

REVIEW

Management of Extracranial Carotid Artery Aneurysm

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WHAT THIS PAPER ADDS

This review provides an overview of the current scarce literature on treatment of extracranial carotid artery aneurysms (ECAAs). This review for the first time identifies a shortcoming of guidance for treatment of patients presenting with ECAA. There is a clear lack of knowledge on the natural course of these aneurysms. Specific essential details on etiology and aneurysm configuration, size, and volume are currently insufficiently available. Furthermore, defining treatment indications for both surgical and endovascular intervention is not possible due to the low quality of studies and confounding by indication. This review supports the need for an international multicenter registry to reveal the optimal treatment for ECAA.

Introduction: Aneurysms of the extracranial carotid artery (ECAA) are rare. Several treatments have been developed over the last 20 years, yet the preferred method to treat ECAA remains unknown. This paper is a review of all available literature on the risk of complications and long-term outcome after conservative or invasive treatment of patients with ECAA.

Methods: Reports on ECAA treatment until July 2014 were searched in PubMed and Embase using the key words aneurysm, carotid, extracranial, and therapy.

Results: A total of 281 articles were identified. Selected articles were case reports ($n = 179$) or case series ($n = 102$). Papers with fewer than 10 patients were excluded, resulting in the final selection of 39 articles covering a total of 1,239 patients. Treatment consisted of either conservative treatment in 11% of the cases or invasive treatment in 89% of the cases. Invasive treatment comprised surgery in 94%, endovascular approach in 5%, and a hybrid approach in 1% of the patients. The most common complication described after invasive therapy was cranial nerve damage, which occurred in 11.8% of patients after surgery. The 30 day mortality rate and stroke rate in conservatively treated patients was 4.67% and 6.67%, after surgery 1.91% and 5.16%. Information on confounders in the present study was incomplete. Therefore, adjustments to correct for confounding by indication could not be done.

Conclusions: This review summarizes the largest available series in the literature on ECAA management. The number of ECAAs reported in current literature is scarce. The early and long-term outcome of invasive treatment in ECAA is favorable; however, cranial nerve damage after surgery occurs frequently. Unfortunately, due to limitations in reporting of results and confounding by indication in the available literature, it was not possible to determine the optimal treatment strategy. There is a need for a multicenter international registry to reveal the optimal treatment for ECAA.

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INTRODUCTION

Invasive treatment for extracranial carotid artery aneurysms (ECAAs) pertains to only 0.6–3.8% of all extracranial carotid interventions,^{1–13} 0.6–2% of all carotid endarterectomies,^{3,5,7,10} and 0.4–2% of all extracranial arterial

aneurysm repairs.^{14–16} A substantial portion of the ECAAs will probably remain clinically silent. However, ECAAs may lead to neurologic symptoms including transient ischemic attacks (TIAs) or ischemic stroke.^{17–19} Other symptoms include pulsating mass and related cranial nerve dysfunction (CND). Information regarding the natural history, indications, and the best treatment in patients with ECAAs is scarce and guidelines are lacking. Both medical, surgical, and endovascular treatment of the aneurysm have been recommended.^{14,15,18,20} The best medical treatment comprises antithrombotic treatment and regular follow up and may have a place in the treatment of asymptomatic patients. Traditional surgical treatment, which is the current treatment of choice of symptomatic or growing ECAAs, consists of open resection of the entire aneurysm with or without arterial replacement with an interposition graft.^{14,20–22} However, this approach has been associated with the risk of stroke and cranial nerve damage.²³ Endovascular ECAA repair has only been described in small case series.²³

For a proper assessment about which treatment should be preferred, a better insight into natural history and risk of complications of the different treatments is needed. This paper is a review of all available literature on the risk of complications and long-term outcome after conservative or invasive treatment of patients with ECAA.

METHODS

Search strategy

In July 2014 a search was performed of all literature since 1900 in Medline (with Pubmed as interface) and Embase combining the following search terms: aneurysm, carotid, extracranial, therapy (and all synonyms for all treatment options). The search was performed according to the search strategy and data collection guidelines of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) Group.²⁴

Definition of ECAA

Because no generally accepted definition of ECAA exists, all aneurysms defined as such by the authors of the parent paper, regardless of the definitions used, located in the internal carotid artery (ICA) or in the common carotid artery (CCA) were included. Only aneurysms located between the CCA origin at the aortic arch and base of the skull were included.

Selection of studies

Retrieved records were independently screened by two authors (J.W., G.B.) on title, abstract, and full text. All discrepancies (3%) were discussed until final agreement was reached. If necessary, a third opinion could be obtained, but agreement between authors was reached in all papers. Inclusion criteria were (a) adult patients with an ECAA; (b) description of the type of intervention (conservative treatment, surgery, endovascular treatment, or any combination); (c) report of data on outcome during follow up (case

fatality, fatal or non-fatal stroke, or local cervical symptoms); and (d) series describing 10 patients or more.

Language of publications was restricted to Dutch and English. Studies regarding aneurysms located at the level of the skull base or above, aneurysms located in the external carotid artery (ECA), non-human data, and unavailable full text papers were excluded. Studies presenting data at a group level containing the ECA were included because of the low number of ECAs in these series and the relevance to present these large series.^{12,19,25–27} The reference list of all selected articles was hand searched to retrieve additional studies. Selected studies were critically appraised based on study design, study quality, consistency, and directness using the GRADE system.²⁸ Subsequently, the level of evidence of the studies was graded by one author (J.W.). The level was graded high, moderate, low, or very low.

Data extraction

Three authors (J.W., B.N., G.B.) independently extracted data by means of predefined parameters. Individual patient data were obtained when available. The following data were retrieved: publication year, country of origin, number of patients, study design, patient characteristics (age, gender, history of smoking, diabetes, hypertension, and hyperlipidemia), aneurysm characteristics (affected vessel, exact location, aneurysm shape, affected side, and aneurysm size), etiology, and detailed method of treatment.

Outcome measurements included case fatality, stroke, and local cervical symptoms. Local cervical symptoms are defined as any symptom, most likely related to the aneurysm, in the cervical region on the ipsilateral side of the aneurysm. Local cervical symptoms were scored as reported by authors. Furthermore, any neurological deficit with an acute onset persisting for at least 24 hours for which no other cause could be found was considered a stroke. Early complications included all events that occurred within 30 days after intervention, or after detection of the ECAA in patients who received conservative treatment. Late outcome consisted of death from any cause and any stroke that occurred after at least 30 days.

Statistical analyses

A pooled or summary estimate of the risk of all cause mortality and of all and non-fatal strokes across all studies was calculated together with a 95% confidence interval using a random effects model. The heterogeneity in results among studies was evaluated by I^2 statistics and by prediction intervals. A 95% prediction interval shows the likely range of values for the risks than can be expected if a new and large study would be performed similar to those included in this review. The prediction interval provides insight into the variability or consistency between the results of individual studies whereas a 95% confidence interval around the pooled estimates provides insight into how certain we are about the significance of the pooled estimate. The amount of between study variation (tau-squared value of a random effects model) is a key factor

determining the width of a 95% prediction interval: large values of between study variation will result in a large prediction interval, even if a large number of studies is included in a review.²⁹

RESULTS

After removing duplicates, the search identified 3,711 articles (Fig. 1). Following screening of title, abstract, and full text, 278 articles were selected. Hand searching the reference lists of selected articles revealed three more articles, resulting in a final selection of 281 articles. Selected articles were case reports ($n = 179$) or case series ($n = 102$). Exclusion of papers with fewer than 10 patients resulted in the final selection of 39 articles on a total of 1,239 patients (a complete list of all included articles can be found in the Appendix I).^{1-4, 6-8,11,12,14-16,18,19,25-27,30-51} The level of evidence from 23 studies was graded low and 16 records very low.

Patient and aneurysm characteristics

At presentation, 1,150 aneurysms (87%) were symptomatic, 476 (36%) presented with cerebral ischemia (120 strokes,

291 TIAs, and in 56 patients cerebral ischemia was not further specified). Other symptoms at presentation were a cervical mass, a hematoma or rupture, pain or CND (Table 1, Fig. 2).

Aneurysm size was defined, by only two reports, as a localized increase of the caliber in the carotid artery of more than 50% compared to reference values or to the expected vessel diameter.^{2,8}

The main cause of the ECAA was atherosclerotic disease, followed by trauma, but for 275 aneurysms (21%) no specific cause was given (Table 1, Fig. 2). Most aneurysms, 608 (46%), were located in the ICA (Table 1, Fig. 2). Since information on aneurysm shape was missing in over 50% of cases this item was not reported in this paper.

Treatment

A minority of aneurysms, 145 (11%), was treated without an invasive intervention (Table 2). Invasive treatment consisted of surgery in 1,102 (94%) aneurysms, endovascular treatment in 57 (5%) aneurysms, or a combined approach in 18 (1%) (Table 2).

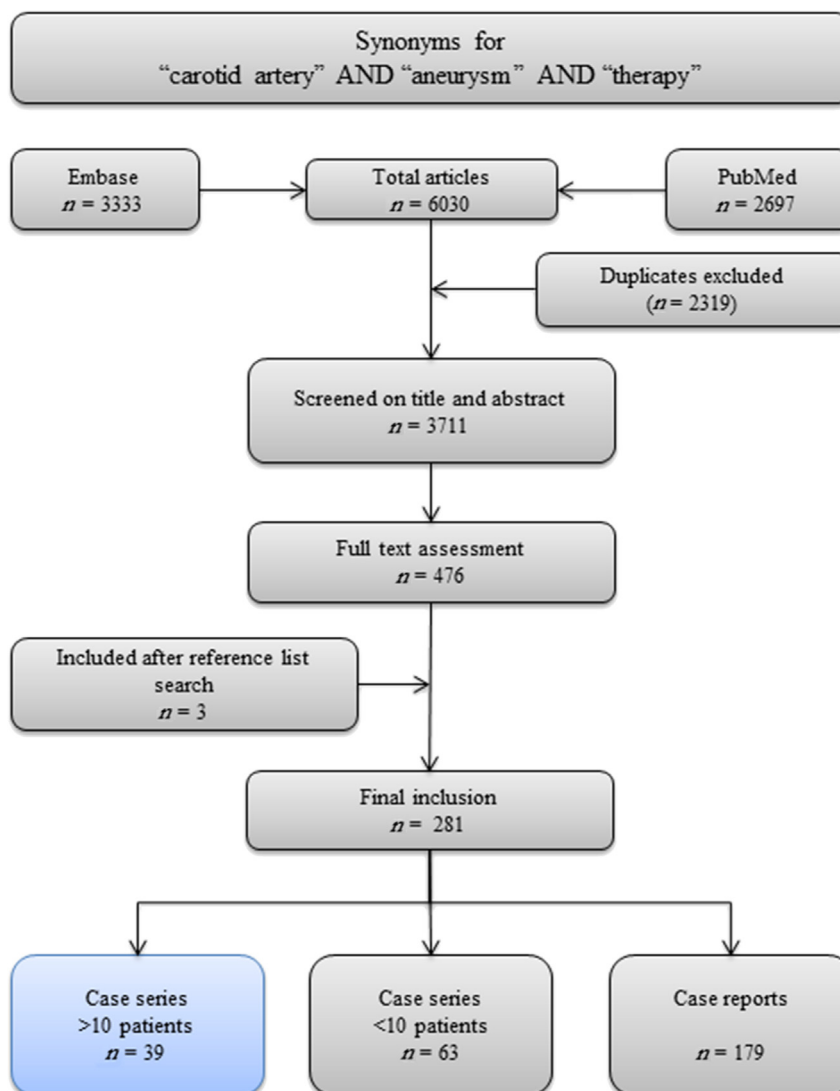


Figure 1. Literature search flow chart.

Table 1. Aneurysm characteristics.

Variables	N	(%)
Reports included	39	
Patients	1239	
Aneurysms	1322	
Etiology		
Atherosclerosis	509	38
Traumatic	144	11
Mycotic	65	5
Other	329	25
Not reported	275	21
Symptoms^a		
Cerebral ischemia	476	36
Mass	442	33
Asymptomatic	172	13
Compression	119	9
Local pain	39	3
Other	185	14
Location		
ICA	608	46
Bifurcation	261	20
CCA	108	8
ECA	9	1
Not reported	336	25

Note. Other etiology includes granulomatous diseases, connective tissue disorders, iatrogenic aneurysms, post carotid endarterectomy cystic medial necrosis, and arteritis. ICA = internal carotid artery; CCA = common carotid artery; ECA = external carotid artery.

^a Some patients experienced multiple symptoms from one aneurysm.

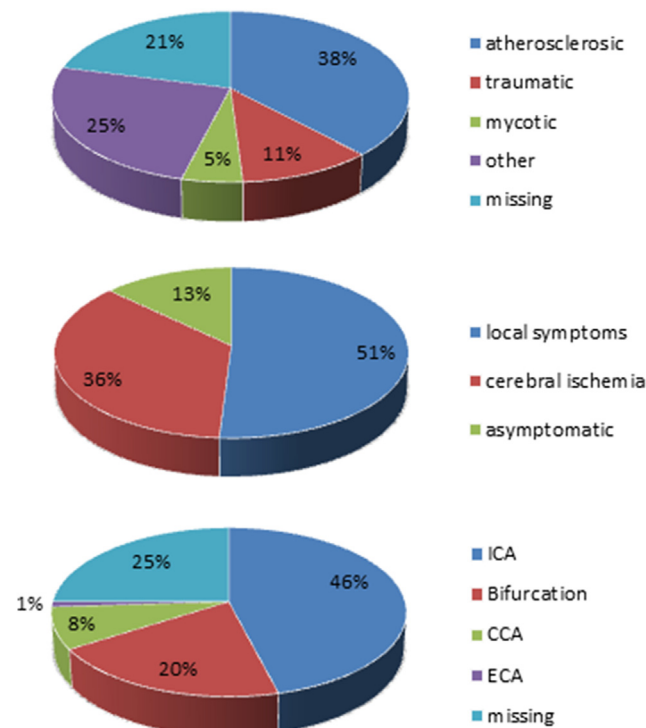


Figure 2. Symptoms at presentation, etiology and location of the extracranial carotid artery aneurysms. ICA = internal carotid artery; CCA = common carotid artery; ECA = external carotid artery.

Table 2. Treatment details.

	Intervention	n
Conservative therapy	Anticoagulant therapy	24
	No therapy	6
	Medical management n.s.	2
	Antiplatelet therapy	1
Endovascular treatment	Conservative therapy n.s.	112
	Stent placement	22
	Balloon exclusion ^a	9
	Stent placement with coil embolization	6
	Embolization	1
	Endovascular n.s.	19
Surgery	Resection with interposition graft	376
	Resection with direct anastomosis	264
	Partial resection with reconstruction	107
	Ligation	61
	Aneurysmorrhaphy	34
	ECA to ICA transposition	11
	Bypass	39
	Surgery n.s.	210
Combined approach	Combined approach n.s.	16
	ECIC bypass with balloon occlusion ^a	2

n.s. = not specified; ECA = extracranial carotid artery; ICA = internal carotid artery; ECIC = extracranial—intracranial.

^a In this procedure a balloon is placed (and left behind) in the aneurysm or parent vessel. Balloon occlusion may also be accompanied with concomitant ECIC bypass.

Early outcome

In total 24 (2.05%, 95% CI 1.14–3.57) patients died, of whom 13 had a stroke (5.04%, 95% CI 3.81–6.62), and 34 (3.05%, 95% CI 1.97–4.70) had a non-fatal stroke within 30 days (Table 3). The pooled estimate of the risk of all cause mortality and of all and non-fatal strokes across all studies describing conservative and surgical treatment are reported in Table 3. The pooled estimates could not be calculated for the endovascular and combined approach due to low study numbers. CND occurred in 110 (12%) patients after surgery and was never reported after endovascular treatment or combined surgical and endovascular treatment.

Long-term outcome

Follow up duration was most often presented as a mean follow up of the study population and patients lost to follow up was not reported in the majority. Therefore, it is not possible to present the number of patients available for follow up or the exact duration. During follow up 81 patients died, of whom eight had a fatal stroke, and 11 had a non-fatal stroke. Most deaths (n = 68, 83%) were reported as not aneurysm related.

Confounding by indication

An important issue considered in the evaluation of which treatment option is superior using observational data is confounding by indication. Patients with certain characteristics

Table 3. Treatment outcome.

	<i>n</i>	30 day mortality, % (95% CI)	30 day stroke, % (95% CI)	30 day non-fatal stroke, % (95% CI)
Conservative	39	4.67 (0.60–28.42)	6.67 (2.17–18.73)	2.22 (0.31–14.16)
Surgery	934	1.91 (1.01–3.57)	5.16 (3.94–6.73)	4.15 (3.07–5.59)
Overall	988	2.05% (1.14–3.63)	5.04 (3.81–6.62)	3.05 (1.97–4.70)

The data of the following articles was not included in this analysis because the data could not be split for the different interventions: Higashida et al.,³⁸ Aleksic et al.,³⁰ De Jong et al.,³⁵ McCollum et al.,¹⁵ Padayachy and Robbs,⁴¹ Frankhauser et al.²⁷

receive a certain treatment, but these specific characteristics could be associated with a worse or beneficial outcome. For correcting confounding by indication, completeness of potential confounders is needed. However, information on confounders in the present study is far from complete and could not be retrieved from the papers. Therefore, adjustments could not be made and therefore, no valid comparison of outcome for the four different treatments was possible.

DISCUSSION

ECAAs are rare, leading to retrieval of only 39 case series containing 10 or more patients. Early mortality and number of strokes is low in surgical and endovascular treatment. Furthermore, the long-term follow up demonstrates low stroke numbers in both intervention groups, which supports the assumption that invasive treatment could prevent stroke. These findings are in line with other publications.^{2,14,23} The high CND in surgically treated patients is probably related to the distal location of aneurysms in the ICA and to the extensive dissection needed to perform complete aneurysm resection. The available information on ECAA treatment in the literature suffers greatly because of its rarity, from small case series, missing data, publication bias, and confounding by indication. Furthermore, the level of evidence in the available literature is low to very low; therefore, any estimate of effect based on these records is very uncertain. Therefore, no evidence based recommendation can be given for an individual patient with an ECAA.

The natural course of ECAs is still hardly understood. Since knowledge of the natural course is required to balance the benefit of any type of intervention, thus far no treatment guideline or expert consensus for the management of ECAA has been developed. Probably, the main goal in the management of ECAs is to prevent thrombo-embolic complications of the aneurysm. In aneurysms in other vascular territories, size is often used as an indication for intervention. Aneurysm size may probably be most related to aneurysm rupture. However, rupture is considered very unusual in ECAs, and most surgeons may only intervene in patients with thrombo-embolic symptoms or proven progressive ECAA growth.

Medical therapy in ECAs, including medication choice, remains unexplored and needs to be further investigated. However, ECAs can occur after dissection in the carotid artery or in patients with generalized atherosclerotic disease. In these diseases, medical therapy has long been used and is scientifically substantiated. Following the medical treatment guidelines for the most probable underlying disease is recommended until more evidence is available regarding medical treatment in ECAA patients.

Operative therapy has been advocated for any ECAA because of the high mortality risk in non-operated cases.^{15,18,20,22} Nowadays, small case series advocating an endovascular approach to treat ECAA have reported favorable procedural results but with a limited number of cases and no mid- or long-term follow up.^{23,52} Endovascular treatment with a stent may be the most favored option of the invasive treatments, mainly because of a high prevalence of CND associated with surgical treatment.

Although the approach of this study allowed presentation of early and late outcomes of ECAA treatment, the present study has several limitations. First of all, no randomized controlled trials have been published on ECAA treatment, and data for the present analysis were obtained from case series only. Inherently, the assessment was limited to information provided in these articles resulting in a high rate of missing data. The reported rates for neurological complications may be biased because none of the studies performed independent and structured confirmation of these events. Furthermore, publication bias may have occurred while case series regularly present only striking and/or invasively treated cases. Another disadvantage is that physicians may tend to publish successful rather than unsuccessful cases. However, by excluding small case series the risk of publication bias was reduced. Because of this publication bias, the results of this study may not be generalizable to the ECAA population. In addition, since this was an observational study, the baseline characteristics of the patients undergoing different treatments were not completely identical. In this study there was confounding by indication because treatment choice was based on patient and aneurysm characteristics. Some of these characteristics may give rise to a different prognosis. Unfortunately, due to incomplete data and low patient numbers, this confounding by indication could not be corrected and comparison between treatment outcomes for the different treatment groups was not possible. Because in 31 of 39 studies the data were presented at a group level, performing any sub-analyses was not possible.

The present study does represent the largest evaluation of treatment in patients with an ECAA. This review for the first time clearly shows the lack of knowledge on the natural course of ECAs, and the fact that population based reporting makes it impossible to perform an individualized patient data analysis. To gain more accurate information regarding the prognosis and results of both conservatively and invasively treated ECAs more research is needed. Initiating a randomized controlled trial is not feasible because of the low incidence of ECAs and the low case fatality rates, but more knowledge regarding natural history and treatment indications might be obtained from a well

designed prospective study. Consequently, the authors have designed a prospective web-based international registry to collect data on ECAA (www.carotidaneurysmregistry.com).⁵³

CONCLUSION

This review summarizes the largest available series in the literature on ECAA treatment. The few data consist of a mix of conservative, open surgical, and a growing number of endovascular interventions. There is no consensus in ECAA treatment. The early and long-term outcome of invasive treatment in ECAA is favorable; however, cranial nerve damage after surgery occurs frequently. This review supports the need for an international multicenter registry to reveal the optimal treatment for ECAA.

CONFLICT OF INTEREST

None.

FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.ejvs.2015.05.002>

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