

Cervical Artery Dissection, Imaging, Trauma and Causal Inference

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There is little doubt that cervical artery dissection causing stroke is associated with major trauma.¹ Willis et al² described several cases of unstable cervical fractures through the transverse foramina, among which 46% had associated asymptomatic vertebral artery dissection. Dissection is quite probably asymptomatic in many unrecognized posttraumatic cases. Indeed, many patients in the series reported in this issue of the Journal³ had suffered major trauma. The implication is that vertebral artery injury may be common while remaining asymptomatic.

What has emerged more vociferously in the recent past is the suggestion that minor trauma can also be associated with vertebral and carotid artery dissection and further, that symptoms may be delayed from the time of the trauma.^{4,5} Patients have been described with stroke or TIA and cervical artery dissection associated with neck turning, swinging a golf club, in-line skating and other sporting activities,⁶ extension of the neck over a hairdresser's sink,⁷ roller coasters⁸ and therapeutic neck adjustment by chiropractors, physiotherapists or other practitioners.⁹⁻¹² Other techniques such as Shiatsu have been implicated.¹³ Two retrospective studies suggest a significant statistical association between chiropractic neck adjustment and stroke.^{14,15} The issue of "chiropractic stroke" has been covered by the Canadian media,¹⁶ coroner's inquests have been held in Saskatchewan and Ontario and lawsuits against chiropractors have proliferated.

Despite strong circumstantial reports and opinions, the quality of evidence that minor neck trauma including chiropractic neck adjustment causes vertebral or carotid artery dissection remains weak. A majority of papers are case reports or series only representing the weakest tier of clinical evidence. While these case series lend credence to the temporal association between neck adjustment and dissection, some patients suffer the hallmark neck pain of dissection prior to neck adjustment and seek chiropractic assistance for relief of their neck pain. Neck manipulation may then dislodge a preexisting thrombus. Still, the evidence to support other important factors that lead to causative inference remains modest at best. Because major trauma is clearly associated with dissection, a dose-response relationship may be implied. However, it is unclear whether more frequent episodes of minor trauma might lead to dissection. The statistical magnitude of effect for the association between chiropractic neck adjustment and subsequent stroke, characterised by odds ratios derived from retrospective case-control studies are supportive.¹⁴ However, retrospective case-control studies are subject to many potential biases allowing for continuing uncertainty.

Most importantly, some patients with spontaneous cervical artery dissection or dissection associated with minor trauma have well-defined abnormalities of connective tissue such as one of

the Ehlers-Danlos syndromes,¹⁷ Marfans syndrome, fibromuscular dysplasia,¹⁸ osteogenesis imperfecta,¹⁹ multiple exostosis syndrome, Turner's syndrome²⁰ or others. It has been suggested that the ultrastructural appearance of skin connective tissue among patients with dissection is pathological compared to normals.²¹ Similarly, one study observed that aortic root dilatation was more common among patients with spontaneous dissection than controls.²² Others have noted clear pathological evidence of pre-existing vessel wall structural abnormalities.²³ No common single genetic mutations have been uncovered among the majority of dissection patients suggesting that dissection may be a multigene phenotype.^{24,25} Other factors that may predispose to dissection include migraine,²⁶ the postpartum period^{27,28} and recent upper respiratory tract infection.^{29,30} Despite these associations, a majority of dissections causing stroke are idiopathic.

The low incidence of clinically evident dissection at 3/100 000 per year³¹ also suggests that a combination of factors may be required. In Rothman's paradigm of causal inference,³² a disease occurs only when a necessary cause exists. A necessary cause may be a single factor or composed of multiple component causes. Minor trauma is, therefore, a component cause but not a necessary cause of arterial dissection. A genetic diathesis such as Marfans syndrome or recent upper respiratory tract infection are both possible additional component causes. These component causes summate, probably in a temporally ordered fashion, to a necessary cause and dissection occurs. Major trauma may act as both a component cause and a sole necessary cause. Further prospective evidence is needed to define what factors are and are not component causes and what the interactions among these component causes might be. Meanwhile, physicians must investigate patients with possible dissection comprehensively.

Noninvasive investigations such as CT angiography and MR angiography must be interpreted without reference to the history so that nonspecific irregularities on arterial images are not interpreted as dissection because of the history, but because of intrinsic characteristics on the images that lead to the diagnosis of dissection. Exactly because CTA and MRA lead to both non-specific arterial findings and lack sensitivity for subtle arterial lesions, formal selective cerebral angiography must be performed more frequently to ensure that the correct diagnosis is made.^{33,34} These characteristics make noninvasive imaging reasonable triage procedures before proceeding to angiography; however, in my opinion, a "negative" CTA or MRA should lead to angiography more frequently, not less. Angiography may be supplemented by high resolution axial MR imaging of the neck searching for evidence of intramural blood products in the relevant artery.³⁵

Beaudry and Spence³ speculate that many of the symptoms

associated with the postconcussive syndrome are potentially accounted for by vertebrobasilar ischemia. No convincing evidence is presented to support this assertion. The suggested pathophysiology according to neurovascular anatomy would support a biological mechanism. No evidence in the literature exists describing investigation of patients with postconcussive syndromes with angiography.

These observations do challenge conventional thinking about the common problems of acute and delayed posttraumatic neck pain, vertigo and cognitive changes seen by neurologists and neurosurgeons across Canada. Lateral thinking leading to hypothesis generation is the first step in the scientific method. Are vertebral and carotid artery dissection underrecognized and underinvestigated? Is dissection caused by minor trauma? Are some patients with postconcussive syndrome suffering from unrecognized vertebrobasilar ischemia?

Unfortunately, these questions may not be answerable definitively because of the limitations of current diagnostic technology. Common symptoms such as headache are too non-specific to justify rapid arterial imaging for all such patients.³⁶ Noninvasive angiography using MR or CT is simply not sensitive enough to detect subtle endothelial defects representing minor regions of dissection. Better noninvasive techniques or combinations of techniques are needed. Formal selective angiography would be required and even then, as pointed out by the authors, angiography may have a significant false negative rate compared to histological analysis. Physicians may be reluctant to pursue formal selective angiography when the perceived yield is low and the risks of the procedure may be higher than the chance of making a positive diagnosis of dissection. Because clinically evident dissection is rare, a prospective cohort study could be both prohibitively expensive and logistically difficult. A prospective case-control study would be the most appropriate approach to providing further insight into these questions.

Neurologists and neurosurgeons should consider arterial dissection, search for it with due diligence and in clinical practice, the history must not colour the radiological interpretation of noninvasive arterial imaging. The controversies and hypotheses presented by the authors will only be solved with better data.

*Michael D. Hill
Calgary, Alberta*

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