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ABSTRACT

BACKGROUND AND PURPOSE: Various endovascular techniques have been applied to the treatment of vertebrobasilar dissecting aneurysms, including parent artery preservation with coiling, stent placement or flow diverter placement, and trapping and proximal occlusion. We performed a systematic review and meta-analysis to study clinical and angiographic outcomes of patients undergoing endovascular treatment of vertebrobasilar dissecting aneurysms.

MATERIALS AND METHODS: We performed a comprehensive literature search for studies on the endovascular treatment of vertebrobasilar dissecting aneurysms. From each study we abstracted the following data: immediate occlusion, long-term occlusion, long-term good neurologic outcome, perioperative morbidity, perioperative mortality, rebleed (ruptured only), recurrence, and retreatment. We performed subgroup analyses of patients undergoing deconstructive-versus-reconstructive techniques. Meta-analysis was performed by using a random effects model.

RESULTS: Seventeen studies with 478 patients were included in this analysis. Sixteen studies had at least 6 months of clinical/angiographic follow-up. Endovascular treatment was associated with high rates of long-term occlusion (87.0%; 95% CI, 74.0%–94.0%) and low recurrence (7.0%; 95% CI, 5.0%–10.0%) and retreatment rates (3.0%; 95% CI, 2.0%–6.0%). Long-term good neurologic outcome was 84.0% (95% CI, 65.0%–94.0%). Deconstructive techniques were associated with higher rates of long-term complete occlusion compared with reconstructive techniques (88.0%; 95% CI, 35.0%–99.0% versus 81.0%; 95% CI, 64.0%–91.0%; $P < .0001$). Deconstructive and reconstructive techniques were both associated with high rates of good neurologic outcome (86.0%; 95% CI, 68.0%–95.0% versus 92.0%; 95% CI, 86.0%–95.0%; $P = .10$).

CONCLUSIONS: Endovascular treatment of vertebrobasilar dissecting aneurysms is associated with high rates of complete occlusion and good long-term neurologic outcomes. Deconstructive techniques are associated with higher occlusion rates. There was no statistical difference in neurologic outcomes between groups, possibly due to low power.

ABBREVIATION: VBDA = vertebrobasilar dissecting aneurysms

The best therapeutic choice for treatment of vertebrobasilar dissecting aneurysms (VBDA) is controversial. Ruptured VBDA are associated with a poor natural history with high rates of rebleed, stroke, and death when left untreated.[1] Unruptured VBDA have a benign clinical course when not associated with stroke or mass effect; however, they are prone to rupture and stroke when symptomatic.[2,3] Surgical and endovascular treatment of these lesions has proved successful. Endovascular therapies have emerged as the treatment of choice due to perceived lower rates of treatment-related morbidity as well as their efficacy. However, a number of endovascular approaches to the treatment of VBDA exist. Parent artery occlusion or trapping of the aneurysm was the initial treatment of choice. With the advent of stents and flow diverters however, parent artery preservation has emerged as an effective treatment technique.

Because most series on the treatment of VBDA are small single-center case series, the safety and efficacy of the various endovascular treatments for these lesions have not been well established. Specifically, little is known regarding whether newer, parent artery preservation techniques are associated with similar

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Table 1: Summary of studies

Author, Year	No. of Patients	No. Ruptured	No. Unruptured	Reconstructive Techniques	Deconstructive Techniques	Mean Follow-Up
Jin et al, 2009[15]	42	29	13	9	33	30 Mo
Kai et al, 2011[18]	8	0	8	0	8	24 Mo
Kashiwazaki et al, 2013[13]	73	45	28	0	73	56 Mo
Kim et al, 2011[7]	119	73	46	62	57	13 Mo
Luo et al, 2005[22]	10	0	10	0	10	15 Mo
Park et al, 2009[12]	27	11	16	27	0	12 Mo
Purkayastha et al, 2006[23]	8	8	0	0	8	37 Mo
Rabinov et al, 2003[16]	26	21	5	0	26	40 Mo
Rho et al, 2013[24]	5	5	0	5	0	40 Mo
Suh et al, 2009[25]	11	11	0	11	0	15 Mo
Tsuura et al, 1999[26]	12	12	0	0	12	6 Mo
Wakhloo et al, 2008[8]	8	2	6	8	0	37 Mo
Wang et al, 2013[27]	11	3	8	2	9	10 Mo
Yamaura et al, 1999[28]	6	6	0	0	6	12 Mo
Yoon et al, 2010[11]	24	6	18	24	0	16 Mo
Yuki et al, 2005[17]	29	29	0	0	29	5.3 Days
Zhao et al, 2013[10]	57	57	0	57	0	27 Mo

rates of angiographic occlusion and improved clinical outcomes. Therefore, we performed a systematic review of the literature examining the overall efficacy of endovascular treatments for VBDA and comparing outcomes of reconstructive techniques such as stent placement, flow diversion, and stent-assisted coiling with deconstructive techniques such as parent artery occlusion and trapping.

MATERIALS AND METHODS

Literature Search

A comprehensive literature search of the data bases PubMed, Ovid MEDLINE, and Ovid EMBASE was designed and conducted by an experienced librarian with input from the authors. The key words, "endovascular," "catheterization," "percutaneous," "embolization," "coil," "stent," "flow diverter," "intracranial," "vertebrobasilar," "posterior circulation," "aneurysm," "dissecting," and "dissection," were used in both "AND" and "OR" combinations. The search was limited to articles published from 1980 to June 2014 in the English language only. All studies reporting patients treated with endovascular therapy for VBDA were selected. Inclusion criteria were a series of >5 patients, with available data on clinical and/or angiographic outcomes. Two reviewers selected the included studies.

For each study, we extracted the following information: patient presentation (ruptured or unruptured), treatment technique (stent, stent-assisted coiling, coiling, parent artery occlusion, trapping), long-term good neurologic outcome, immediate angiographic occlusion, long-term angiographic occlusion, perioperative morbidity (resulting from procedural complications), perioperative mortality (all cause), rebleeding (for ruptured only), recurrence, and retreatment. Good neurologic outcome was defined as a modified Rankin Scale score of ≤2. In cases in which a modified Rankin Scale score was not available, good neurologic outcome was determined if the study used terms such as "no morbidity" or "good recovery."

Outcomes were obtained for the overall population of patients receiving endovascular treatment of VBDA, in addition to determining outcomes by aneurysm rupture status. Separate analyses were also performed comparing outcomes between patients receiving reconstructive techniques with preservation of the parent artery including stent placement and stent-assisted coiling and those undergoing deconstructive techniques such as trapping or parent artery occlusion.

Statistical Analysis

All included studies were noncomparative. We estimated from each cohort the cumulative incidence (event rate) and 95% confidence interval for each outcome. Event rates for each intervention were pooled in a meta-analysis across studies by using the random effects model.[4] Anticipating heterogeneity among studies, we chose this model a priori because it incorporates within-study variance and between-study variance. Heterogeneity of the treatment effect across studies was evaluated by using the I^2 statistic and the Cochrane Q test for heterogeneity.[5,6] We considered an I^2 statistic of >50% or a P value for the heterogeneity test of <.05 to suggest significant heterogeneity. We were unable to test for publication bias due to the noncomparative nature of the studies.

RESULTS

Literature Review

The initial literature search yielded 615 articles. On initial abstract and title review, 552 articles were excluded because they were deemed not relevant to the current study. Sixty-three studies were reviewed in additional detail. Twenty-five studies were excluded because they dealt with outcomes of treatment of vertebrobasilar dissections, not vertebrobasilar dissecting aneurysms. Twenty-one studies were excluded because they were either case reports or had too few patients. In total, 17 studies with 476 patients were included. Three hundred eighteen patients (66.8%) presented with ruptured VBDA, and 158 patients (33.2%) presented with unruptured VBDA. Two hundred five patients (43.1%) were treated with reconstructive techniques, and 271 patients (56.9%) were treated with deconstructive techniques. Mean follow-up was at least 6 months for 16 of the 17 studies. Mean follow-up was only 5.3 days for 1 study. These data are summarized in Table 1.

Table 2: Meta-analysis outcomes

Outcome	All Patients		Deconstructive		Reconstructive		
	Event Rate (95% CI)	I^2	Event Rate (95% CI)	I^2	Event Rate (95% CI)	I^2	*P* Deconstructive versus Reconstructive
All patients							
Immediate occlusion	75.0 (55.0–88.0)	83	88.0 (47.0–98.0)	86	53.0 (31.0–74.0)	71	<.0001
Long-term occlusion	87.0 (74.0–94.0)	82	88.0 (35.0–99.0)	91	81.0 (64.0–91.0)	62	<.0001
Perioperative morbidity	12.0 (9.0–16.0)	0	12.0 (7.0–18.0)	0	4.0 (2.0–10.0)	0	.04
Perioperative mortality	8.0 (6.0–11.0)	0	10.0 (6.0–17.0)	0	4.0 (2.0–10.0)	0	.11
Recurrence	7.0 (5.0–10.0)	0	5.0 (2.0–10.0)	0	5.0 (2.0–11.0)	0	.89
Retreatment	3.0 (2.0–6.0)	0	5.0 (2.0–10.0)	0	3.0 (1.0–8.0)	0	.25
Long-term good clinical outcome	84.0 (65.0–94.0)	89	86.0 (68.0–95.0)	68	92.0 (86.0–95.0)	0	.10
Patients with rupture							
Immediate occlusion	78.0 (55.0–91.0)	78	94.0 (84.0–98.0)	0	43.0 (18.0–73.0)	57	<.0001
Long-term occlusion	88.0 (83.0–92.0)	0	95.0 (86.0–98.0)	0	83.0 (74.0–90.0)	0	.02
Perioperative morbidity	16.0 (11.0–22.0)	10	14.0 (8.0–23.0)	0	7.0 (3.0–17.0)	0	.82
Perioperative mortality	11.0 (8.0–16.0)	0	13.0 (8.0–22.0)	0	7.0 (3.0–15.0)	0	.82
Rebleed	9.0 (6.0–13.0)	0	9.0 (4.0–20.0)	12	7.0 (3.0–14.0)	0	.75
Recurrence	8.0 (5.0–13.0)	0	6.0 (2.0–13.0)	0	7.0 (2.0–17.0)	1	1.00
Retreatment	5.0 (3.0–8.0)	0	6.0 (2.0–13.0)	0	5.0 (2.0–15.0)	0	.25
Long-term good clinical outcome	79.0 (68.0–87.0)	59	83.0 (62.0–94.0)	64	88.0 (79.0–94.0)	0	.19
Patients without rupture							
Immediate occlusion	80.0 (48.0–94.0)	74	94.0 (68.0–99.0)	28	57.0 (25.0–84.0)	65	<.0001
Long-term occlusion	86.0 (69.0–94.0)	64	97.0 (81.0–100.0)	0	68.0 (47.0–83.0)	31	<.0001
Perioperative morbidity	6.0 (3.0–12.0)	0	7.0 (2.0–19.0)	0	7.0 (2.0–19.0)	0	.58
Perioperative mortality	4.0 (2.0–9.0)	0	4.0 (1.0–18.0)	0	5.0 (1.0–15.0)	0	1.00
Recurrence	7.0 (4.0–13.0)	0	4.0 (1.0–18.0)	0	7.0 (2.0–20.0)	0	1.00
Retreatment	4.0 (2.0–9.0)	0	4.0 (1.0–18.0)	0	5.0 (1.0–15.0)	0	1.00
Long-term good clinical outcome	95.0 (89.0–98.0)	0	93.0 (76.0–98.0)	0	94.0 (84.0–98.0)	0	1.00

Overall Outcomes of Endovascular Treatment of VBDA

Considering all patients treated by either reconstructive or deconstructive techniques, immediate occlusion rates were 75.0% (95% CI, 55.0%–88.0%) and long-term occlusion rates were 87.0% (95% CI, 74.0%–94.0%). Angiographic recurrence rates were 7.0% (95% CI, 5.0%–10.0%) with a retreatment rate of 3.0% (95% CI, 2.0%–6.0%). Perioperative morbidity was 12.0% (95% CI, 9.0%–16.0%), and all-cause perioperative mortality was 8.0% (95% CI, 6.0%–11.0%). Patients with ruptured VBDA made up a majority of patients with VBDA with perioperative mortality (11.0%; 95% CI, 8.0%–16.0%). All-cause perioperative mortality for unruptured VBDA was 4.0% (95% CI, 2.0%–9.0%). The overall rebleed rate for patients with ruptured VBDA was 9.0% (95% CI, 6.0%–13.0%). These data are summarized in Table 2. Forest plots for the overall outcomes are provided in On-line Figs 1–8.

Deconstructive versus Reconstructive Techniques: All Patients with VBDA

Patients treated with deconstructive techniques had higher rates of complete occlusion on immediate posttreatment angiography than those treated with reconstructive techniques (88.0% versus 53.0%, $P < .0001$). The same was true for long-term posttreatment angiography (88.0% versus 81.0%, $P < .0001$). Perioperative morbidity was lower in the reconstructive group compared with the deconstructive group (4.0% versus 12.0%, $P = .04$). There was a trend toward decreased perioperative mortality rates in the reconstructive group (4.0% versus 10.0%, $P = .11$) and a trend toward higher rates of long-term good clinical outcome in the reconstructive group (92.0% versus 86.0%, $P = .10$). These data are summarized in Table 2.

Deconstructive versus Reconstructive Techniques: Patients with Ruptured VBDA

Patients treated with deconstructive techniques had higher rates of complete occlusion on immediate posttreatment angiography than those treated with reconstructive techniques (94.0% versus 43.0%, $P < .0001$). The same was true for long-term posttreatment angiography (95.0% versus 83.0%, $P = .02$). Perioperative morbidity rates were similar in the reconstructive group compared with the deconstructive group (7.0% versus 14.0%, $P = .82$). Perioperative mortality was 13.0% (95% CI, 8.0%–22.0%) in the deconstructive group versus 7.0% (95% CI, 3.0%–15.0%) in the reconstructive group ($P = .82$). Long-term good clinical outcome rates were similar between the reconstructive (88.0%; 95% CI, 79.0%–94.0%) and deconstructive groups (83.0%; 95% CI, 62.0%–94.0%) ($P = .19$). Rebleeding rates were similar between the deconstructive (9.0%; 95% CI, 4.0%–20.0%) and reconstructive (7.0%; 95% CI, 3.0%–14.0%) techniques ($P = .75$). These data are summarized in Table 2.

Deconstructive versus Reconstructive Techniques: Patients with Unruptured VBDA

Patients treated with deconstructive techniques had higher rates of complete occlusion on immediate posttreatment angiography than those treated with reconstructive techniques (94.0% versus 57.0%, $P < .0001$). The same was true for long-term posttreatment angiography (97.0% versus 68.0%, $P = .02$). Perioperative morbidity rates were similar in the reconstructive group compared with the deconstructive group (7.0% versus 7.0%, $P = .57$). Perioperative mortality was 4.0% (95% CI, 1.0%–18.0%) in the deconstructive group versus 5.0% (95% CI, 1.0%–15.0%) in the

reconstructive group ($P = 1.00$). Long-term good clinical outcome rates were similar between the reconstructive (94.0%; 95% CI, 84.0%–98.0%) and deconstructive groups (93.0%; 95% CI, 76.0%–98.0%%) ($P = 1.00$). These data are summarized in Table 2.

Study Heterogeneity

Significant heterogeneity (I^2 value of >50% and P value for the Cochrane Q test of <.05) was noted in the analyses of 3 outcomes (immediate occlusion, long-term good clinical outcome, and long-term occlusion). Therefore, confidence in a pooled summary estimate for these 3 outcomes is limited. On the other hand, the results were very consistent across studies for all of the remaining outcomes.

DISCUSSION

This systematic review and meta-analysis demonstrated that both deconstructive (parent artery occlusion, aneurysm trapping) and reconstructive (stent placement/stent-assisted coiling) techniques are effective in the treatment of ruptured and unruptured VBDA. Deconstructive techniques achieved higher rates of complete angiographic occlusion compared with reconstructive techniques; however, periprocedural morbidity rates were lower for reconstructive techniques. Both techniques resulted in high rates of good long-term neurologic outcome and similar low rates of recurrence and retreatment. Overall, these findings suggest that reconstructive techniques may be as effective as and possibly safer than deconstructive techniques; especially in cases in which patients lack sufficient collateral circulation.

Comparisons of clinical and angiographic outcomes between reconstructive and deconstructive techniques in the literature are limited, largely due to the small sizes of most case series. The largest study to date comparing deconstructive and reconstructive techniques was that of Kim et al,[7] which compared 62 VBDA treated with reconstructive techniques and 57 treated with deconstructive techniques This study demonstrated no difference in recurrence and rebleeding rates between reconstructive and deconstructive techniques. Recurrence rates were 10.2% for patients treated with reconstructive techniques versus 17.1% for those treated with deconstructive techniques. Although our study found that deconstructive techniques result in higher angiographic occlusion rates, we found no difference in recurrence, retreatment, and rebleeding rates when comparing reconstructive and deconstructive techniques. These findings are important because they run contrary to the expectation that reconstructive techniques result in higher recanalization and rebleeding rates. With the advent of flow diverters and increased use of multiple overlapping stents in the treatment of dissecting VBDA, it is likely that angiographic outcomes of patients treated with reconstructive techniques will improve with time.[7-9] Higher rates of long-term angiographic occlusion with multiple overlapping stents compared with single-stent treatment have been demonstrated in multiple series.[10-12]

Our study found similar rates of good long-term neurologic outcome between patients treated with reconstructive and deconstructive techniques but higher rates of perioperative morbidity among patients treated with deconstructive techniques. Patients treated with deconstructive techniques are at a higher risk of neurologic complications secondary to ischemia resulting from sacrifice of the parent vessel. Most ischemic complications are the result of occlusion and ischemia of perforating arteries and the anterior spinal artery.[13] In a series of 72 patients treated with deconstructive techniques, Kashiwazaki et al[13] reported 2 cases of spinal cord infarction and 7 cases of partial Wallenberg syndrome secondary to occlusion of vertebrobasilar dissecting aneurysms involving the PICA. Despite these perforator complications, only 1 patient died and the remaining patients had mRS ≤2. Perforator infarctions are rare with stent and flow-diverter reconstruction for treatment of vertebrobasilar aneurysms.[14] Large-vessel infarcts resulting from thrombotic complications or hemodynamic alterations in the setting of deconstructive techniques are rare as well.[15-17]

Despite their overall lower rate of perioperative morbidity, reconstructive techniques are far from a panacea in the treatment of VBDA. One major limitation of treatment of VBDA with stents is in the treatment of PICA-origin VBDA. Especially in the setting of ruptured VBDA, complete obliteration of the aneurysm should be the primary goal because recanalization is associated with a high rate of rupture. Deconstructive techniques could be considered in this setting; however, in the absence of adequate cerebellar circulation, these are associated with a high risk of stroke and associated mass effect.[12] Reconstruction of PICA-involving lesions often requires the aneurysm sac to be left partially open to ensure adequate PICA flow.[18] This places the patient at a high risk of recanalization, which, in the setting of ruptured VBDA, can result in hemorrhage. Thus, for these types of lesions, bypass surgery should be considered.[19] Reconstructive treatments are also associated with a host of other complications, including stent migration, in-stent thrombosis leading to stroke, and dissection. However, these complications are rare.[7,10,12]

The most important consideration in the treatment of VBDA is weighing the risks of treatment with the risks of the natural history of these lesions. Ruptured VBDA are known to have a poor natural history with high rates of rebleeding and mortality.[1] Rabinov et al[16] compared mortality rates among patients with ruptured VBDA treated with deconstructive techniques and surgical clipping with a small group of patients managed conservatively and found that mortality rates in the conservative group were 50% compared with 20% in the treatment group. Kobayashi et al[3] followed 113 patients with unruptured VBDA without ischemic symptoms at presentation for a mean of 3 years and found a 3% morbidity at follow-up, with 2 patients having clinical deterioration due to mass effect and 1 patient having ischemic stroke and hemorrhage. Five patients had enlargement of the aneurysm in this series.[3]

Strengths and Limitations

The strengths of this study include following a priori established protocol, the comprehensive literature search that involved multiple databases, and the process of study selection by independent reviewers. The main limitation of this analysis is the noncomparative and nonrandomized nature of the studies. It is difficult to perform comparative studies on treatment of VBDA because treatment decisions for lesions are dependent on multiple factors

such as the presence of collateral circulation, involvement of branch vessels or perforators, and lesion severity. Due to the rarity, variable appearance, and severity of these lesions and the multitude of treatment options available, prospective clinical registries should be considered to determine which treatment modalities provide superior outcomes for various lesion types. Furthermore, development of a validated classification system for vertebrobasilar dissecting aneurysm severity could be considered. There are no validated tools to evaluate the methodologic quality of noncomparative series. Therefore, the risk of bias associated with inferences from studies with this design should be considered high. There are no reliable tests to evaluate publication bias in the setting of noncomparative studies. Publications bias is very likely in the setting of small observational studies because patients who had either uneventful or poor outcomes may have been excluded from published results. Furthermore, when performing single-institution retrospective review series, an investigator can easily look at the outcomes and not publish them when they are not favoring the investigator's point of view. Moreover, treatment modalities have varied during the time course of the published series; this variation makes standardization of treatment paradigms difficult.

Last, uniform assessment and reporting of complications in a standardized fashion was lacking. Using the Grading of Recommendations, Assessment, Development, and Evaluation framework,[20,21] the quality of evidence (confidence in estimates) is very low because of the imprecision, heterogeneity, and methodologic limitations of the included studies, most important because they were noncomparative. Nevertheless, this meta-analysis provides useful data to share with patients and families when assessing the risks of treatment of VBDA and represents a benchmark against which future studies can be compared. With analysis of >470 patients, this is currently the largest study examining outcomes of the endovascular treatment of VBDA.

CONCLUSIONS

Endovascular treatment of VBDA may be associated with high rates of complete occlusion and good long-term neurologic outcomes. Deconstructive techniques may result in higher rates of complete angiographic occlusion, while reconstructive techniques may be associated with less perioperative morbidity. However, long-term neurologic outcomes and retreatment rates are statistically similar between these 2 treatment modalities, possibly due to low power to detect differences between the groups. Comparative studies are needed to further confirm these findings. Use of either of these 2 modalities seems to be safe and effective in the right clinical setting. When deciding to treat unruptured VBDA, the risks of the treatment should be weighed against the risks of the natural history of these lesions.

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