ORIGINAL RESEARCH

Endovascular coiling versus parent artery occlusion for treatment of cavernous carotid aneurysms: a meta-analysis

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ABSTRACT

Background and purpose Endosaccular coil embolization and parent artery occlusion (PAO) are established endovascular techniques for treatment of cavernous carotid aneurysms. We performed a systematic review of published series on endovascular treatment of cavernous carotid aneurysms to determine outcomes and complications associated with endovascular coiling and PAO of cavernous carotid artery aneurysms.

Methods In September 2013, we conducted a computerized search of MEDLINE and EMBASE for reports on endovascular treatment of intracranial cavernous carotid aneurysms from January 1990 to August 2013. Comparisons were made in periprocedural complications and outcomes between coiling and PAO patients who did not receive bypass. Event rates were pooled across studies using random effects meta-analysis.

Results 20 studies with 509 patients and 515 aneurysms were included in this systematic review. Aneurysm occlusion rates at >3 months after operation were significantly higher in the PAO without bypass group (93.0%, 95% CI 86.0 to 97.0) compared with the coiling group (67.0%, 95% CI 55.0 to 77.0) (p<0.01). Retreatment rates were significantly lower in the PAO without bypass group (6.0%, 95% CI 2.0 to 12.0) compared with the coiling group (18.0%, 95% CI 12.0 to 26.0) (p=0.01). Coiling patients had a similar morbidity rate (3.0%, 95% CI 2.0 to 6.0) compared with PAO without bypass patients (7.0%, 95% CI 3.0 to 12.0) (p=0.13). Coiling patients had a similar mortality rate (0.0%, 95% CI 0.0 to 6.0) compared with PAO without bypass patients (4.0%, 95% CI 1.0 to 9.0) (p=0.68).

Conclusions Evidence from non-comparative studies suggests that traditional endovascular options are highly effective in treating cavernous sinus aneurysms. PAO is associated with a higher rate of complete occlusion. Periprocedural morbidity and mortality rates are not negligible, especially in patients receiving PAO.

INTRODUCTION

Aneurysms of the cavernous carotid artery (CCA) are associated with mass effect on adjacent cranial nerves while their risk of rupture with ensuing direct carotid cavernous fistulas or life threatening subarachnoid hemorrhage (SAH) is low.[1–3] Because of the complexity of surgical treatment, endovascular techniques have emerged as the preferred therapy for treatment of symptomatic CCA aneurysms. Endosaccular coil embolization and parent artery occlusion (PAO) are established endovascular techniques for the treatment of carotid cavernous aneurysms. However, in the past few years, flow diversion has emerged as a newer technique for the treatment of these aneurysms although there are no definitive data supporting its superior safety and efficacy over more traditional techniques. A number of case series and retrospective studies have assessed the efficacy of endovascular techniques, such as endovascular carotid occlusion and endosaccular coiling, in treating CCA aneurysms.[4 5] A common limitation in most studies has been the limited number of patients. We sought to perform a systematic review to compare outcomes of endovascular carotid artery occlusion and endosaccular coiling in the treatment of ruptured and unruptured carotid cavernous aneurysms. Given the recent interest in the application of flow diversion to CCA aneurysms, these data provide an important benchmark against which the results of flow diversion can be assessed.

METHODS

In September of 2013, we performed a computerized MEDLINE and EMBASE search of the literature from January 1990 to August 2013 for reports of endovascular embolization of cavernous carotid aneurysms by using the keywords 'cavernous carotid artery', 'intracranial aneurysm', 'endovascular', 'coil', 'embolization', 'occlusion', and 'sacrifice' in both 'AND' and 'OR' combinations. Identified studies from the MEDLINE search were then further evaluated for inclusion in the systematic review. We also searched references from multiple articles to find any additional series on endovascular treatment of cavernous carotid aneurysms not found in our initial literature search. Inclusion criteria were the following: (1) studies reporting a consecutive series of cavernous carotid aneurysms (>5 patients), (2) studies reporting angiographic and/or clinical outcomes following treatment, and (3) studies stratifying outcomes by treatment modality. Studies reporting on patients treated with bypass in conjunction with endovascular PAO were also considered but patients receiving bypass were evaluated in a separate analysis. Exclusion criteria included the following: (1) studies reporting five or less patients, (2) studies reporting outcomes of endosaccular balloon embolization (non-coil embolization), (3) studies reporting endovascular occlusion of vessels other than the internal carotid

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artery and (4) studies in languages other than English. Patients with traumatic carotid cavernous fistulas (CCFs) and pseudoaneurysms were excluded.

Each study was analyzed to collect the following variables: (1) perioperative (procedure related) morbidity, (2) perioperative stroke (both clinical and radiographic), (3) perioperative hemorrhage, (4) perioperative mortality, (5) patient presentation, (6) aneurysm retreatment, (7) long term (>3 month) occlusion rate, and (8) improvement in mass effect. The perioperative period was defined as <30 days after operation. Outcomes were compared across two treatment groups: (1) endovascular coiling (including stent assisted coil patients) and (2) endovascular PAO (excluding patients who received bypass). Patients treated with endovascular PAO in conjunction with bypass were excluded from the comparative analysis in order to allow for direct comparisons between patients receiving endovascular only treatments. Two additional subgroup analyses were performed: (1) a subgroup analysis comparing outcomes of stent assisted and non-stent assisted coiling and (2) a second subgroup analysis of patients treated with bypass in conjunction with endovascular PAO.

Statistical analysis

We estimated from each study the cumulative incidence (event rate) and 95% CI for each outcome. Event rates were pooled across studies using random effects meta-analysis.[6] Subgroup effects were evaluated using an interaction test, as described by Altman.[7] Comparisons were made between the coiling and PAO without bypass groups as well as between stent assisted and non-stent assisted coiling groups. Outcomes of the PAO with bypass group were evaluated separately due to the small number of patients. Heterogeneity across studies was evaluated using the I^2 statistic.[8]

RESULTS

Search results

MEDLINE and EMBASE searches yielded 495 articles; of these, 408 were excluded after reading the abstract alone, 39 additional studies were excluded for not meeting the inclusion criteria of >5 patients, eight studies were excluded for reporting endosaccular balloon occlusion rather than coil embolization, 19 studies were excluded because they reported on traumatic CCFs or post-traumatic pseudoaneurysms, and two studies were excluded as they did not stratify outcomes by PAO and coil embolization. Twenty articles met our inclusion criteria. All studies were retrospective case series. Thirteen studies included patients who underwent endosaccular coiling and 10 studies included patients who underwent PAO. Seven studies included patients who received stent assisted coiling. The smallest study had six patients and the largest study had 113 patients. A total of 509 patients with 515 aneurysms were included in the current analysis. A summary of the included studies is provided in table 1.

Patient presentation and treatment

Seventy-seven per cent of patients (95% CI 65.0 to 86.0) presented with cranial nerve deficits, 7.0% of patients (95% CI 5.0 to 10.0) presented with SAH, and 7.0% of patients (95% CI 5.0 to 9.0) presented with CCF. A total of 176 patients (37.1%) were treated with PAO and 339 patients (62.9%) were treated with endosaccular coiling. Stent assisted coiling was used in 131 cases (37.5%). A total of 135 patients (76.7%) had endovascular PAO without bypass and 41 patients (23.3%) had endovascular PAO with bypass. Table 2 describes the patient characteristics, patient presentations, and treatment modality used.

Outcome, morbidity, and mortality rates

We found that 93.0% (95% CI 86.0 to 97.0) of patients who underwent PAO without bypass demonstrated complete or near complete occlusion of the aneurysm >3 months after the procedure compared with an occlusion rate of 67.0% (95% CI 55.0 to 77.0) in those who underwent endovascular coiling ($p<0.01$). The perioperative morbidity rate for endovascular coiling was 3.0% (95% CI 2.0 to 6.0) compared with 7.0% (95% CI 3.0 to 14.0) for patients receiving PAO without bypass

Table 1 Description of studies

Study	No of patients	No of aneurysms	No of unruptured aneurysms	CCF (n)	SAH (n)	Carotid occlusion (n)	Aneurysm coiling (n)	Stent assist (n)	Mean follow-up (months)	Type of study
Murakami[25]	7	7	6	1	0	7	0	0	NA	R
Hauck[26]	8	8	8	0	0	0	8	6	22	R
Suzuki[27]	10	11	11	0	0	0	11	0	58	R
van Rooij[10]	85	86	77	8	1	55	31	2	42	R
Morita[28]	7	7	7	0	0	0	7	3	53	R
Choulakian[11]	113	113	110	0	3	0	113	53	6	R
Akai[29]	8	8	8	0	0	0	8	0	31	R
Elhammady[19]	15	15	14	0	1	15	0	0	14	R
Kim[20]	19	19	18	0	1	0	19	0	NA	R
Starke[5]	79	82	75	1	6	15	67	53	21	R
Bavinzski[18]	32	33	25	2	6	16	17	0	33	R
Barnett[30]	6	6	5	0	1	6	0	0	6	R
Kupersmith[31]	12	12	12	0	0	12	0	0	24	R
Linskey[32]	6	6	6	0	0	6	0	0	25	R
Lylyk[33]	60	60	40	0	0	40	0	0	NA	R
Raymond[34]	7	7	7	0	0	7	0	0	4	R
Halbach[35]	35	35	32	0	3	0	35	0	NA	R
Weber[36]	6	6	6	0	0	0	6	0	6	R
Mawad[37]	8	8	8	0	0	0	8	8	6	R
Kono[38]	6	6	6	0	0	0	6	6	16	R

CCF, carotid cavernous fistula; R, retrospective; SAH, subarachnoid hemorrhage; NA, not available.

Table 2 Patient characteristics

	Meta-analysis (% (95% CI))	I^2 (%)	Raw numbers
No of patients	–	–	509
No of aneurysms treated	–	–	515
Patient presentations			
Cranial nerve deficit mass effect	77.0 (65.0 to 86.0)	81	310/511
SAH	6.0 (4.0 to 9.0)	0	23/511
CCF	7.0 (5.0 to 9.0)	0	22/511
Treatment modality			
Carotid occlusion	35.0 (18.0 to 58.0)	84	176/515
Endovascular coiling	65.0 (42.0 to 82.0)	84	339/515
Cumulative outcomes			
Complete/near complete occlusion at 3 months	79.0 (69.0 to 87.0)	71	372/477
Improvement in mass effect	82.0 (67.0 to 91.0)	71	218/266
Retreatment rate	14.0 (9.0 to 21.0)	38	52/507
Total periprocedural morbidity	4.0 (3.0 to 7.0)	0	12/514
Periprocedural stroke	4.0 (3.0 to 6.0)	0	11/515
Periprocedural hemorrhage	3.0 (2.0 to 6.0)	0	2/515
Periprocedural mortality	3.0 (2.0 to 6.0)	0	2/515

CCF, carotid cavernous fistula; R, retrospective. SAH, subarachnoid hemorrhage.

(p=0.13). The perioperative mortality rate was 0.0% (95% CI 0.0 to 6.0) for endovascular coiling compared with 4.0% (95% CI 1.0 to 9.0) for PAO without bypass (p=0.68). The coiling group demonstrated a retreatment rate of 18.0% (95% CI 12.0 to 26.0) compared with 6.0% (95% CI 2.0 to 12.0) for PAO without bypass (p=0.01). Improvement in mass effect/cranial nerve compressive symptoms was seen in 83.0% (95% CI 52.0 to 96.0) of patients receiving PAO without bypass compared with 72.0% (95% CI 48.0 to 87.0) of endosaccular coiling patients (p=0.48). These data are summarized in table 3.

In a subgroup analysis of stent assisted versus non-stent assisted coiling, there were 76 patients with stent assisted coiling and 152 patients with non-stent assisted coiling. Patients receiving stent assisted coiling demonstrated a non-significant trend toward better occlusion rates (56.0%, 95% CI 31.0 to 79.0) compared with non-stent assisted coiling patients (45.0%, 95% CI 22.0 to 71.0) (p=0.56). Retreatment rates were similar between the two groups, as stent assisted patients had a retreatment rate of 22.0% (95% CI 14.0 to 33.0) compared with 20.0% (95% CI 12.0 to 31.0) (p=0.80). Periprocedural morbidity was low in the stent assisted (0.0%, 95% CI 0.0 to 21.0) and non-stent assisted (4.0%, 95% CI 2.0 to 9.0) groups (p=0.56). These data are summarized in table 4.

A subgroup analysis of endovascular PAO with bypass found 41 patients. Occlusion rates were 93.0% (95% CI 81.0 to 98.0). Total periprocedural morbidity was 11.0% (95% CI 4.0 to 26.0) and total periprocedural mortality was 7.0% (95% CI 2.0 to 19.0). These data are summarized in table 5.

DISCUSSION

Our systematic review of endovascular treatment of cavernous aneurysms demonstrated remarkably high rates of complete or near complete occlusion following PAO and substantially lower rates of such occlusion following either coil or stent–coil occlusion. The difference in occlusion between reconstructive and deconstructive techniques was not only statistically significant but also clinically relevant; this clinical relevance is further highlighted by a nearly three times higher rate of retreatment among the coil group compared with the PAO group. However, there was a trend towards significantly higher morbidity rates in the PAO compared with the coiling group. We noted a mortality rate of 4% in the former group and no mortality in the latter although this did not reach statistical significance. These findings indicate that the optimal therapy for patients suffering from symptomatic cavernous carotid aneurysms remains difficult to establish.

In a previous systematic review of outcomes of balloon occlusion and endosaccular coiling for treatment of cavernous carotid aneurysms, van der Schaaf *et al* found an ischemic complication rate of 5% for occlusion patients and a 0% complication rate for endovascular coiling patients.[9] They also found a very high rate of long term aneurysmal occlusion in the parent artery embolization group of 97.5% compared with 80% in the coiling group. The study included 247 patients undergoing PAO (with and without bypass) and only 68 patients receiving endosaccular coiling. Our study differs from this previously published systematic review in that we only included patients with non-traumatic aneurysms and only compared outcomes of patients treated with endovascular techniques, excluding patients receiving PAO with bypass from statistical comparisons. Thus our patient population is more homogeneous, potentially allowing for more accurate comparisons between groups.

Other recently published large case series on the endovascular treatment of cavernous carotid aneurysms have demonstrated remarkably low complication rates with both PAO and endosaccular coiling. Van Rooij *et al* demonstrated a complication rate of 1.2% with PAO and 0.0% with endosaccular coiling. Similar to our study however, retreatment rates were significantly higher among endosaccular coiling patients compared with PAO patients.[10] In a series of 113 patients receiving endosaccular

Table 3 Patient outcomes—coiling (combined stent assisted and non-stent assisted) versus parent artery occlusion without bypass

	Endovascular coiling		Endovascular PAO		
	Meta-analysis (% (95% CI))	Raw numbers	Meta-analysis (% (95% CI))	Raw numbers	p Value
Complete/near complete occlusion at 3 months	67.0 (55.0 to 77.0)	203/296	93.0 (86.0 to 97.0)	128/133	<0.01
Improvement in mass effect	72.0 (48.0 to 87.0)	75/103	83.0 (52.0 to 96.0)	63/76	0.48
Retreatment rate	18.0 (12.0 to 26.0)	49/333	6.0 (2.0 to 12.0)	2/134	0.01
Total periprocedural morbidity	3.0 (2.0 to 6.0)	5/339	7.0 (3.0 to 14.0)	5/135	0.13
Periprocedural stroke	3.0 (2.0 to 6.0)	4/339	6.0 (3.0 to 12.0)	4/135	0.31
Periprocedural hemorrhage	3.0 (1.0 to 6.0)	1/339	4.0 (1.0 to 9.0)	1/135	0.68
Periprocedural mortality	0.0 (0.0 to 6.0)	0/339	4.0 (1.0 to 9.0)	1/135	0.68

PAO, parent artery occlusion.

Table 4 Patient characteristics—stent assisted coiling versus non-stent assisted coiling

	Stent assisted coiling		Non-stent assisted coiling		
	Meta-analysis (% (95% CI))	Raw numbers	Meta-analysis (% (95% CI))	Raw numbers	p Value
Complete/near complete occlusion at 3 months	56.0 (31.0 to 79.0)	37/76	45.0 (22.0 to 71.0)	59/109	0.56
Improvement in mass effect	44.0 (26.0 to 64.0)	13/28	75.0 (49.0 to 90.0)	61/75	0.06
Retreatment rate	22.0 (14.0 to 33.0)	15/74	20.0 (12.0 to 31.0)	21/152	0.80
Total periprocedural morbidity	0.0 (0.0 to 21.0)	0/74	4.0 (2.0 to 9.0)	1/152	0.68
Periprocedural stroke	0.0 (0.0 to 21.0)	0/74	0.0 (0.0 to 9.0)	0/152	0.56
Periprocedural hemorrhage	0.0 (0.0 to 21.0)	0/74	4.0 (2.0 to 9.0)	1/152	0.68
Periprocedural mortality	0.0 (0.0 to 18.0)	0/74	0.0 (0.0 to 9.0)	0/152	0.56

treatment for cavernous carotid aneurysms, Choulakian *et al* found a thromboembolic complication rate of 3.5% and a retreatment rate of 11.5%, similar to our study.[11]

These current findings are very important as in the past few years flow diversion has been proposed as the treatment of choice in patients with aneurysms of the cavernous carotid artery. Larger studies examining outcomes of flow diverter treatment of cavernous carotid aneurysms demonstrated complete occlusion rates of 70–100% and symptom improvement in upwards of 90% of patients.[12] However, flow diversion therapy is not devoid of important and often unpredictable complications, such as delayed aneurysm rupture and distal intraparenchymal hemorrhage. A meta-analysis performed by Brinjikji *et al* found procedure related morbidity and mortality rates of 5% and 4%, respectively, among all patients treated with flow diverters. Furthermore, they found an intraparenchymal hemorrhage rate of 3%, and a stroke rate of 6%.[13]

Complications are perhaps less acceptable in the case of intracavernous aneurysms which may present with symptoms of mass effect and cranial neuropathy but generally have a more benign natural history than intradural aneurysms. Placement of a flow diverter requires the ability to cross the aneurysm neck with the microcatheter and microguidewire, and this may be particularly difficult in patients with very large and giant dysplastic intracavernous aneurysms. Many of these patients are elderly with diseased and tortuous vessels, which may increase the difficulty of the distal navigation. One of the advantages of flow diversion is that, unlike PAO, it allows for preservation of the parent artery while also allowing for very high rates of complete occlusion at follow-up. Indeed, in an analysis of practice changes since the introduction of flow diverters, we have observed a significant reduction in the rate of PAO since flow diverters become available.[14] A potential shortcoming of PAO is the risk of developing aneurysms along the collateral pathways in relation to the increased hemodynamic stress.[15–17] This risk is theoretically higher in patients with intracavernous aneurysms as these patients often have dysplastic vessels and often already have mirror aneurysms on the contralateral carotid.[15–17]

Table 5 Outcomes of parent artery occlusion with extracranial to intracranial bypass

	Meta-analysis (% (95% CI))	Raw numbers
Complete/near complete occlusion at 3 months	93.0 (81.0 to 98.0)	40/41
Improvement in mass effect	87.0 (57.0 to 97.0)	30/33
Retreatment rate	8.0 (3.0 to 22.0)	1/41
Total periprocedural morbidity	11.0 (4.0 to 26.0)	3/41
Periprocedural stroke	11.0 (4.0 to 26.0)	2/41
Periprocedural hemorrhage	9.0 (3.0 to 24.0)	1/41
Periprocedural mortality	7.0 (2.0 to 19.0)	1/41

With advances in endovascular techniques, a number of operators have tried to avoid PAO because of the above mentioned limitations in favor of reconstructive techniques such as flow diversion and/or endosaccular coil embolization with or without stent or balloon assistance. Our review suggests that endosaccular coiling can be conducted with a low complication rate with a trend suggesting rates lower than with PAO without bypass. Shortcomings of endosaccular occlusion include the lower rate of complete occlusion compared with PAO and the high recurrence rate, as many of these aneurysms are very large or giant and with wide necks. PAO alone may compare favorably with flow diversion in terms of complete occlusion rates and complications but the complication rates are likely much higher if bypass is needed. In this respect, after a period of over enthusiasm with flow diverters for symptomatic and expanding cavernous sinus aneurysms, our group now considers the use of PAO without bypass, especially in elderly patients or in cases where placing a flow diverter across the aneurysm neck may be difficult.

Limitations

Our study has several limitations. As noted above, the cases are likely highly selected, and our systematic review does not provide information on the exact proportion of all cavernous carotid aneurysms amenable to endovascular treatment. The data on which the systematic review are based may be affected by publication bias. It is possible that studies with favorable results are more likely to be published. Moreover, the limitations of single center experiences for potential complication under reporting are well known. Many details were lacking from the studies included in our analysis. For example, data on aneurysm size and geometry were not available in many studies. Assessment of geometric characteristics of intracranial aneurysms is an important factor in treatment decisions, such as whether or not to use adjunctive devices. Many studies did not stratify outcomes by aneurysm size and patient presentation (SAH, CCF, unruptured, etc), however, a vast majority of the patients in this study presented with unruptured aneurysms. An equal proportion of patients presented with CCF and SAH in our analysis, which may seem unexpected in a series of cavernous carotid aneurysms. However, among series reporting the size of cavernous carotid aneurysms causing SAH, all aneurysms were large or giant.[11 18–20] Furthermore, in the International Study of Unruptured Intracranial Aneurysms, large and giant cavernous carotid aneurysms had a 3.0% and 6.4% risk of SAH, respectively.[21]

In addition, many of the series analyzed and reported in our analysis included cases collected over several years, and it is also possible that complication rates have improved as a result of increased operator experience and skill, and improved devices and technology. In general, many studies did not report why patients were treated with PAO versus coiling. However, most of the PAO patients included in our analysis were treated prior to the widespread utilization of endosaccular coiling. Factors such as personal preference and aneurysm size also contributed to the decision to perform PAO over coiling.[19] Among the studies included in this meta-analysis, the decision to perform bypass in addition to PAO was based on the results of carotid occlusion tests.[5 10 18–20] If the occlusion test revealed non-tolerance, patients generally received bypass or conservative therapy. If coil modifications and flow diverter techniques prove to be safe and effective in preventing recurrences, the results reported in this systematic review will likely improve over time.

The comparisons reported in this meta-analysis were made across studies, not within studies, which greatly weakens inference. Using the Grading of Recommendations, Assessment, Development and Evaluation framework, the quality of evidence (confidence in estimates) was very low because of imprecision, heterogeneity, and methodological limitations of the included studies.[22–24] Nevertheless, this meta-analysis provides useful data to share with patients and families when assessing the risks of treatment of cavernous carotid aneurysms, and represents a benchmark against which future studies, especially those on flow diverters, can be compared. With analysis of over 500 patients, this is currently the largest study examining outcomes of endovascular coiling of cavernous carotid aneurysms.

CONCLUSION

Carotid occlusion and endovascular coiling are both effective means for the treatment of cavernous carotid aneurysms. Non-comparative evidence suggests that endovascular carotid occlusion is associated with higher occlusion rates while endosaccular coiling is associated with slightly lower complication rates. Endovascular PAO paired with bypass is associated with high morbidity and mortality rates and should not be considered, except in select cases. Further research is needed to compare the efficacy of carotid occlusion, endosaccular coiling, and newer flow diverters in the treatment of cavernous carotid aneurysms.

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