

# Recanalization after Extracranial Dissection: Effect of Antiplatelet Compared with Anticoagulant Therapy

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**Background:** Cervical arterial dissection is a leading cause of stroke in young patients, yet optimal management remains controversial. Existing studies focusing on recurrent stroke were underpowered to demonstrate differences between antithrombotic strategies. Vessel recanalization is a more prevalent outcome and is potentially clinically important. We aimed to assess recanalization rates with anticoagulation compared with antiplatelet therapy. **Methods:** We studied a single-center retrospective cohort of patients with extracranial carotid or vertebral artery dissection. Subjects with baseline and follow-up imaging between 1999 and 2013 were included. Stenosis was measured using North American Symptomatic Carotid Endarterectomy Trial methodology. Univariate and multivariable analyses were performed to determine factors associated with recanalization, defined as  $\geq 50\%$  relative improvement in stenosis from baseline to follow-up imaging. Secondary analyses assessed absolute and relative stenosis change and limited the cohort to  $>50\%$  stenosis at diagnosis. **Results:** We identified 75 patients with 84 dissections, mean age 47 years, 43% female, 39% non-white. Patients treated with anticoagulation had worse stenosis at baseline (median 99% versus 50%,  $P = .02$ ). Comparing anticoagulation with antiplatelet therapy in the first month, there were no differences in the rates of  $\geq 50\%$  relative improvement in stenosis (50% versus 48%,  $P = .84$ ) nor in absolute (median 16% versus 7%,  $P = .34$ ) or relative (median 48% versus 43%,  $P = .92$ ) change in stenosis from baseline to follow-up. In multivariable analysis, anticoagulation was not associated with recanalization (odds ratio [OR] 1.41, 95% confidence interval [CI]: .5-4.1,  $P = .52$ ), whereas hypertension was negatively associated (OR .26, 95% CI: .09-.72,  $P = .009$ ). **Conclusions:** Anticoagulation was not associated with greater likelihood of recanalization compared with antiplatelet medication therapy. **Key Words:** Dissection—antiplatelet—anticoagulation—stroke.

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## Introduction

Extracranial cervical arterial dissection is a leading cause of ischemic stroke in young patients, although optimal medical management for stroke prevention has been controversial.<sup>1,2</sup> The dissection site is highly thrombogenic, which can lead to in situ stenosis, occlusion, or thromboembolism. For stroke prevention, the current American Heart Association guidelines suggest treatment with either antiplatelet therapy or anticoagulation for at least 3-6 months.<sup>3-5</sup> In previous studies of patients with

dissection and stroke or transient ischemic attack (TIA) at presentation, recurrent strokes have been relatively infrequent.<sup>3,6-8</sup> As a result, these studies have been underpowered to demonstrate statistical differences between treatments, leaving the question of optimal medical management largely unanswered.

The Cervical Artery Dissection in Stroke Study (CADISS) study was the first randomized controlled, prospective trial that compared antiplatelet and anticoagulation treatment.<sup>6</sup> Of the 250 patients enrolled, only 4 (2%) had recurrent strokes; 3 in the antiplatelet treatment arm and 1 in the anticoagulation treatment arm ( $P = .63$ ). Notably, a power calculation suggested that it would require a sample size of ~10,000 patients to identify a difference in stroke outcomes. Given that CADISS was a large multicenter study and required 7 years to complete enrollment of 250 patients, a definitive clinical trial with appropriate power to detect differences in recurrent stroke is likely not feasible.

In addition to stroke risk, vessel recanalization is also a potentially important outcome. It is self-evident that having a patent and non-stenosed vessel is preferred over an occluded or highly stenosed artery, particularly given the long-term potential for any particular patient to subsequently develop atherosclerotic stenosis. Fortunately, recanalization is common after acute cervicocephalic dissection, with previous studies reporting recanalization in 30%-70% of cases.<sup>9-11</sup> As a result, vessel recanalization is an important surrogate end point that provides greater sensitivity to determine the efficacy of differing medical treatments. The aim of this study was to identify patients with acute extracranial carotid or vertebral dissections and to compare rates of recanalization on subsequent imaging between patients on anticoagulation and those on antiplatelet therapy, and to identify factors independently associated with vessel recanalization. We hypothesized that anticoagulation would be associated with a higher likelihood of recanalization.

## Methods

### *Study Design and Participants*

We conducted a single-center retrospective cohort study of patients with acute extracranial carotid or vertebral artery dissection at the Hospital of the University of Pennsylvania between January 1, 1999 and December 31, 2013. Patients were included if they were over 18 years of age and had evidence of acute carotid or vertebral artery dissection on dedicated neurovascular imaging within the first 2 weeks of symptom onset. Patients were excluded if they exclusively had intracranial dissection, if they did not obtain any follow-up vascular imaging, or if patients were managed non-pharmacologically (e.g., stent placement). Local institutional review board approval was obtained before initiation of study activities.

Patients were identified using the Penn Data Store, an internal web-based search application that incorporates data from inpatient and outpatient visits as well as radiology results, using the search terms "carotid dissection," "vertebral dissection," "evidence of dissection," "extracranial dissection," "arterial dissection," "artery dissection," and "[carotid dissection] or [vertebral dissection] not [no evidence of dissection]." The medical records, including inpatient admission and discharge records, daily inpatient progress notes, and outpatient documentation, were then reviewed for all patients to identify those who met inclusion/exclusion criteria. The following information was obtained for each included patient: age, sex, race, medical history (hypertension, hyperlipidemia, history of prior dissection, peripheral vascular disease, cerebral aneurysms, prior stroke or TIA, diabetes, atrial fibrillation), social history (tobacco, alcohol, or drug use), and home medications (statins, antiplatelet medications, anticoagulants); the location of the dissected vessel; etiology of dissection (prior trauma, iatrogenic); evidence of cerebrovascular infarct on imaging; date and type of baseline and follow-up imaging (computed tomography angiography, magnetic resonance angiography, or conventional cerebral angiography); medical management initiated (antiplatelet, anticoagulation, dual therapy, etc.) and continued through 1 week, 1 month, and 3 months; treatment side effects including bleeding; and recurrent strokes.

### *Vessel Measurements*

The degree of stenosis on both initial and follow-up imaging was independently calculated manually by 2 of the authors (P.R. and A.B.) using the North American Symptomatic Carotid Endarterectomy Trial methodology, which has been used in studies of vertebral artery stenosis as well.<sup>12,13</sup> Luminal diameters were measured at 2 points: (1) at the narrowest point within the dissection and (2) at a distal point where the vessel appeared normal. The diameter at the stenotic segment was divided by the diameter at the normal segment, and subtracted from 1, to obtain a percent stenosis. If there was discrepancy between the readers of >20%, vessels were re-read together to reach a consensus. The stenosis on follow-up was subtracted from the stenosis on acute imaging to obtain an absolute percent change, and then divided by the acute stenosis to determine the relative percent change. Measurements were performed without knowledge of clinical information, including antithrombotic therapy given to the subject.

### *Treatment*

The primary analysis compared patients who were treated with anticoagulation for the majority of the first month (i.e., greater than 2 weeks) after diagnosis with those who were not. Patients who received no treatment or treatment with either single or dual antiplatelet therapy alone for greater than 50% of the first month after

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