### **REVIEW**

## Antithrombotic Treatment for Acute Extracranial Carotid Artery Dissections: A Meta-Analysis

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#### WHAT THIS PAPER ADDS

The article summarises a meta-analysis of antithrombotic treatment for extra cranial carotid artery dissections and concludes that there is no clear evidence for one type of treatment over another. In short, medical treatment lies at the discretion of the treating surgeon.

**Introduction:** Carotid artery dissection is a leading cause of stroke in younger patients, with an associated prevalence of 2.6–3.0 per 100,000 population. This meta-analysis aims to determine whether in patients managed medically, treatment with anticoagulants or antiplatelet agents was associated with a better outcome with respect to mortality, ischaemic stroke, and major bleeding episodes.

Patients and methods: A comprehensive search strategy was employed of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (January 1966 to March 2015), and EMBASE (January 1980 to March 2015) databases. Primary outcomes were death (all causes) or disability. Secondary outcomes were ischaemic stroke, symptomatic intracranial haemorrhage, and major extracranial haemorrhage during the reported follow-up period.

**Results:** No completed randomized trials were found. Comparing antiplatelets with anticoagulants across 38 studies (1,398 patients), there were no significant differences in the odds of death (effects size, ES, -0.007, p = .871), nor in the death and disability comparison or across any secondary outcomes.

**Conclusion:** There were no randomised trials comparing either anticoagulants or antiplatelets with control, thus there is no level 1 evidence to support their routine use for the treatment of carotid artery dissection. Also, there were no randomised trials that directly compared anticoagulants with antiplatelet drugs, and the reported non-randomised studies did not show any evidence of a significant difference between the two.

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#### **INTRODUCTION**

The incidence of carotid artery dissection (CAD) is quoted as 2.6-3.0 per 100,000 population,<sup>1</sup> although the true incidence may be higher as many remain undiagnosed.<sup>2</sup> CAD is the most common cause of stroke in males under 45 years of age,<sup>3</sup> and has an associated mortality of

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up to 5% with a full resolution occurring in excess of 90% of cases.<sup>4</sup> CAD is associated with trauma, aneurysm, hypertension, and atherosclerosis.<sup>5</sup> Presentation can vary from incidental findings of asymptomatic disease to cerebrovascular events, regional pain, and Horner's syndrome.

Although recent developments in noninvasive imaging have led to more frequent diagnoses, there is no consensus or high-level evidence on optimal management. Management strategies are aimed predominantly at limiting progression of dissection, preventing thromboembolic complications and maintaining cerebral perfusion.<sup>1</sup> The majority of patients are managed by antithrombotic treatment through anticoagulation or antiplatelet therapy,

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although endovascular intervention or surgery may be considered on an individualised basis.  $^{1}$ 

The aim of this study is to compare anticoagulation and antiplatelet treatment outcomes including death, ischaemic stroke, and intra- and extra-cranial haemorrhage in patients with extracranial carotid artery dissection using metaanalysis techniques.

#### **METHODS**

An electronic search was undertaken using the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (January 1966 to March 2015), and EMBASE (January 1980 to March 2015) databases. The search employed the term(s) "Carotid dissection," which was combined with each of the following Boolean operators: "antiplatelet," "anticoagulation," "extracranial." Abstracts of the citations identified by the search were then scrutinised by two authors to determine eligibility for inclusion in the analysis (MC, CS). The Cochrane Stroke Group Trials Register was also searched for relevant studies. Comprehensive searches were carried out and relevant papers were also interrogated for additional eligible studies including recent review papers. The search method adhered to the PRISMA statement for reporting systematic reviews (Fig. 1).<sup>6</sup> Outcome measures identified included death from all cause, death and disability, ischaemic strokes, symptomatic intracranial haemorrhage, and major extracranial haemorrhage.

All forms of trials and studies including at least 10 patients with carotid artery dissection that allowed comparisons between antiplatelet therapy and anticoagulation for the treatment of CAD were deemed eligible for inclusion. Any study analysing only one form of antithrombotic therapy was excluded. Further exclusion criteria included studies involving less than 10 patients, review articles, duplicate data (only the most recent series was included), and studies where no division was made between carotid and vertebral artery dissections. Patients with severe infarction (defined in line with the Modified Rankin Scale as severe disability, requiring constant nursing care and attention, bedridden, incontinent) or with significant comorbidity that were not given any antithrombotic therapy were also excluded from the analysis. Data were collected by two authors (MC, CS) and the quality of the nonrandomised studies was assessed using the Newcastle-Ottawa Scale (NOS) (Fig. 2). The NOS is primarily formulated by a point allocation system, assigning a maximum of nine points for the risk of bias in three areas: (i) selection of study groups (four points), (ii) comparability of groups (two points), and (iii) outcomes and/or exposure for cohort studies and case-control studies (two points). Studies looking at surgical intervention were not included in the analysis, because of a lack of substantial data.

Information was sought regarding diagnosis, clinical presentation, and diagnostic findings. All studies that



Figure 1. Study selection.

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