Anticoagulant therapy has been advocated consistently as the treatment of choice for cervical arterial dissection in numerous published studies and reviews, but there is little evidence-based data to justify this assumption. Although dissection of the cervical arteries has long been established as a cause of ischemic and hemorrhagic stroke, the major obstacle to planning therapeutic studies has been the perception that this is a relatively rare phenomenon. However, rapid developments in accurate noninvasive imaging have shown cervical arterial dissection as a common, if not the most common, cause of ischemic stroke in persons <50 years of age. This has raised for the first time the realistic concept of a therapeutic trial of anticoagulants versus antiplatelet treatment. A recent Cochrane review cited a figure of 1000 patients in each therapeutic arm, and similar figures were calculated from the only prospective study published to date.

Arterial dissection can theoretically cause ischemic stroke either by embolism from the site of the intimal tear, or hemodynamically from luminal obstruction. Available evidence strongly favors artery-to-artery embolism as the most common cause, and the pattern of cerebral infarction in stroke from dissection is typical of that seen in other types of cerebral embolism. Even more interesting, microemboli have not only been detected by transcranial Doppler in acute cervical arterial dissections, but they also correlate with the presence of stroke in patients with traumatic and "spontaneous" dissections.

All these factors intuitively favor the use of anticoagulant therapy, at least in the immediate poststroke phase, to minimize distal embolism from the site of the tear, but accumulating data of the underlying pathology of dissection indicate that its mechanics are more complex than previously believed. Carotid endarterectomy in patients with acute dissection may reveal previously healed asymptomatic dissections in the same vessel. Also, neurovascular imaging sometimes shows silent redissection in the same cervical artery in patients receiving anticoagulants for previous dissection, raising the possibility that these drugs encourage further dissection of the vessel wall, though most observers believe this is a rare event and should not discourage anticoagulant therapy.

However, these findings do raise another caveat for the use of heparin or warfarin in acute dissection; the occurrence of unsuspected subarachnoid hemorrhage from intracranial involvement, which is probably much more frequent than generally believed. Dissections may track silently along the course of the extracranial part of the cervical artery, only to declare themselves as subarachnoid hemorrhage when they arrive at the intracranial portion. The structure of the intracranial cervical vessels differs from that of the extracranial arteries. Once they pierce the dura, there is anatomical attenuation and weakening of the media, which facilitates rupture of the vessel wall, allowing blood to track right through to the subadventitia, and so into the subarachnoid space. Clearly, when there is the slightest doubt, lumbar puncture should be performed to exclude dissection before administering anticoagulant therapy, especially in patients where headache is a major symptom.

In spite of these reservations, most neurologists use anticoagulants as the first line of treatment in acute cervical arterial dissection. In a recent nationwide survey of Canadian neurologists, anticoagulant therapy was the treatment of choice for 81% of physicians, though admittedly on empirical grounds only. The usual regimen is to follow immediate heparin therapy with longer-term warfarin for 3 months and then decide on further management depending on vascular imaging. Enhanced magnetic resonance angiography is now almost as accurate as catheter angiography, but without the complications of the invasive procedure, and computerized tomographic angiography is proving even better. Angiography should be performed urgently because imaging abnormalities are often very transient. Doppler ultrasound is in general disappointing, even for screening purposes, because although it is sensitive to flow changes, it has limited anatomical range in the neck and limited ability to show minor but critical damage to the vessel wall, such as intimal flaps, minor wall irregularities, or “false” aneurysms.

In the presence of these structural abnormalities, it is customary to continue anticoagulant therapy for another 3
months even in the absence of symptoms, but if the vessel has returned to normal, as in most cases, aspirin treatment is usually given for another 3 months. In the internal carotid artery, dissections occur 1 to 2 cm more distally to the bulb than in atherosclerosis, where the wall changes from an elastic to a muscular structure, which is an ideal location for stenting should symptoms continue in spite of adequate anticoagulation.10

All these uncertainties would be dispelled if a randomized controlled trial could be undertaken. Two separate and independent studies have arrived at similar numbers for such a trial, involving a total of \( \approx 2000 \) patients.2,3 This number would be large but not unwieldy using present information technology. The time for this trial has arrived.

References


KEY WORDS: treatment

Extracranial Arterial Dissection
Anticoagulation Is the Treatment of Choice: Against

P.A. Lyrer, MD

Carotid artery dissection (CAD) was first recognized as a cause of ischemic stroke in the mid-1950s, although there were pathological reports on the condition dating from 1872.2 The incidence of extracranial internal CAD is \( \approx 2 \) to 3 per 100,000 per year.3 For extracranial vertebral artery dissection (VAD), community-based epidemiological data are not available. Data from hospital-based case series show the extracranial VAD incidence to be estimated \( \approx 1 \) to 1.5 per 100,000 per year.3 The recurrence rate of stroke in CAD is estimated to be \( < 1\% \) per year.4

The pathogenesis of ischemic strokes in CAD is still a matter of debate. Former studies showed a high frequency of angiographic findings suggesting embolism with cerebral arterial branch occlusions in \( \approx 15\% \), and cases with free-floating intraarterial thrombi were occasionally reported. Recently, transcranial doppler monitoring studies revealed microembolic signals downstream of the dissected arteries.6 In extracranial internal CAD, high-intensity transient signals suggesting embolism were detected in the middle cerebral artery in up to 60% of cases. Together with brain imaging features of stroke lesions, one may assume that extracranial arterial dissections cause embolic stroke. However, most data are based on small, presumably highly selected case series. Hence, from these impressions many authors suggested that immediate anticoagulation may be the right thing to do.7

Although CAD has been known to cause ischemic stroke for almost 50 years, at present no data based on randomized controlled trials are available.8 But there are arguments against routine anticoagulation. First: extracranial CAD is caused by intramural arterial bleeding. At least theoretically, anticoagulation may promote enlargement of the mural bleed. This may lead to worsening of the hemodynamic condition. It may also cause intracranial bleeding, mostly feared in cases with VAD. In extracranial VAD, there are single case reports about subarachnoid hemorrhage as the presenting feature in which any antithrombotic treatment, and particularly anticoagulation, is considered deleterious. Delayed occlusion of the internal carotid artery during heparin therapy have recently been reported in 5 of 20 patients with extracranial internal CAD. Thus, the likelihood for delayed ICA occlusion seems to increase with higher degrees of anticoagulation.9 Second: recurrent stroke does not very often occur in CAD and no data are available for VAD. The magnitude of the potential therapeutic benefit of anticoagulation in reducing the occurrence of ischemic strokes may be very limited and moreover may be counteracted by bleeding complications. Third: at least some strokes may be due to hemodynamic impairment, rather than thromboembolism, especially when collaterals from the circle of Willis are lacking.9 Stroke occurrence or recurrence was reported in extracranial internal CAD patients.
treated with antiplatelets as well as in patients with sufficient anticoagulation, indicating that protection even with anti-coagulation—not surprisingly—is not absolute. For other stroke pathogeneses it was shown by means of a systematic meta-analysis that immediate anticoagulant therapy in patients with acute ischemic stroke is not associated with net short- or long-term benefit. Forth: a recent Cochrane meta-analysis targeting the effect of antithrombotic drugs for extracranial internal CAD did not show any data from controlled trials. Further anticoagulants were not superior for primary outcomes, such as death or dependency. Twenty-six studies including 327 patients (who either received antiplatelets or anticoagulants) were eligible. Two of 109 patients (1.8%) treated with antiplatelets were reported dead, and 4 of 218 (1.8%) treated with anticoagulants were reported dead. The weighted estimates across studies showed that the likelihood of death within the follow-up period does not differ between both treatment groups as indicated by a Peto odds ratio of 1.59, with a 95% confidence interval of 0.22 to 11.59.

To conclude, there is no evidence from any controlled data that anticoagulation for extracranial internal CAD might be helpful. It could be that, in a subset of patients with proven embolism, immediate anticoagulation may protect from first or recurrent strokes. But this has not been shown yet. Furthermore, there is even less data for VAD. As there are safety concerns and the benefit–risk ratio is not established, patients with CAD are unlikely to be harmed by antiplatelets, and there seems little justification for giving anticoagulants as a first line therapy in all patients. Therefore it is more appropriate not to recommend anticoagulation on a routine basis for CAD or VAD.

As a consequence, a large randomized controlled trial comparing anticoagulants with antiplatelets is desirable and ethically justified. Its protocol should include a stringent definition of carotid dissection, a standardized diagnostic protocol, strictly random allocation to different types of antithrombotic treatment, as well as accurate and unbiased assessment of outcome.

References


Key Word: treatment

Extracranial Arterial Dissection
Anticoagulation Is the Treatment of Choice

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One of the most frustrating experiences we have as stroke clinicians is the lack of high level evidence for the management of patients with symptomatic and asymptomatic extracranial arterial dissection. Interestingly, this has become even more pressing since the introduction of magnetic resonance angiography (MRA) and computerized tomography angiography (CTA), where we are more frequently identifying dissections, typically in young adults and often with minimal symptoms. Moreover, with increased vascular screening of patients presenting with head and neck trauma, or postchiropractic manipulation, even the numbers currently detected may be the tip of the iceberg. Indeed, in 1978, Fisher et al stated that “spontaneous dissection is more common than the literature indicates.” What do we do in these circumstances and how should the dilemma be resolved?

Given the absence of a definitive clinical trial, it seems reasonable to use a pathophysiological basis for the decision-making process. Both our protagonists have presented very
adequate evidence that there is usually a thromboembolic basis for recurrent cerebral ischemic events, although hemodynamic factors may also be relevant. In fact, both recommend antithrombotic therapy, but the main debate is the use of anticoagulants versus antiplatelet agents.

Interestingly, those who have been avidly reading the Controversies Section of this Journal for the past 3 years will have noted that we generally agree on stroke management strategies, even in controversial areas. However, in some instances, this collegial approach cannot be maintained! This is one such example. One of us (G.A.D.) routinely uses antiplatelet agents alone in cases of extracranial arterial dissection (symptomatic and asymptomatic) and reserves the use of heparin for those cases where recurrent symptoms occur. However, the other (S.M.D.) would routinely use anticoagulation, especially for symptomatic cases, provided that there is no evidence of either large acute infarction or intracranial extension. This is despite the fact that both co-editors were once stroke fellows at the MGH—"Must Give Heparin"!

Apart from the issues we asked our protagonists to address, there are many other interesting questions surrounding arterial dissection and stroke, all of which need to be addressed. For example, the use of tPA in patients with dissection and acute ischemic stroke is feasible, but remains somewhat uncertain. Also, optimal management, and particularly the role of endovascular treatment of intracranial arterial dissection, with and without subarachnoid hemorrhage, is uncertain.

Where does this leave us concerning the central question of the role of anticoagulation in the management of patients with extracranial arterial dissection? Both protagonists are in accord, as are we, that a clinical trial is a priority. This would need to be large, investigator-driven trial, probably involving an international collaboration. A call to arms!

References


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Extracranial Arterial Dissection: Anticoagulation Is the Treatment of Choice: For
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