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Review

Impact of aneurysm morphology on safety and effectiveness of flow diverter treatment of vertebrobasilar aneurysms

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Introduction

Flow diversion is a novel technique for endovascular treatment of complex intracranial aneurysms, in which deployment of a low-porosity endoluminal device across the diseased vessel segment promotes stagnation of intra-aneurysmal flow and eventual aneurysm thrombosis [1]. The struts of the device also act as a scaffold for neointimal overgrowth, leading to endoluminal parent vessel reconstruction [2], while covered branch arteries arising from or in close proximity to the aneurysm generally remain patent due to flow demand [3]. Flow diversion of anterior circulation aneurysms has shown impressive effectiveness, with reported aneurysm occlusion rates typically exceeding 85% [4–10] and morbidity rates of less than 7% [10,11].

Off-label utilization of flow diversion to treat posterior circulation aneurysms has yielded mixed initial results. In a recent meta-analysis by Wang et al. [12] of 14 publications with 225 posterior circulation aneurysms, flow diversion achieved a 6-month angiographic occlusion rate of 84% [95% CI, 68–94%], with ischemic stroke and perforator infarction rates of 11% (95% CI, 7–17%) and 7% (95% CI, 3–13%), respectively. However, an important limitation of this meta-analysis, and the majority of its constituent case series, is cohort heterogeneity in terms of aneurysm morphology and location. In contrast, in a case series by Siddiqui et al. [13], 5 of 7 patients (71%) with basilar or vertebrobasilar aneurysms treated with flow diversion were dead or severely disabled at last clinical follow up.

The purpose of this study is to separately assess the clinical and angiographic outcomes of saccular and fusiform vertebrobasilar aneurysms treated with flow diversion. In animal models, neointimal lining of the Pipeline Embolization Device (PED) has been demonstrated as early as 4 weeks after device implantation across the neck of saccular aneurysms [14,15]. However, a histopathologic analysis of giant fusiform aneurysms treated with the PED found that endothelialization across the device did not occur for up to 13 months [16]. Moreover, while the ostia of covered branch vessels arising from parent artery adjacent to the neck of saccular aneurysms are opposed to the flow diverter, intervening clot may form between the flow diverter and branch vessels arising from fusiform aneurysms. These physiologic mechanisms may result in differences in outcomes between saccular and fusiform aneurysms treated with flow diversion, and warrant consideration of aneurysm morphology in choosing an endovascular treatment strategy.

Methods

Systematic review

The search and selection process applied during the systematic literature search and critical review is detailed in Fig. 1.

Relevant published reports were identified via electronic search of the PubMed database in March 2017 for the term “Flow diverter” or “Flow diversion”. Additional records were identified by reviewing references of records obtained through database search. Studies that did not specify details of individual cases were excluded. From the selected studies, individual cases of saccular or fusiform vertebrobasilar aneurysms treated with flow diversion were identified. Dissecting intracranial aneurysms were excluded from this review due to their unique pathophysiology. Patient ages listed only by decade were estimated as being midway through the decade (e.g. “50s” was estimated as 55). If previous treatment was not reported, we assumed that aneurysms were not previously treated. Aneurysms described as “giant” or “large” were considered to be 25 and 20 mm, respectively. The following angiographic descriptions were considered near-complete occlusion: “significant involution”,

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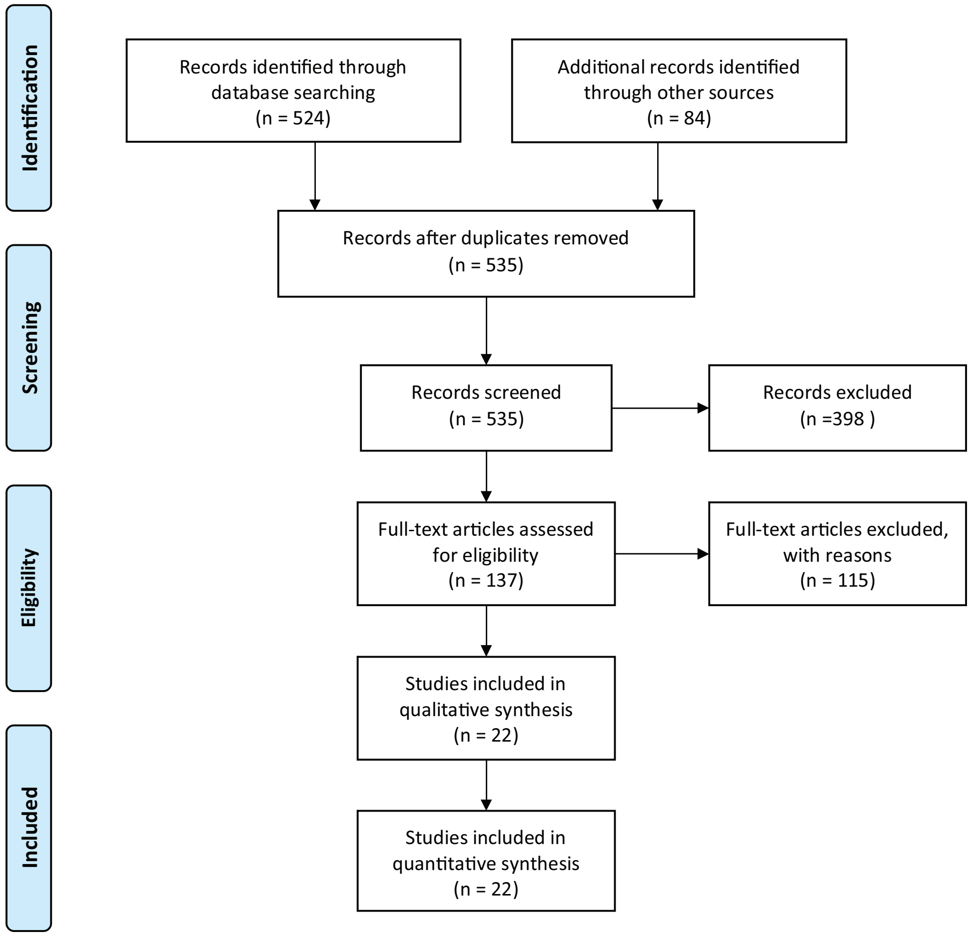

Fig. 1. PRISMA diagram detailing the search and selection process applied during the systematic literature search and critical review.

"minimal filling", "slight neck filling", "residual neck", "neck remnant" and O'Kelly-Marotta 3B [17].

Statistical analysis

Complications, angiographic outcomes, and clinical outcomes (good clinical outcome defined as a post-procedure mRS ≤ 2), were estimated separately for subgroups of aneurysms categorized on the basis of morphology (saccular vs fusiform), size (small, medium, large, giant), and location (vertebral artery, basilar artery, vertebrobasilar junction). For fusiform aneurysms, the likelihood of a good clinical outcome was calculated for subgroups of patients categorized by the presence or absence of aneurysm-related symptoms and preoperative functional status. Rates of each outcome were compared for fusiform and saccular aneurysms and for aneurysm subgroups described above. Statistical analysis was performed using Graphpad Prism version 6.0a (GraphPad Software, San Diego California, USA).

Results

Saccular aneurysms

Seven publications containing patient-level data on 25 patients were identified (Table 1) [18–25]. Mean patient age was 51.1 ± 16.1 years (range, 8–82 years), with 24% (6/25) men and 76% (19/25) women (genders of two patients were not reported). Aneurysm locations included the basilar artery (60%; 15/25), vertebral artery (20%; 5/25), and vertebrobasilar junction (20%; 5/25). Mean aneurysm size was 15.4 ± 7.2 mm (range, 3.5–27 mm), of which 12% (3/25) were small (< 6 mm), 44% (11/25) medium (7–15 mm), 20% (5/25) large (16–25 mm), and 24% (6/25) giant (> 25 mm). Fifty two percent (13/25) of patients were symptomatic preoperativelyThese patients' symptoms are included in Table 1 Twenty four percent (6/25) of aneurysms had been previously treated.

Flow diverter devices included the PED (60%, 15/25) and Silk (40%, 10/25). The mean number of devices used was 1.4 (range, 1–3) overall; 1.6 for the PED, and 1.0 for the Silk. One Silk construct was reinforced with a Neuroform stent. Adjunctive coiling was performed in 48% (12/25) of cases. Unilateral vertebral artery sacrifice was performed in 16% (4/25) of cases. All patients received dual antiplatelet therapy with aspirin and a P2Y12 antagonist. Platelet function testing was performed in 48% (12/25) of cases.

The neurologic complication rate was 36% [9/25, 95% confidence interval (CI) 20-56%] owing to stroke (28%, 7/25), intraparenchymal hemorrhage (4.0%, 1/25), and one case of delayed in-stent thrombosis 11 months post-procedure (4.0%, 1/25). Complication rates as a function of aneurysm size and location are listed in Table 2. The incidence of complications did not vary significantly by aneurysm size or location ($P = 0.90$ and 0.71 respectively).

Angiographic follow up was reported for 96% (24/25) of cases. The precise duration of follow up was reported for 76% (19/25) of cases, the mean of which was 16.3 months (range, 3–34 months). Degree of occlusion was reported heterogeneously. Unambiguous complete aneurysm occlusion was reported in 71% (17/24, 95% CI 51-85%) of cases. Complete or near-complete occlusion rate was 88% (21/24, 95% CI 69-96%). Complete angiographic occlusion rates as a function of aneurysm size and location are listed in Table 3.

Table 1
Patient-level data of saccular vertebrobasilar aneurysms treated with flow diversion identified during systematic review. Abbreviations: BA: basilar artery; mRS: modified rankin score; NR: not reported; OKM: O'Kelly-Marotta; PED: pipeline embolization device; SCA, superior cerebellar artery; VA: vertebral artery; VBJ: vertebrobasilar junction. *Pre-procedure functional status not reported.

First author (year of publication)	Age, gender	Aneurysm location	Aneurysm size (mm)	Preoperative symptoms	Previous treatment(s)	Flow diverter	# devices	Adjunctive stent	Adjunctive coiling?	Unilateral VA sacrifice?	Platelet function testing	Neurologic complications	Angiographic follow up (mo)	Aneurysm occlusion	Δ mRS	Post-procedure mRS
Kulcsar (2010)	51F	BA turnk	20	Brainstem Compressive Syndrome	None	Silk	2	Enterprise	No	No	NR	Stroke	nr	Complete	1	5
	69F	BA tip	18	Recurrence	Coils	Silk	1	–	Yes	No	NR	None	23	Neck remnant	0	0
	17M	BA trunk	8	Headaches	Stent-coiling x 2	Silk	1	–	No	No	NR	None	nr	Complete	0	0
	50F	BA trunk	26	Brainstem Compression Syndrome	None	Silk	1	–	Yes	No	NR	Stroke	32	Complete	0	4
	42F	BA trunk	10	Incidental	Stent-coiling x 2	Silk	1	–	No	No	NR	None	nr	Complete	0	2
	8M	BA trunk	7	Incidental	None	Silk	1	–	No	No	NR	None	12	Sac filling	0	0
	49F	BA tip	5.5	Incidental	None	Silk	1	–	Yes	No	NR	Stroke	4	Complete	0	0
	50M	BA tip	14	Incidental	None	Silk	1	–	Yes	No	NR	Stroke	6	Neck remnant	3	3
	59F	BA trunk - SCA	3.5	Incidental	None	Silk	1	–	Yes	No	NR	None	nr	Complete	0	0
Toth (2015)	40s	VA	11.5	SAH	None	PED	1	–	Yes	No	Yes	None	28	OKM C3	-1	0
	40s	VA	7	SAH	None	PED	2	–	Yes	No	Yes	Stroke	25	Complete	0	1
	30s	BA	27	Cranial Neuropathy (Mass Effect)	None	PED	2	–	No	No	Yes	None	12	Complete	-2	1
	50s	VA	12	Headache	None	PED	1	–	Yes	No	Yes	None	6	Complete	-1	0
Chalouhi (2013)	61M	VA	6	No	Coils	PED	1	–	No	No	Yes	None	7	Complete	–	0
	73F	VBJ	12	No	Stent-coiling, coiling	PED	2	–	No	No	Yes	None	6	Complete	–	0
	43F	VA	16	No	None	PED	1	–	Yes	No	Yes	None	3	Complete	–	0
	82F	VA	15	Yes (NR)	None	PED	2	–	No	No	Yes	None	-	-	–	–
Meckel (2013)	60F	VBJ	25	Mass Effect	None	PED	2	–	No	Yes	Yes	None	18	Complete	–	0
	51F	VBJ	25	Mass Effect	None	PED	2	–	Yes	Yes	Yes	None	34	Neck remnant	NR*	1
	61F	VBJ	25	Mass Effect	stent-coiling	PED	3	–	Yes	Yes	Yes	Delayed in-stent thrombosis	26	Complete	-–	0
	43M	VBJ	20	Unclear	stent-coiling	PED	1	–	Yes	Yes	Yes	Stroke	22	Complete	NR*	1
Lubicz (2010)	62F	BA trunk - SCA	15	No	None	Silk	1	–	No	No	NR	Stroke	3 or 6	Incomplete	2	NR
John (2016)	NR	BA	19	No	None	PED	NR	–	No	No	NR	None	12	OKM 3B	–	NR
	NR	BA	25	Headache	None	PED		–	No	No		None	28	Complete	–	NR
McAuliffe (2012)	64M	BA tip-P1	12	Mass Effect	None	PED	1	–	No	No	NR	Intraparenchymal hematoma	6	Complete	–	0

Table 2
Complication rates of saccular vertebrobasilar aneurysms treated with flow diversion as a function of aneurysm size and location.

Aneurysm size	Aneurysm location			
	BA	VA	VBJ	Total
Small (< 6 mm)	1/2	0/1	0	33% (1/3)
Medium (7–15 mm)	3/6	1/4	0/1	36% (4/11)
Large (16–25 mm)	1/4	0	1/1	40% (2/5)
Giant (> 25 mm)	1/3	0	1/3	33% (2/6)
Total	40% (6/15)	20% (1/5)	40% (2/5)	36% (9/25)

Table 3
Saccular vertebrobasilar aneurysms that were complete or near complete occlusion at last angiographic follow up as a function of aneurysm size and location.

Aneurysm Size	Aneurysm location			
	BA	VA	VBJ	Total
Small (< 6 mm)	2/2	1/1	0	100% (3/3)
Medium (7–15 mm)	4/6	2/3	1/1	70% (7/10)
Large (16–25 mm)	4/4	0	1/1	100% (5/5)
Giant (> 25 mm)	3/3	0	3/3	100% (6/6)
Total	82% (13/15)	75% (3/4)	100% (5/5)	88% (21/24)

Occlusion rates did not vary by size or location ($P = 0.18$ and 0.52 respectively).

Clinical outcome could be ascertained for 88% (22/25) of cases. Good clinical outcome was reported or could be inferred in 82% (18/22, 95% CI 61–93%) of cases. While there was no reported mortality at clinical follow up, one patient (4.5%, 1/22) was severely disabled (mRS 5).

None of the three patients for whom clinical outcome could not be ascertained experienced a periprocedural complication.

Fusiform aneurysms

Fifteen publications containing patient-level data on 64 patients were identified (Table 4) [13,19–21,25–35]. Mean patient age was 53.8 ± 15.1 years (range, 13–77 years), with 61% (38/62) men and 39% (24/62) women, (gender of two patients was not reported). Aneurysm locations included the basilar artery without vertebral artery involvement in 41% (26/64), vertebral artery alone in 17% (11/64), and the basilar and at least one vertebral artery in 42% (27/64) of cases. Mean aneurysm maximum diameter size was 18.3 ± 9.5 mm (range, 4.5–46 mm), of which 1.6% (1/64) were small (< 6 mm), 45% (29/64) were medium (7–15 mm), 25% (16/64) were large (16–25 mm), and 28% (18/64) were giant (> 25 mm). Eighty nine percent (57/64) of patients were symptomatic preoperatively with specific symptoms listed in Table 4. Thirteen percent (8/64) of aneurysms had been previously treated.

Flow diverters used included the PED (84%, 54/64), Silk (14%, 9/64), and Surpass (1.6%, 1/64). The mean number of devices used was 2.9 (range, 1–9) overall, 3.1 (range, 1–9) for the PED, and 1.9 (range, 1–4) for the Silk. Four Silk constructs were reinforced with LEO stents and one PED was deployed in conjunction with three Neuroform stents. Adjunctive coiling was performed in 28% (18/64) of cases. Unilateral vertebral artery sacrifice was performed in 19% (12/64) of cases. All patients received dual antiplatelet therapy with aspirin and a P2Y12 antagonist. Platelet function testing was performed in 86% (55/64) of cases.

Whether procedure-related neurologic complications occurred could be ascertained for 86% (55/64) of patients. Of these, the neurologic complication rate was 35% (19/55, 95% CI 23-48%) owing to stroke (15%, 8/55), transient ischemic attack (5.5%, 3/55), intraparenchymal hemorrhage (1.8%, 1/55), and spontaneous aneurysm rupture (5.5%, 3/55). Complication rates as a function of aneurysm size and location are listed in Table 5. The complication rate was higher for aneurysms involving the basilar artery compared with those involving only the vertebral artery, however, this did not reach statistical significance [41% (18/44) vs 9.1% (1/11), OR 6.9, $P = 0.07$]. Complication rates were also higher for giant aneurysms compared with non-giant aneurysms [56% (10/18) vs. 24% (9/37), OR 3.9, $P = 0.03$]. The overall complication rates for flow diverter treatment of fusiform and saccular aneurysms were comparable [35% (19/55) vs. 36% (9/25), OR 1.1, $P = 1.0$].

Angiographic follow up was reported for 88% (56/64) of cases. The mean duration of follow up was 9.9 months (range, 7 days–39 months). Degree of occlusion was reported heterogeneously. Unambiguous complete aneurysm occlusion was reported in 52% (29/56) of cases. The complete or near-complete occlusion rate was 71% (40/56, 95% CI 59–82%). Complete angiographic occlusion rates as a function of aneurysm size and location are listed in Table 6. Occlusion rates were higher for vertebral artery aneurysms compared with basilar or vertebrobasilar aneurysms [100% (10/10) vs. 65% (30/46), OR 11, $P = 0.05$] and lower for giant aneurysms compared with non-giant aneurysms [56% (40/56) vs. 78% (31/40), OR 1.4, $P = 0.63$].The overall occlusion rate for fusiform aneurysms was lower than that of saccular aneurysms but the difference was not statistically significant [88% (21/24) vs. 71% (40/56), OR 2.8, $P = 0.16$].

Clinical outcomes were also reported heterogeneously. Post-treatment mRS was reported or could be inferred for 97% (62/64) of patients. Good clinical outcome was achieved in 60% (37/62, 95% CI 46–69%) of cases, and 35% (22/62, 95% CI 24–47%) of patients were dead or severely disabled (mRS 5 or 6). Clinical outcomes as a function of preoperative symptomatology and functional status are listed in Table 7. Patients with preoperative symptoms were less likely to have a good clinical outcome compared with asymptomatic patients [54% (31/57) vs. 86% (6/7), OR 18.0, $P = 0.02$]. Patients with fusiform aneurysms were less likely than those with saccular aneurysms to have a good clinical outcome [60% (37/62) vs. 82% (18/22), OR 3.3, $P = 0.07$], but the difference was not statistically significant

Discussion

Saccular vertebrobasilar aneurysms treated with flow diversion

In this analysis of saccular vertebrobasilar aneurysms treated with flow diversion, complete occlusion was achieved in 88% (21/24) with a complication rate of 36% (9/25), including seven strokes, one intraparenchymal hemorrhage, and one delayed in-stent thrombosis. Good clinical outcome was achieved in 82% (18/22) of cases, with only one patient (4.5%, 1/22) becoming severely disabled by treatment. Though subgroup sample sizes were small, aneurysms arising from the basilar artery, vertebral artery, and vertebrobasilar junction did not differ significantly in terms of occlusion rates or procedural complications. These results should be evaluated in the context of alternative management options. The 5-year cumulative rupture rates for saccular posterior circulation aneurysms are 2.5% for aneurysms smaller than 7 mm and 50% for giant aneurysms [36]; therefore, the threshold for treating these aneurysms is relatively low. Endovascular treatment of vertebrobasilar aneurysms is generally preferred to microsurgical clipping owing to multiple studies showing worse outcomes after surgical treatment [37,38]. However, approximately 10–20% of coiled aneurysms require retreatment [39–42], and the recurrence rate is approximately three times higher in aneurysms larger than 10 mm with a neck greater than 4 mm [41]. A meta-analysis of 10 studies found that stent-assisted coiling significantly reduced recurrence rates (16 vs 34%, $P < 0.01$) with a comparable complication rate to coiling alone (17.6 vs. 15.9%, $P = 0.56$)

Table 4
Patient-level data of fusiform vertebrobasilar aneurysms treated with flow diversion identified during systematic review.

First author (year of publication)	Age, gender	Aneurysm location	Aneurysm size (mm)	Preoperative symptoms	Previous treatment	Flow diverter	# devices	Adjunctive stent	Adjunctive coiling?	Unilateral VA sacrifice?	Platelet function testing	Neurologic complications	Angiographic follow up (mo)	Aneurysm occlusion	Δ mRS	Post-procedure mRS
Ahmed (2015)	56M	VB	4.5	Dizziness, Nausea, Emesis	–	PED	6	–	No	No	Yes	Stroke	Follow up range 12-25 months with mean of 14.25 months	Incomplete	4	6
	67M	BA	10	Slurred Speech	–	PED	3	–	No	No	Yes	Stroke		Ňo retreatment¨	2	4
	56M	VB	11.9	Dizziness, Numbness	–	PED	8	–	No	No	Yes	–		Incomplete	4	6
	72M	VB	33	Mass Effect (Leg weakness)	–	PED	1	Neuroform x 3	Yes	No	Yes	Stroke		-	2	6
Chalouhi (2013)	58M	VA	10	No	–	PED	3	–	No	No	Yes	–	7	šignificant involution¨	0	0
	48 F	VB	14.5	No	Yes (details NR)	PED	1	–	No	No	Yes	–	7	šignificant involution¨	NR	NR
	76M	BA	25	Brainstem Compression	–	PED	1	–	No	No	Yes	–	3	Ňo change¨	0	0
De Vries 2013	73M	BA	20	Yes (n/a)	–	Surpass	2	–	No	No	Yes	–	6	Near complete (95-100%)	0	4
Ertl (2014)	64M	VB	22	Mass Effect (Cranial Nerve Neuropathy)	–	PED	6	–	No	No	Yes	–	17	Incomplete	3	6
	71M	BA	28	Mass Effect (Diplopia, insecure gait)	–	Silk	2	LEO x 3	No	No	Yes	–	5	Incomplete	3	6
	58M	VB	13	SAH	–	Silk	2	LEO x 3	Yes	Yes	Yes	Stroke	17	Incomplete	4	5
	54M	BA	30	Mass Effect	–	Silk	4	LEO x 4	Yes	Yes	Yes	Stroke	29	Incomplete	2	5
	49M	BA	21	Mass Effect	–	Silk	3	–	No	No	Yes	–	9	Complete	3	6
Fiorella (2008)	47M	VA	14	Headaches and Neck Pain	Stent-coiling	PED	3	–	No	No	No	–	4.5	Near complete	0	0
	57M	VA	14	Mass Effect (gait instability)	–	PED	3	–	Yes	No	Yes	–	6	Complete	0	0
Fiorella (2009)	13F	BA	39	Mass Effect (Gait instability)	–	PED	7	–	No	No	Yes	–	0.25	Complete	0	0
Martin (2015)	50F	BA	30	SAH	Coiling	PED	1	–	No	No	No	–	36	Complete	0	0
	62F	BA	8	Headache, numbness	–	PED	2	–	No	No	No	–	24	Complete	0	0
	56F	BA	21	Weakness	–	PED	1	–	Yes	No	No	Stroke	6	Near-occlusion	NR	NR
Meckel (2013)	58M	VB	>25	Ischemia	–	PED	2	–	Yes	Yes	Yes	Stroke	6	Complete	NR	2
	48M	VB	>25	Mass Effect	–	PED	9	–	No	Yes	Yes	–	11	Minimal filling	NR	6
	34F	VB	>25	Mass Effect/Ischemia	Stent-coiling	PED	2	–	Yes	Yes	Yes	Stroke	22	Minimal filling	NR	1
	72M	VB	>25	Mass Effect	–	PED	4	–	No	No	Yes	–	5	Residual filling	NR	6
	57M	VB	>25	Mass Effect	–	PED	6	–	Yes	Yes	Yes	IPH	0.5	Complete	NR	6
Mohammad (2017)	15M	BA	27	Hearing Loss/Gait imbalance	–	PED	1	–	Yes	No	No	–	9	Complete	NR	0

Table 4 (*Continued*)

First author (year of publication)	Age, gender	Aneurysm location	Aneurysm size (mm)	Preoperative symptoms	Previous treatment	Flow diverter	# devices	Adjunctive stent	Adjunctive coiling?	Unilateral VA sacrifice?	Platelet function testing	Neurologic complications	Angiographic follow up (mo)	Aneurysm occlusion	Δ mRS	Post-procedure mRS
Monteith (2014)	74F	VA	11	No	Stent-coiling	PED	2	–	NR	No	Yes	–	6	Complete	0	0
	60M	VA	10	No	–	PED	3	–	NR	No	Yes	–	12	Minimal filling	0	0
	50F	BA	28	No	Yes (details NR)	PED	1	–	NR	No	Yes	–	14	50% size decrease	0	0
	43F	BA	14	TIA/headache	–	PED	1	–	NR	No	Yes	–	10	Complete	0	0
	77M	BA	23	Ataxia/ CN VI palsy	–	PED	1	–	NR	No	Yes	SAH	–	–	0	2
	32M	BA	46	Multiple Cranial Neuropathies	Stent-coiling	PED	4	–	NR	No	Yes	Stroke	5	Ongoing filling	1	5
	44F	VB	20	No	Yes (details NR)	PED	1	–	NR	No	Yes	–	6	Slight neck filling	0	1
Munich 2014	56F	VB	6.7	LE weakness	–	PED	2	–	No	No	Yes	NR	Mean, 4.9 mo Range, 2-6 mo	Complete	-1	1
	65M	VB	9.8	Syncope	–	PED	5	–	No	No	Yes			–	6	6
	53F	VB	15.3	Supraclavicular Edema	–	PED	2	–	No	No	Yes			Complete	0	0
	64M	VB	23.2	Gait Instability	–	PED	6	–	No	No	Yes			–	1	5
	46M	VB	12	Headaches, Nausea and Vomiting	–	PED	4	–	No	No	Yes			Complete	0	0
	30F	VB	11.4	Headaches	–	PED	4	–	No	No	Yes			Complete	0	0
	46F	VB	10.3	Headaches	–	PED	2	–	No	No	Yes			Complete	0	0
	69F	VB	12.9	Headaches	–	PED	1	–	No	No	Yes			Complete	-1	0
Natarajan 2016	58 F	VB	10	Headaches, dizziness, nausea	–	PED	4	–	No	Yes	Yes	–	39	Complete	NR	0
	57 M	VA	6	Headaches, Extremity numbness	–	PED	2	–	No	No	Yes	–	26	Complete	NR	0
	66 M	VA	7	No	–	PED	1	–	No	No	Yes	–	23	Complete	NR	0
	68 M	VA	14	Amnesia	–	PED	1	–	No	No	Yes	–	22	Complete	NR	0
	29 M	VB	14	Dizziness, slurred speech, headaches	–	PED	1	–	No	No	Yes	–	6	Complete	NR	0
	70 F	BA	17	Headaches, CN III and CN VI palsy	–	PED	2	–	Yes	No	Yes	–	3	Complete	NR	1
	36 F	VA	17	Headaches	–	PED	3	–	Yes	No	Yes	–	15	Complete	NR	0
	54 M	VA	20	Headaches, generalized weakness	–	PED	1	–	Yes	Yes	Yes	–	3	Complete	NR	0
	71 F	BA	10	Headaches	–	PED	1	–	Yes	No	Yes	–	6	Complete	NR	0
	54 M	VB	10	Neck pain	–	PED	1	–	No	Yes	Yes	Stroke	6	Complete	NR	4
	62 F	VB	18	Headaches	–	PED	2	–	Yes	Yes	Yes	–	12	Complete	NR	0
Raphaeli (2011)	17F	BA	16	Headache, transient bilateral arm anesthesia	–	Silk	1	–	No	No	No	–	NR	Incomplete (flow reduction)	NR	0
	23M	BA	11	Transient Ischemic Attack	–	Silk	1	–	No	No	No	–	NR	Incomplete (flow reduction)	NR	0
	31M	VA	16	Prior SAH	–	Silk	1	–	No	No	No	TIA	NR	Incomplete	NR	0
	57M	BA	40	Quadriparesis, pneumopathy	–	Silk	1	–	No	No	No	–	NR	No follow up	NR	6

Table 4 (*Continued*)

First author (year of publication)	Age, gender	Aneurysm location	Aneurysm size (mm)	Preoperative symptoms	Previous treatment	Flow diverter	# devices	Adjunctive stent	Adjunctive coiling?	Unilateral VA sacrifice?	Platelet function testing	Neurologic complications	Angiographic follow up (mo)	Aneurysm occlusion	Δ mRS	Post-procedure mRS
Siddiqui (2012)	75M	VB	14.3	Difficulty Ambulating, Dizziness	–	Silk	2	Leo	No	No	Yes	–	12	Complete	0	1
	66M	VB	23.3	Slurred speech, recurrent aspirations, gait instability, cognitive impairment, hydrocephalus, quadriparesis	–	PED	9	-	Yes	Yes	Yes	NR	NR	Residual filling	2	6
	57F	VB	17.5	Headache, incidental	–	PED	5	-	Yes	Yes	Yes	TIA	4	Near complete (>95%)	-1	0
	42M	BA	35.6	Hemiparesis, Facial Weakness	–	PED	3	-	No	No	Yes	TIA, SAH	–	–	4	6
	42F	BA	37.1	Facial Numbness, Vertigo & ataxia	–	PED	3	-	Yes	No	Yes	SAH	1	Residual neck	4	6
	51M	BA	9.5	Thalamus & pons stroke; only dysarthria after tPA 2 weeks prior to treatment	–	PED	9	-	No	No	Yes	Stroke	1	Residual filling	2	5
	55F	BA	8.5	Pontine stroke, dysphagia, L hemiplegia	–	PED	3	-	Yes	No	Yes	–	–	–	1	6
Toth (2015)	60s	BA	29	Stroke	–	PED	2	-	No	No	Yes	Stroke	1	OKM B3	5	6
	50s	BA	29	Mass Effect/Stroke	–	PED	5	-	No	No	Yes	Stroke	4.5	Complete	2	5

IPH: intraparenchymal hemorrhage; mRS: modified Rankin score; NR: not reported; OKM: O'Kelly-Marotta; PED: pipeline embolization device; SAH: subarachnoid hemorrhage; TIA: transient ischemic attack.

Table 5
Complication rates of fusiform vertebrobasilar aneurysms treated with flow diversion as a function of aneurysm size and location.

	Aneurysm location			
Aneurysm Size	BA	VA	VB	Total
Small (< 6 mm)	0	0	1/1	100% (1/1)
Medium (7–15 mm)	2/7	0/8	2/7	18% (4/22)
Large (16–25 mm)	2/7	1/3	1/4	29% (4/14)
Giant (> 25 mm)	6/12	0	4/6	56% (10/18)
Total	38% (10/26)	9.1% (1/11)	44% (8/18)	35% (19/55)

Table 6
Fusiform vertebrobasilar aneurysms that were completely occluded at last angiographic follow up as a function of aneurysm size and location.

	Aneurysm location			
Aneurysm size	BA	VA	VB	Total
Small (< 6 mm)	0	0	0/1	0% (0/1)
Medium (7–15 mm)	3/5	8/8	11/14	82% (22/27)
Large (16–25 mm)	4/5	2/2	3/5	75% (9/12)
Giant (> 25 mm)	5/10	0	4/6	56% (9/16)
Total	60% (12/20)	100% (10/10)	69% (18/26)	71% (40/56)

Table 7
Percentages of patients with good clinical outcome (mRS ≤ 2) after flow diversion of fusiform vertebrobasilar aneurysms as a function of preoperative symptoms and functional status.

	Preoperative Functional Status			
Preoperative Symptoms	mRS ≤ 2	mRS > 2	NR	Total
Yes	10/18	0/12	21/27	54% (31/57)
No	4/4	-	2/3	86% (6/7)
Total	64% (14/22)	0% (0/12)	77% (23/30)	58% (37/64)

[43]. Meta-analyses and large case series of posterior circulation aneurysms treated with endovascular coiling with or without stent assistance have reported complete or near-complete occlusion rates of approximately 90%, recurrence rates of 5–20%, and complication rates of less than 20% [42,44,45], which are similar to those reported in series primarily containing anterior circulation aneurysms [46,47]. Additionally, a case series of 501 aneurysms treated with stent-assisted coiling found no difference in recurrence rates of anterior versus posterior circulation aneurysms [48], and another case series by Johnson et al. of 486 aneurysms treated with stent-assisted coiling found comparable complication rates during treatment of anterior and posterior circulation aneurysms [45].

The results of this analysis cannot be compared with other case series without acknowledging important caveats. Even pooling 7 publications produced a relatively small sample size of only 25 aneurysms with patient-level data. Also, the results may have been biased by a sample that included 44% (11/25) large or giant aneurysms, 52% (13/25) of which were symptomatic preoperatively, or other confounding factors that prompted treatment with flow diversion instead of well-established conventional endovascular techniques. Still, the derived occlusion and complication rates are useful when considering treatment options and counseling patients. The 88% complete occlusion rate in this review is comparable to reported rates achieved for anterior circulation aneurysms, which are approximately 75–85% for large or giant aneurysms [11,49,50] and 85-95% for small aneurysms [4,5], as well as those reported for stent-assisted coiling. However, unlike the latter, recurrence of a completely occluded aneurysm treated with flow diversion has yet to be reported. Still the effectiveness of flow diversion of saccular posterior circulation aneurysms may be offest by a higher complication rate that appears to be independent of aneurysm size or location within the posterior circulation. Therefore, flow diversion should only be considered in saccular posterior circulation aneurysms that cannot be treated with coiling alone or stent-assisted coiling and for which the cumulative risk of surveillance warrants the risk of perioperative complications.

Fusiform vertebrobasilar aneurysms treated with flow diversion

In this analysis of vertebrobasilar aneurysms treated with flow diversion, complete or near-complete aneurysm occlusion was achieved in 71% (40/56) of cases with a complication rate of 35% (19/55) and 60% (37/62) likelihood of a good clinical outcome.

The natural history of fusiform vertebrobasilar aneurysms was recently described in a systematic review that included nine studies with 440 cases of non-saccular vertebrobasilar aneurysms. The overall mortality of initially asymptomatic patients was 0.4% per year. However, 46% of aneurysms in this review demonstrated growth on serial imaging, which was associated with an annual mortality rate of 6.1%. Prognosis was especially poor once patients became symptomatic. Patients presenting with stroke had an annual recurrent stroke risk of 5.9%, and 40% of patients with symptoms related to brainstem compression died after 3.7 years of follow up [51].

Endovascular techniques have been the mainstay of treatment, as these aneurysms are typically inaccessible surgically. Endovascular parent artery occlusion is a viable option for patients who pass balloon occlusion testing, but a third of patients still worsen clinically despite treatment [52]. Patients who do not tolerate temporary balloon occlusion have been successfully treated with stent-assisted reconstructive techniques. In a retrospective study of fusiform dissecting and atherosclerotic aneurysms treated with stenting alone or stent-assisted coiling, complete and subtotal aneurysm occlusion were initially achieved in 50% (12/24) and 46% (11/24) of cases, respectively, with no periprocedural complications, and 89% (25/28) of patients experienced clinical stability or improvement. However, as is seen with saccular aneurysms, the recanalization rate of completely occluded aneurysms was 17% (4/24) [53].

Flow diverter treatment of fusiform aneurysms has the advantage of parent artery preservation, with no reported cases of aneurysm recurrence, and the overall occlusion and complication rates for fusiform aneurysms in this analysis were comparable to those for saccular aneurysms. However, unlike saccular aneurysms, our analysis found that the safety and effectiveness of flow diverter treatment of fusiform aneurysms in the posterior circulation depends on aneurysm size and location. Occlusion rates of fusiform aneurysms involving the basilar artery, with or without vertebral artery involvement, were 65% (30/46) overall and 56% (9/16) for giant aneurysms, with complication rates of 41% (18/44) overall and 56% (10/18) for giant aneurysms. In the absence of alternative treatment options, these statistics may be acceptable when treating an aneurysm with a poor natural history. However, clinicians and patients must understand that flow diversion of fusiform basilar aneurysms is likely less effective and higher risk than for other types of aneurysms. In contrast, all 10 vertebral artery aneurysms with angiographic follow up completely occluded, with a complication rate of 9.1% (1/11) due to a transient ischemic attack. In their systematic review of dissecting vertebral artery aneurysms treated with flow diversion, Cerejo et al. [54] reported similarly positive results, including complete aneurysm occlusion and periprocedural complication rates of 82% (36/44) and 8.3% (3/36). Potential explanations for the relative safety and effectiveness of vertebral artery flow diversion may be the smaller number of brainstem perforator arteries arising from the vertebral artery compared with the basilar artery [55]. Also, publications typically don't report the lengths of treated fusiform aneurysms.

Aneurysms involving only the vertebral artery may tend to be shorter than those involving the basilar or vertebrobasilar arteries, and endothelialization across flow diverter constructs may occur more readily over shorter segments of diseased vessel.

The results of this review also highlight a clinical dilemma as to the appropriate timing of flow diverter treatment. Although the sample size of asymptomatic patients was small, 86% (6/7) had a good functional outcome. In contrast, only 56% (10/18) of patients with symptomatic aneurysms remained functionally independent after treatment and no patients with a preoperative mRS > 2 regained independence. These results appear to argue in favor of early treatment before the aneurysm becomes symptomatic. However, as previously discussed, the prognosis of stable, asymptomatic fusiform vertebrobasilar aneurysms is relatively good, with mortality rates escalating dramatically only after the aneurysm enlarges or causes symptoms. Therefore, since the strategy that minimizes overall risk is unclear, the asymptomatic patient must choose which set of risks he or she is willing to accept. However, if the aneurysm enlarges over the course of imaging surveillance, treatment should be offered before symptoms develop and the likelihood a good functional outcome diminishes.

Limitations

Although the results of this analysis provide insight regarding the safety and effectiveness of flow diverter treatment of vertebrobasilar aneurysms, several limitations must be considered. Publications included in this review were primarily retrospective with self-reported outcomes, and therefore subject to the biases inherent to these methodologies. Additionally, while pooling data from multiple small case series enabled outcome rates to be calculated with narrower confidence intervals and facilitated comparisons of different subgroups, it also increased cohort heterogeneity and potentially introduced confounding variables into the analysis, such as variations in antiplatelet medication dosing and testing protocols, and use of adjunctive coiling or unilateral vertebral artery sacrifice. Despite pooling data from several studies, the number of aneurysms in each subgroup was relatively small, which precluded multivariable analysis. Lastly, our analysis may have been skewed by publication bias, as studies with more dramatic results may have been more likely to be published.

Conclusion

Flow diversion is an option for the treatment of saccular posterior circulation aneurysms that cannot be treated with conventional strategies. Flow diversion of fusiform basilar aneurysms, particularly those that are giant or symptomatic, is likely less effective and higher risk than flow diversion of fusiform vertebral artery aneurysms.

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