similar among groups of age, aneurysm size, and anterior-versus-posterior circulation. Among saccular aneurysms, the rate of complications was 23% (95% CI, 2%–40%), whereas no data were available for fusiform aneurysms (On-line Table 5).

Deconstructive Group. Complete/near-complete aneurysm obliteration was higher among younger patients (95.9% versus 78%) (P = .007, OR = 2.5). No differences in occlusion rates were found in relation to aneurysm size, location, and shape. Complication rates were comparable between younger and older patients and aneurysm sizes, whereas posterior circulation aneurysms treated with PAO showed higher rates of complications (36%) compared with anterior circulation aneurysms (15%) (P = .001, OR = 3.6). Although few studies were available for the analysis, complications were statistically similar between fusiform and saccular aneurysms (On-line Table 5).

Comparison among Coiling/BAC, SAC, and Flow Diversion for the Treatment of Unruptured Aneurysms

Complete/near-complete occlusion was 59% and 73% after coiling/BAC and SAC, respectively (P = .3) (On-line Table 6). Flow-diversion treatment resulted in 72% occlusion rates, with comparable rates between treatment with flow diverter alone versus flow diverter with adjunctive coils (75% versus 70%, respectively). The rates of early aneurysm rupture after coiling and SAC were approximately 6% and 9% (P = .5), whereas 7% of cases were reported after flow diversion alone, and no cases were described after flow diversion with adjunctive coils. The rate of late aneurysm rupture was 7% after coiling/BAC, whereas there were no cases of late rupture after SAC and flow diversion. The overall rate of treatment-related complications was higher after SAC (39%) compared with coiling/BAC (20%) (P = .001). Complications after flow diversion were 29%, and there were no significant differences between flow diversion alone and flow diversion plus coiling (32% versus 26%, P = .8). Treatment-related complications among anterior circulation aneurysms were slightly lower compared with posterior circulation aneurysms after coiling/BAC (15% versus 20%, P = .7) and SAC (38% versus 43%, P = .9), whereas flow diversion was associated with significantly lower rates of complications in the anterior circulation (17% versus 41%, P = .02). The most common complications were ischemic events, particularly among the SAC group (32%). Worsening of mass effect was close to 6% after coiling and SAC, whereas it was lower after flow diversion (1.6%). Hemorrhagic complications were between 5% and 10% among the different treatment groups. Overall, the rate of good neurologic outcome was between 60% and 72%.

Study Heterogeneity

High rates of heterogeneity were reported in the following: treatment-related complications, improvement of mass effect among unruptured lesions, rates of occlusion and recanalization among reconstructive treatments of unruptured aneurysms, and factors related to complications and aneurysm occlusion.

DISCUSSION

Our meta-analysis of nearly 900 very large/giant intracranial aneurysms treated endovascularly shows important differences between reconstructive and deconstructive techniques. Overall, among unruptured aneurysms, deconstructive treatments allowed higher rates of occlusion (93% versus 71%) and lower rates of complications (16% versus 30%), compared with reconstructive techniques. However, among posterior circulation aneurysms, treatment-related morbidity was not negligible after PAO (36%). Coil embolization of unruptured lesions was associated with lower rates of complication and aneurysm occlusion (20% and 59%) compared with SAC (39% and 73%) and flow diversion (29% and 72%). Most interesting, flow-diverter stents were significantly safer among anterior circulation aneurysms (17% versus 41% complications), whereas the safety of coiling and SAC was comparable for anterior and posterior circulation lesions. Although ruptured aneurysms were effectively treated with both techniques (70%–80% occlusion), reconstructive treatments were associated with a lower rate of complication and morbidity (34% and 20%) compared with PAO (38% and 29%). Younger patients had higher odds of aneurysm occlusion after reconstructive (OR = 1.9) and deconstructive treatments (OR = 2.5) compared with older patients. These findings are important, and they provide more information to guide the endovascular treatment/management of these lesions.

Reconstructive Treatments

Although exclusion of aneurysms with preservation of the parent vessel should be the first option, complication rates of reconstructive treatments seem nonnegligible. We found 30% treatment-related complications with 15% morbidity after reconstructive treatments of giant unruptured aneurysms. Most complications were ischemic (15%): They may be related to the complexity of the procedure, longer duration of the treatment, and use of adjunctive devices (SAC, flow diverter and coiling, or multiple flow diverters).[1,10] Ischemic events were particularly high after SAC (30%), which may be a reflection of a longer procedure time, technical challenges encountered during stent deployment, and the need for dual-antiplatelet therapy. According to our results, in a large series of 512 patients treated with coiling alone and SAC, Yang et al[11] showed that larger aneurysm size was a predictor of procedural morbidity after SAC. In our study, the rate of complications after flow-diversion treatment ranged from 25% to 30%, without significant differences between flow diversion alone and flow diversion with adjunctive coils. This finding is in accordance with findings reported in other studies comparing the 2 groups of treatments.[12] Most interesting, flow diversion was safe and effective among anterior circulation lesions, whereas it was associated with a high incidence of complications in the vertebrobasilar region. In the International Retrospective Study of Pipeline Embolization Device (IntrePED), among the subgroup of giant aneurysms, Kallmes et al[13] reported 40% of complications after Pipeline treatment in the posterior circulation, compared with 23% in the anterior circulation. Among unruptured aneurysms, there was a trend toward higher rates of worsening of mass effect after coiling and SAC (6%) compared with flow diversion (1.6%), whereas the rates were comparable between reconstructive and deconstructive techniques.

Aneurysms presenting with mass effect are usually treated by a surgical approach (and decompression of the mass effect) with evacuation of the aneurysmal sac. However, our meta-analysis showed improvement of mass effect in about 50% and 77% of reconstructive and deconstructive treatments of unruptured aneurysms, respectively. Compressive symptoms in giant aneurysms seem to be a combination between direct compression/deformation of the neural structures and irritation caused by aneurysm sac pulsation. Accordingly, improvement leads independently to aneurysmal shrinkage because of the decreased pulsation, resolution of the perianeurysmal edema, and partial shrinkage.[14] In a series of 19 aneurysms treated with coiling, Hassan and Hamimi[14] reported 63% complete resolution of mass effect and 32% symptom improvement, without strict correlation with aneurysm shrinkage on the MR imaging.

Long-term occlusion of giant aneurysms is notoriously challenging after selective endovascular treatment,[1,6] and the rates complete/near-complete occlusion are reported to be between 35% and 90%.[1,3,15-17] Our study, the largest to date, demonstrated roughly 70% complete/near-complete occlusion after reconstructive treatment, with 40% and 32% recanalization and retreatment, respectively. In addition, we found a higher rate of occlusion after flow diversion and SAC (72% and 73%) compared with coiling alone (59%). Although currently it is common practice to perform coil embolization of giant aneurysms in addition to flow diversion, no significant differences in occlusion rates were found between flow diverter alone and flow diverters plus coils. Most interesting, after reconstructive treatments, the occlusion rate seems to be slightly higher among younger patients (80% versus 70%, OR = 1.9) with smaller aneurysms in the anterior circulation. In general, reconstitution of the endothelial lining of the neck with thrombus organization inside the sac is an important factor related to stable aneurysm occlusion. In giant wide-neck aneurysms, insufficient stent wall apposition, low density of coil packing, and coil migration into the thrombotic wall can decrease the neoendothelization of the neck and the thrombotic process inside the sac.[1,18,19]

Postprocedural aneurysm rupture is a serious complication, and prior studies demonstrated a higher risk of rupture in giant aneurysms. After reconstructive treatments of unruptured lesions, we found 5% and 3% early and late aneurysm rupture. The incidence of rupture in the first 30 days was slightly higher in the ruptured group (8%, $P = .08$). Most interesting, the rate of rupture was comparable among coiling, SAC, and flow diversion. However, we found 7% early rupture (within 30 days) of aneurysms treated with flow diversion alone, and no cases of rupture in the group of lesions treated with adjunctive coils. These results support the recommendation to treat very large and giant aneurysms with concomitant coiling and flow diverters to prevent delayed ruptures. In a recent review of the literature, Rouchaud et al[20] reported that 76% of the ruptures after flow diversion occurred in the first month: Giant aneurysms accounted for about 50% of ruptures, and 80% of lesions were not previously coiled.

Overall, the rate of good neurologic outcome was approximately 80% and 60% for unruptured and ruptured treated aneurysms.

Deconstructive Treatments

Among unruptured aneurysms, PAO had lower complications (16%) and morbidity (9%) compared with reconstructive treatments. The most frequent complications were ischemic events (11%), whereas hemorrhagic complications seem to be significantly lower compared with reconstructive treatments (2% versus 6%, $P = .03$). Better results of PAO could be related to a careful patient selection with balloon test occlusion and rigorous postoperative management. In addition, deconstructive treatments allow better results in terms of improvement of mass effect compared with coiling or flow diversion (77% versus 48%, $P = .02$). In a series of 19 patients with giant aneurysms, Clarençon et al[4] reported an 85% reduction of ocular symptoms, with a complete cure in 75% of cases. However, treatment-related outcomes after PAO in ruptured giant aneurysms were poor, with high rates of complications (38%) and morbidity (29%). The incidence of stroke seems to be high after PAO with SAH (33%). Several factors may explain the high rate of ischemic events in the acute phase: 1) difficulty in testing the hemodynamic tolerance to vessel occlusion, 2) management of the platelet antiaggregation therapy, 3) the hypercoagulability status after SAH, and 4) decreased blood flow compensation after cerebral vasospasm.

Most interesting, posterior circulation giant aneurysms treated with PAO had a remarkable complication rate compared with anterior circulation aneurysms (36% versus 15%, $P = .001$). Lubicz et al[21] reported 40% early complications and 8% mortality after PAO of 13 giant vertebrobasilar aneurysms. The high morbidity rate can be related to the lower compliance of the posterior cranial fossa to mass effect lesions, high risk of injury to the perforating vessels, and difficulty in assessing the tolerance to occlusion of the vertebrobasilar territory. The size of the posterior communicating arteries represented a good predictor of long-term tolerance to basilar artery occlusion.[22] However, giant vertebrobasilar aneurysms are challenging lesions with a poor prognosis after treatment, and survival as low as 20% after a few years if they are left untreated.[22]

Overall, long-term occlusion was achieved in about 90% of patients, with low recanalization and retreatment rates among unruptured lesions (5% and 4%, respectively), a low risk of rupture after treatment, and a high rate of good neurologic outcome.

Strength and Limitations

Our study has limitations. There was substantial heterogeneity among the analyzed outcomes ($I^2 > 50\%$). The series are often small, retrospective, and single-institution experiences. Half of the reported studies were of low quality. Details of the antiplatelet therapy were infrequently specified. Finally, the small number of cases in some subgroups may not provide sufficient power to demonstrate a statistically significant difference in the rates of complications and occlusion among age groups and aneurysm size, location, and shape. However, although retrospective data are low in quality, our meta-analysis is the best available evidence to evaluate reconstructive and deconstructive treatments of very large/giant aneurysms.

CONCLUSIONS

The treatment of very large and giant intracranial aneurysms remains extremely challenging. Sacrifice of the parent artery is a reasonable approach for complex unruptured, anterior circulation aneurysms, allowing high rates of occlusion with an acceptable rate of complications. Among reconstructive techniques, coiling should be preferred for the treatment of posterior circulation aneurysms and for ruptured lesions, whereas flow diversion is relatively safe and effective for unruptured anterior circulation aneurysms.

Disclosures: Federico Cagnazzo—*UNRELATED*: *Employment*: University of Florence. Paolo Perrini—*UNRELATED*: *Employment*: University of Pisa, *Comments*: I am an associate professor of neuroradiology. Vincent Costalat—*UNRELATED*: *Grants/Grants Pending*: Medtronic, Stryker*; *Payment for Development of Educational Presentations*: Medtronic, Stryker, Balt, MicroVention. Alain Bonafe—*UNRELATED*: *Employment*: Hopital Gui de Chauliac service de neuroradiology. Waleed Brinjikji—*UNRELATED*: *Consultancy*: Johnson and Johnson, *Comments*: $500 consulting fee; *Patents (Planned, Pending or Issued)*: intellectual property in balloon catheter technology; *Stock/Stock Options*: Superior Medical Editing stock options; *Travel/Accommodations/Meeting Expenses Unrelated to Activities Listed*: Johnson and Johnson; *Other*: CEO of Marblehead Medical LLC. Carlos Riquelme—*UNRELATED*: *Employment*: Hopital Gui de Chauliac service de neuroradiology. *Money paid to institution.

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