Manual Therapy 21 (2016) 2–9

Contents lists available at ScienceDirect

Manual Therapy

journal homepage: www.elsevier.com/math

Masterclass

Cervical arterial dissection: An overview and implications for manipulative therapy practice

Lucy C. Thomas*

School of Health and Rehabilitation Sciences, The University of Queensland, St Lucia 4072, QLD, Australia

ARTICLE INFO

Article history:
Received 24 January 2015
Received in revised form
24 June 2015
Accepted 19 July 2015

Keywords:
Carotid artery
Internal dissection
Manipulation
Spinal
Risk factors
Neck

ABSTRACT

Introduction: Cervical arterial dissection (CAD) is a common cause of stroke in young people under 55 years. It can occur spontaneously or subsequent to minor trauma or infection. The incidence is difficult to determine accurately as not all CAD progress to stroke. CAD is the most catastrophic adverse event associated with cervical manipulative therapy but it is rare. Early features of CAD can mimic a painful musculoskeletal presentation and a patient may present for treatment of neck pain and headache with a dissection in progress. Whether the manipulative technique is responsible for dissection or whether the diagnosis of CAD has been missed is unclear. Identification of individuals at risk, or early recognition of CAD could help expedite medical intervention and avoid inappropriate treatment.
Purpose: The aims of this masterclass are to outline current research into the pathophysiology, aetiology and clinical presentation of CAD, to place the risk in context in a manipulative therapy setting and to discuss its possible clinical recognition.
Implications: For those patients presenting with recent onset, moderate to severe unusual headache or neck pain, clinicians should perform a careful history, in particular questioning about recent exposure to head/neck trauma or neck strain. Cardiovascular factors may not be particularly useful indicators of risk of dissection. Clinicians should also be alert to reports of transient neurological dysfunction such as visual disturbance and balance deficits, arm paraesthesia and speech deficits, as these may be subtle. If clinicians suspect arterial dissection is in progress patients should be urgently referred for medical evaluation.

1. Introduction

Cervical artery dissection (CAD) is a tear or haematoma in the wall of the internal carotid or vertebral artery (Debette, 2014). CAD accounts for up to 25% of all ischaemic strokes in people under 55 years and 2% of all ischaemic stroke. It occurs spontaneously or commonly, subsequent to minor trauma (Debette, 2014). CAD can occur at any age, even childhood. It is more common between 35 and 50 years of age, peaks in the fifth decade and rare in people over 65 years. CAD occurs slightly more frequently in men (Thanvi et al., 2005; Debette, 2014). Not all dissections will progress to an ischaemic event, as ischaemia and infarction of brain tissue only occur if the blood supply is critically reduced. Ischaemic stroke or transient ischaemic attack (TIA) occurs in 67–77% of cases (Debette, 2014). Other cases may be asymptomatic or cause minor symptoms, heal spontaneously and may not be reported (Debette and Leys, 2009). The true incidence is difficult to determine (Thanvi et al., 2005; Grond-Ginsbach et al., 2013b).

CAD is the most catastrophic adverse event associated with cervical manipulative therapy. Accounts of CAD following neck manipulation have received wide and often emotive coverage in the popular press. This has led to suggestions that cervical manipulation be abandoned altogether (Lee et al., 1995; Norris et al., 2000; Wand et al., 2012). At the least it has spurred the development of demanding frameworks guiding clinical reasoning for cervical manipulation (Rushton et al., 2012, 2014). The aims of this masterclass are; to outline current research into the pathophysiology, aetiology and clinical presentation of CAD, to place the risk in context in a manipulative therapy setting and to discuss its possible clinical recognition.

2. Pathophysiology

Dissections of the vertebral and internal carotid arteries usually arise from a tear of the inner wall (tunica intima) or outer

* Tel.: +61 7 36615644.
E-mail address: l.thomas2@uq.edu.au.

http://dx.doi.org/10.1016/j.math.2015.07.008
1356-689X/

adventitial layer; commonly due to damage to the vaso vasorum (Fig. 1). Blood under arterial pressure enters the deeper layers forming an intramural haematoma 'dissecting' the artery and causing alteration of blood flow (Schievinck, 2001; Haneline and Lewkovich, 2005). These changes are detected radiologically by the classic 'crescent sign' where the haematoma partially obstructs the lumen of the artery (Fig. 2a, b). Alteration to blood flow may trigger the clotting cascade or an embolus may break off and propagate to the brain, causing ischaemic stroke (Schievinck, 2001). Most spontaneous CADs result from a sub-adventitial tear caused by haemorrhage in the tunica media or tunica adventitia (Volker et al., 2011). This creates a pseudo-aneurysm or degeneration of the media-adventitial border with formation of micro-haematomas, thus weakening the vessel wall (Volker et al., 2011). Degeneration may result from inflammatory changes in the vessel wall (Pfefferkorn et al., 2011). Such weakening is relevant clinically, as the artery potentially has increased vulnerability to vigorous or end-range cervical movement.

3. Aetiology

The pathogenesis of CAD is not fully understood but is multi-factorial (Debette, 2014). It involves a pre-existing intrinsic susceptibility, which predisposes the artery to damage in the presence of a precipitating extrinsic event which may be fairly innocuous (Rubinstein et al., 2005; Volker et al., 2005; Debette and Leys, 2009; Schievink and Debette, 2011).

The intrinsic predisposition is an underlying arteriopathy, anatomical variant or genetic pre-disposition (Brandt et al., 1998; Debette and Markus, 2009). Arteriopathy is probably in part genetically determined and permanent, but may be transient, possibly triggered by pro-inflammatory states (Schievink and Debette, 2011).

The extrinsic precipitating event may be minor mechanical trauma to the vessel, an infection or pro-inflammatory state causing temporary friability or weakness of the arterial vessel wall, rendering it vulnerable to damage (Grau et al., 1999; Debette and Leys, 2009). Cervical manipulation is one potential form of minor trauma, but the trauma can have various origins including sporting or recreational activities, sustained or jerky head movements and heavy lifting (Caso et al., 2005; Thomas et al., 2011; Engelter et al., 2013). Common to these activities is some degree of rotation or hyperextension of the neck or increased intra-thoracic pressure e.g. from lifting or paroxysmal coughing (Caso et al., 2005). Trauma to the internal carotid artery likely occurs due to cervical extension or sudden neck movement compressing the artery over the bodies or transverse processes of the upper cervical vertebrae or mastoid process (Caso et al., 2005). The vertebral artery is most commonly injured at the atlanto-axial segment (C1-2) where most cervical rotation occurs (Bogduk and Mercer, 2000; Haneline and Triano, 2005; Lleva et al., 2012; Biller et al., 2014) (Fig. 3).

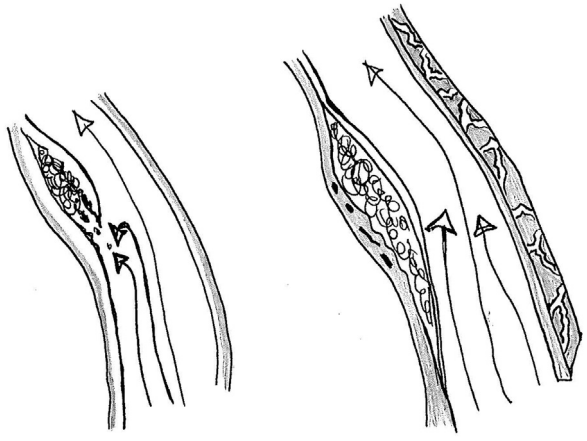

Fig. 1. Cervical arterial wall showing an intimal tear (left) and sub-adventitial intramural haematoma (right) and the effects on blood flow.

4. CAD and manipulative therapy practice

Cervical spine manipulation is one type of minor trauma which may cause CAD (Haldeman et al., 1999; Thiel et al., 2007; Cassidy et al., 2008). The questions raised are whether the nature of a manipulative technique is responsible for the dissection, or whether the diagnosis of CAD has been missed (Biller et al., 2014).

4.1. Missed diagnosis

The early clinical presentation of CAD typically includes neck pain or headache which may mimic migraine or a musculoskeletal disorder (Schievinck, 2001; Arnold et al., 2006; Debette and Leys, 2009). A dissection might not be recognised, particularly in the absence of clear ischaemic (or neurological) features. The patient may present for treatment for painful 'cervical' symptoms which are, in reality, a dissection in progress (Cassidy et al., 2008). Clinicians may be erroneously blamed due to the temporal relationship of the manipulative treatment with the eventual diagnosis of dissection. Thus early recognition of a CAD in progress is essential.

4.2. Can manipulation cause CAD?

There are four mechanisms from which cervical manipulative therapy, in particular high velocity manipulation, is purportedly implicated in the aetiology of CAD: (i) the force of the manipulative thrust damages the arterial wall; (ii) manipulative therapy in the presence of an existing dissection may propagate embolic material to the brain (Haldeman et al., 1999; Mitchell and Kramschuster, 2008); (iii) the positions in which manipulative manoeuvres are performed may alter blood flow in the craniocervical arteries (Mitchell, 2009) and (iv) although never demonstrated in vivo, the manipulative thrust might cause vertebral artery vasospasm, temporarily altering blood flow to the brain (Mann and Refshauge, 2001; Haneline and Lewkovich, 2005). These mechanisms require appraisal.

4.2.1. *Forces associated with manipulation*

Animal studies using dogs and pigs, whose cervical arterial structure is similar to humans, have assessed the effect of manipulative thrusts. Researchers were unable to produce sufficient force to cause any arterial damage (Licht et al., 1999; Kawchuk et al., 2008; Wynd et al., 2008). Similarly, cadaver studies have shown that far greater forces than those capable of being produced by manipulation were required to cause damage to the arterial wall (Wuest et al., 2010). Thus the manipulative thrust is unlikely to be forceful enough to cause damage to a normal artery.

A study using a canine model assessed the effect of manipulation on abnormal vertebral arteries created artificially with an angioplasty. Here again investigators were unable to produce sufficient force to cause tearing of the arterial wall (Wynd et al., 2008). There are limitations to this experimental model and different mechanisms may be involved in a human artery weakened by inflammatory factors.

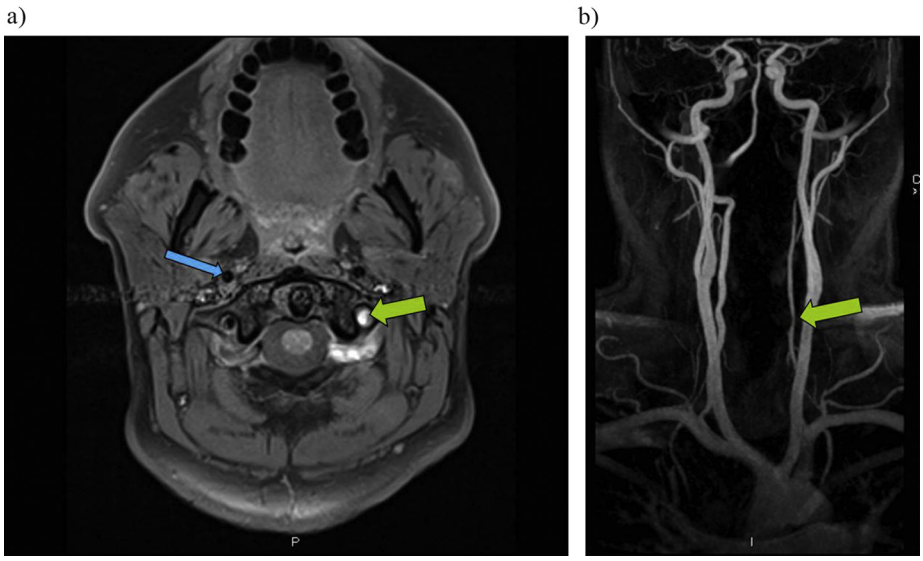

Fig. 2. a) MRI showing intramural haematoma 'crescent sign' in the left vertebral artery (green arrow) and thrombotic material in the atlanto-axial segment of the artery. Internal carotid artery (right) is also shown (blue arrow). b) MRA showing narrowed lumen of left vertebral artery (green arrow) in the same patient. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

4.2.2. Effects of manipulative therapy on a dissection in progress

Manipulative therapy performed when a dissection is present could further damage the artery or propagate an embolus. This proposal is based on the close time frame between onset of CAD and cervical manipulative therapy (Lee et al., 1995; Rothwell, 2001). There are case reports where manipulative treatment has continued in the presence of apparent or worsening neurological symptoms where CAD might have been prevented (Puentedura et al., 2012). Other case reports identify patients having CAD despite negative pre-manipulative screening tests, which suggests that CAD is idiosyncratic and hard to predict (Haldeman et al., 2002).

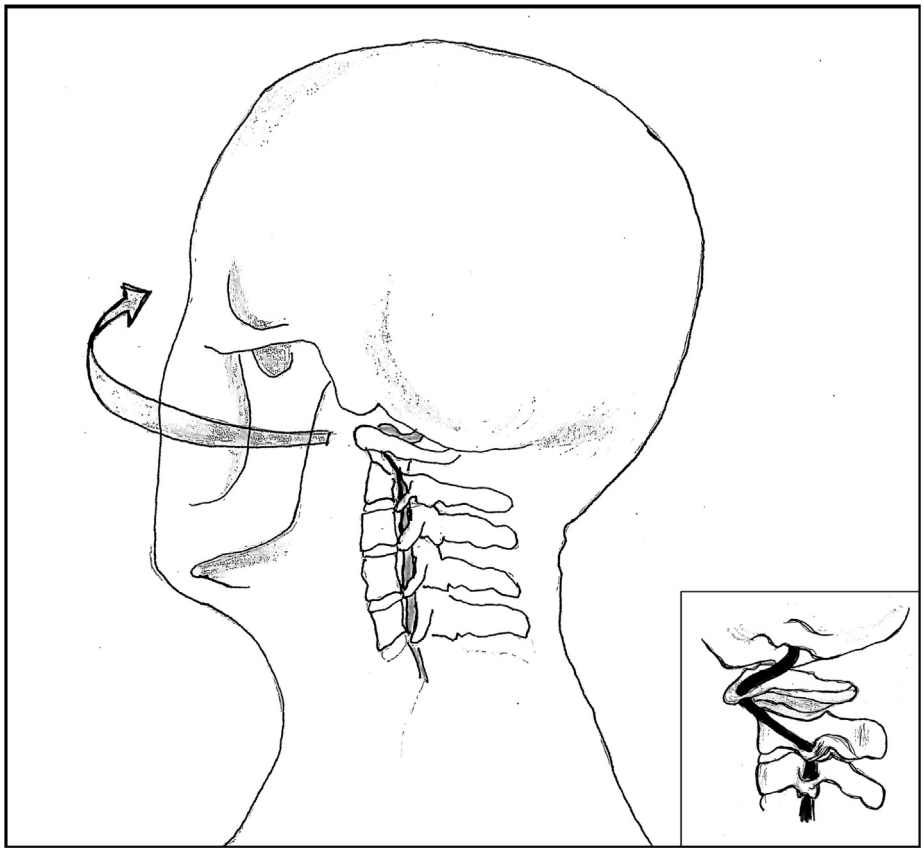

Fig. 3. Diagram of the vertebral artery in the atlanto-axial segment showing stress on the artery in contralateral rotation of the head.

4.2.3. Effects on blood flow

There have been extensive investigations of effects of head position on blood flow, but what are the effects and how relevant is blood flow to the evaluation of risk of adverse neurovascular events? Ultrasound imaging studies show that certain neck movements, in particular cervical rotation, can significantly alter blood flow velocities in the cervical arteries in some individuals (Stevens, 1991; Licht et al., 1998; Li et al., 1999; Johnson et al., 2000; Mitchell, 2003; Zaina et al., 2003; Arnold et al., 2004). This might be an indicator of increased biomechanical stress on the artery, rendering it more susceptible to insult (Refshauge, 1994). Yet there are conflicting results from these studies. Some demonstrate blood flow changes in the vertebral artery contralateral to the direction of cervical rotation, but others report no change (Arnetoli et al., 1989; Weingart and Bischoff, 1992; Thiel et al., 1994; Haynes et al., 2002; Mitchell, 2003; Zaina et al., 2003). There is natural variability in blood flow between individuals which does not support theories of biomechanical strain on the artery or risk of arterial dissection. Likewise, examining blood flow in one vessel does not necessarily give any indication of the overall effect on cerebral perfusion via the Circle of Willis.

A recent MRI study imaged all four cervical arteries simultaneously (Thomas et al., 2013, 2014) and again demonstrated that blood flow in various neck positions can vary widely between individuals. Some vessels showed marked flow reduction yet signs of brain ischaemia were not provoked, leading to conclusions that with an intact Circle of Willis, the body can compensate for changes in flow without incident (Thomas et al., 2013). The risk is when more than one vessel is compromised or there is an incomplete Circle of Willis. It is these individuals whom clinicians should be attempting to identify with provocative physical testing.

4.2.4. Summary

It seems unlikely that either the force of the manipulative thrust or the position in which the technique is performed can cause dissection in a normal cervical artery. What cannot be ruled out is the possibility that a manipulative technique or trivial neck strain may cause dissection in a susceptible artery, extend a CAD or propagate an embolus. The critical issues are recognising a patient with a dissection in progress or identifying a susceptible individual. Blood flow studies indicate how well the body compensates for lack of flow in one vessel but not risk of dissection.

5. Can those at risk be recognised?

CAD is the most catastrophic event associated with cervical manipulative therapy. However to avoid unreasonable alarmism, it is important to place the risk in perspective. Firstly, the annual incidence of internal carotid dissection (ICAD) is estimated as 2.5–3 per 100,000 (around 0.0025% of the population); for vertebral artery dissection (VAD), as 1–1.5 per 100,000 or 0.001% (Schievinck, 2001). Secondly, estimates of CAD following cervical manipulation range at worst, from 1 in 100,000 (0.001%), to 1 in 6,000,000 manipulations (Lee et al., 1995; Albuquerque et al., 2011). The chances that a clinician will actually encounter a patient with dissection are extremely small as is the likelihood of CAD occurring in a clinician's career. Nevertheless, the aim is to avoid all catastrophic events.

For safe practice, clinicians should recognise: (i) the potential for manipulative therapy to cause CAD in a susceptible patient; (ii) a patient presenting with CAD in progress; (iii) patients with abnormal/altered blood flow in whom cervical manipulative therapy should be approached with caution. The importance of a comprehensive history cannot be overemphasised to both identify indicative clinical features and the patient's exposure to putative risk factors. Important historical features are presented.

5.1. Unilateral neck pain and headache

Unilateral neck pain and headache are both common presenting complaints to manipulative therapists and presenting features of CAD (Debette, 2014). Most presentations of neck pain and headache are benign. It may be difficult to distinguish between early symptoms of dissection and other headache forms in the absence of clear neurological features (Debette and Leys, 2009). The site of pain is probably not useful and there is considerable overlap between VAD and ICAD. Patients with VAD commonly present with posterior neck pain or occipital headache on the side of the dissection. The presentation is less distinct than for ICAD and more likely to be interpreted as musculoskeletal in origin (Arnold and Bousser, 2005a). ICAD presents with unilateral frontal or retro-orbital pain.

In most cases of CAD, onset of headache and neck pain is acute/recent and pain is moderate to severe. This should alert clinicians to the potential for more serious pathology. In patients with pre-existing migraine, differential diagnosis may be more challenging since high levels of pain are common. However migraine is present in only around 8% of CAD cases. Nevertheless, differentiation from first episode or familiar migraine is important because ischaemic features may be similar to those of basilar migraine (Arnold and Bousser, 2005b). Importantly, CAD patients usually report their pain as unusual, different to any previously experienced (Biousse et al., 1994; Silbert et al., 1995). This may be helpful in differentiating CAD from other headache forms. In contrast to cervicogenic headache and migraine, this is usually the first episode of headache. Similarly if neck pain and headache precede any ischaemic features, this is strongly suggestive of dissection (Arnold and Bousser, 2005a; Debette, 2014). Notably, some patients present with mild or no pain and only neurological features.

5.2. Local and ischaemic signs and symptoms

Reports of neurological or ischaemic signs should provide a clear indication of more serious pathology. Notably, these are often subtle and transient and may not be recognised as significant by either patient or clinician (Thomas et al., 2015). Typically, patients present with local symptoms such as pain and then progress to an ischaemic event (i.e. stroke or TIA) in the following hours, days or even weeks (Biousse et al., 1995; Arnold and Bousser, 2005b).

Neurological features will depend on the area of the brain supplied by the dissected artery (Fig. 4). Early signs of ICAD may include partial Horner's syndrome – ptosis, miosis or facial palsy, due to pressure on sympathetic fibres from the enlarged artery. Cranial nerve palsies are rare (incidence 8–16%), and affect the lower cranial nerves, in particular the hypoglossal (swallowing), and less commonly the trigeminal and facial nerves (Baumgartner and Bogousslavsky, 2005). Signs result from local compression of the artery and progression to ischaemic stroke may not occur. The carotid arteries supply the anterior cerebral circulation and ischaemic symptoms of general stroke such as limb weakness or paraesthesia and speech disturbance result if there is progression.

The vertebral arteries feed into the posterior circulation which supplies the brainstem, cerebellum and posterior cerebral cortex. Ischaemic signs occur more commonly in VAD than in ICAD (>80% patients) but may be delayed by days or weeks (Silbert et al., 1995; Schievinck, 2001). Signs include balance disturbance, ataxia, syncope, drop attacks, dysphagia, dysarthria, and visual deficits eg diplopia. Notably, dizziness only occurs in around 50% of patients.

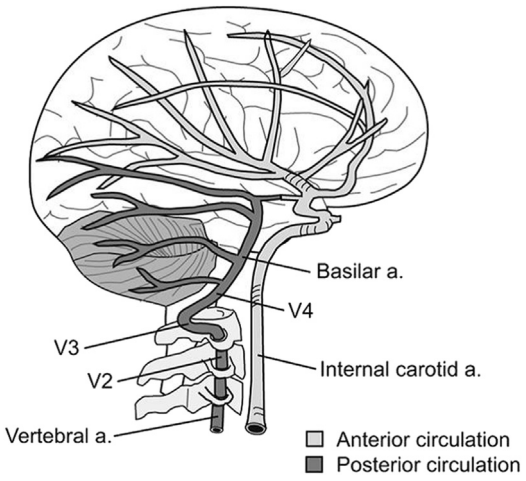

Fig. 4. Distribution of the internal carotid and vertebral artery via the Circle of Willis. Reprinted from Journal of Chiropractic Medicine, Vol 6, Haneline, M, The etiology of cervical artery dissection, page 111, Copyright 2007, with permission from Elsevier.

5.3. *Transient antecedent ischaemic features*

Many CAD patients have transient antecedent neurological signs and symptoms for days or weeks prior to their dissection. These symptoms were identifiable in the patient's history with specific questioning but often patients did not think to mention them spontaneously (Thomas et al., 2015). Most common were visual disturbance, dizziness and imbalance. It is critical that clinicians question for and recognise transient yet possibly subtle signs and symptoms. Good history taking is the key. Delayed stroke in CAD patients is not uncommon (Lichy et al., 2015).

5.4. *Exposure to risk factors for CAD*

5.4.1. *Recent minor trauma and infection*

As early diagnosis can be difficult, it is important to consider exposure to risk factors for CAD. Extrinsic or environmental risk factors include recent minor head and neck trauma, recent infection or viral illness (Grau et al., 1999; Lindsberg and Grau, 2003; Dittrich et al., 2007; Thomas et al., 2011; Engelter et al., 2013). Studies confirmed that recent neck strains, blows to the head or neck, or activities involving jerky uncontrolled head movement are common in CAD (Thomas et al., 2015). Patients presenting with recent onset, unusual neck pain or headache should be questioned about these features to determine exposure to potential risk. Similarly, the clinician should enquire about recent gastroenterological or respiratory infections (particularly with violent retching or coughing) as well as any other valsalva type activities (lifting or intensive/heavy gym work). These increase intrathoracic pressure and place strain on the artery/neck.

It is more difficult to identify factors implicating susceptibility to dissection. Exposure to recent infection or viral illness may increase a patient's susceptibility to CAD. Findings of elevated inflammatory factors (Grond-Ginsbach et al., 2013a) and seasonal variation in CAD presentation indicate the possibility of an infective cause (Micheli et al., 2010; Kloss et al., 2012). This is more likely in ICAD with the close proximity of the upper respiratory tract to the artery (Grau et al., 1999).

5.4.2. *Cardiovascular risk factors for stroke*

The importance of cardiovascular risk factors in the pathogenesis of CAD is controversial. Arnold et al. (2009) found that in comparison to healthy matched controls, CAD patients were more likely to have hypertension but less likely to have hypercholesterolaemia or be overweight. Hypertension might increase arterial stiffness predisposing the artery to CAD but (Calvet et al., 2004) found no consistent evidence of atherosclerosis from their imaging studies suggesting it is not a predisposing factor for CAD. Atherosclerosis might even be protective due to increased collagen and elastin synthesis making the arterial wall less vulnerable to tears (Debette, 2014).

There may be a slightly increased frequency of smoking in CAD patients but is inconsistent (Arnold and Bousser, 2005a; Thomas et al., 2011). Even though migraine without aura has been linked with CAD, it is only present in 8% of patients (Metso et al., 2012). Thus the contribution of vascular risk factors to increased susceptibility to CAD is unclear and they may not be particularly informative in determining risk.

5.4.3. *Vascular anomalies*

Anomalies of craniocervical circulation include; aplasia or hypoplasia of one vertebral artery; failure of the vessel to join directly into the posterior Circle of Willis; or no posterior cerebral artery. Anomalies could compromise the homeostatic function of the Circle in maintaining constant blood flow to the brain but have been identified in only a portion of CAD patients (Guillon et al., 2000, 2003). Moreover, patients with a vascular anomaly often have well-developed, compensatory collateral circulation from other small cerebral vessels (Kathuria et al., 2011). The presence of vascular anomaly may not represent a true risk for dissection.

6. Screening for CAD or susceptibility to CAD

With concern about the safety of neck manipulation (Lee et al., 1995; Norris et al., 2000; Wand et al., 2012), some argue against manipulation and others for much more rigorous screening of patients. Extensive documentation has been introduced to guide clinical reasoning for all patients in whom cervical manipulative therapy is planned (Kerry et al., 2008; Rushton et al., 2014). In light of more recent research into CAD, it is important to consider essential elements of screening. Effective screening needs to identify patients with a dissection in progress and those susceptible to dissection. The history is the most important aspect of assessment to identify a CAD dissection in progress. Features do not fit a regular musculoskeletal pattern. A patient with CAD in progress may present only with local symptoms of neck pain and headache, but alerting features are recent/acute onset of moderate to severe, quite unusual pain. Often, symptoms worsen over hours/days. This should prompt the clinician to question about risk factors such as recent exposure to minor trauma or recent infection (Biller et al., 2014). Follow-up questions should seek in some detail, information about any ischaemic features such as visual disturbance, balance or gait disturbance, speech difficulties or limb weakness or paraesthesia. A clinical pattern may emerge just from the history which directs immediate action.

Other tests are advocated to detect patients who may be susceptible to or at risk of CAD. The evidence for routine screening for cardiovascular risk factors for general stroke is tenuous (Caso et al., 2005; Arnold et al., 2009; Debette and Leys, 2009). For example, hypertension is not present in all CAD patients and there is no evidence that it increases risk. Restricting treatment in patients with hypertension is not supported by evidence to date. Similarly migraine is present in 8% of CAD patients but with such a low incidence, migraine may not be particularly useful to predict risk.

The validity of screening tests utilising sustained rotation and extension positions to provoke dizziness, pre-syncope or nystagmus have caused debate over several years (Rushton et al.,

Table 1
Differentiation between features of CAD and VBI.

CAD	VBI
Acute onset neck pain or headache	Long standing neck pain or headache
Young-middle age 30–50	Older person >65
History of recent trauma or infection	No report of recent trauma or infection
No clear link of signs and symptoms with head movement	Link of symptoms with head position or neck movement
Headache, neck pain	Neck pain
Moderate/severe pain	Mild-moderate pain
5 Ds and other neurological symptoms eg limb paraesthesia or weakness, Horner's syndrome,	5 Ds (dizziness, diplopia, dysarthria, dysphagia, drop attacks), pre-syncope

2012). Recent MRI studies evaluating all four craniocervical vessels suggest that even if flow is substantially reduced in one vessel, the other three will compensate (Thomas et al., 2013, 2014). Thus the provocative physical tests more generally assess the adequacy of collateral flow to the brain than the competency of one artery. The significance for clinicians is that for the majority of patients, the physical tests will be negative if vessels are normal. Physical tests arguably still have a place to identify the few individuals with abnormal vessels in whom collateral compensation is insufficient.

There is no evidence that haemodynamic testing such as carotid palpation or measurement of blood flow is relevant (Kerry et al., 2008; Rushton et al., 2014). Some suggest that quantitative measurement of blood flow could be used in screening using devices such as a hand-held velocimeter (Haynes et al., 2000; Kerry et al., 2008). However both ultrasound and MRI studies have shown that even in those with hypoplastic vessels and low or even absent flow in contralateral rotation, signs and symptoms of VBI did not necessarily ensue (Rivett, 2000; Thomas et al., 2008, 2013). Blood flow, particularly in the vertebral arteries, is so variable between individuals that its assessment in pre-manipulative screening protocols may not be helpful.

6.1. How does VBI fit into the picture?

Past guidelines for pre-manipulative testing have focussed on recognising signs and symptoms of VBI, in particular dizziness. While signs and symptoms of VBI may be indicative of CAD, CAD is better identified through its association with other historical features such as exposure to risk factors and acute onset of neck pain and headache. A useful point for differentiation is that VBI generally occurs in older people, while CAD is rare over 65 years. Table 1 summarises some key points of difference.

7. Actions if CAD is suspected

If a dissection in progress is suspected, time is the most important factor. The patient should be referred immediately to the nearest emergency department for medical evaluation. Several cases have been reported where patients have attended emergency departments in the days or weeks preceding dissection but were sent home without imaging evaluation only to return with a full blown ischaemic event (Grond-Ginsbach et al., 2013b). The clinician must communicate (verbally and letter) specific concerns about the possibility of CAD, identifying key points of suspicion e.g. recent/acute onset, moderate-severe, unusual neck pain or headache combined with recent exposure to trauma as well as the need for investigative imaging (CT or MRI angiography).

8. Future research

There are many areas for future research in the area of risk to better understand arterial susceptibility. This could include further research into the influence of infective factors, such as the effects of pro-inflammatory mediators on arterial walls. Clinical screening needs to align better with research findings and be simplified. There is room to revise/develop a screening tool or clinical decision rule to more readily identify those with dissection or susceptible to dissection. Likewise it is important to better define which manipulative techniques are more risky from a biomechanical perspective.

9. Conclusion

CAD is the most serious and life threatening adverse event associated with cervical manipulative therapy. Yet, it is a rare event, and there needs to be caution against over-stating the risk and denying patients helpful treatment for conditions such as neck pain, cervicogenic headache and cervical vertigo. Nevertheless, it is critical for clinicians to identify a CAD in progress, susceptible individuals, and those with poor flow generally in whom high velocity techniques and extreme positions of the neck may compromise blood flow to the brain. The most appropriate way to screen patients prior to cervical manipulative therapy with current knowledge seems to lie in taking an effective history. Suspicion would be heightened with presentation of acute/recent onset of unusual neck pain or headache, with recent exposure to minor trauma or infection in conjunction with any ischaemic features even if transient and subtle.

References

Albuquerque FC, Hu YC, Dashti SR, Abla AA, Clark JC, Alkire B, Theodore N, McDougall CG. Craniocervical arterial dissections as sequelae of chiropractic manipulation: patterns of injury and management. J Neurosurg 2011;115(6):119–1205.

Arnetoli G, Amadori A, Stephani P, Nuzzaci G. Sonography of vertebral arteries in De Kleyn's position in subjects and in patients with vertebrobasilar transient ischemic attacks. Angiology 1989;40:716–20.

Arnold C, Bourassa R, Langer T, Stoneham G. Doppler studies evaluating the effect of a physical therapy screening protocol on vertebral artery blood flow. Man Ther 2004;9:13–21.

Arnold M, Bousser M. Carotid and vertebral artery dissection. Pract Neurol 2005a;5:100–9.

Arnold M, Bousser M. Clinical manifestations of vertebral artery dissection. In: Baumgartner RW, Bogousslavsky J, Caso V, Paciaroni M, editors. Handbook of cerebral artery dissection. Basel: Karger; 2005b. p. 77–86.

Arnold M, Cumurciuc R, Stapf C, Favrole P, Berthet K, Bousser MG. Pain as the only symptom of cervical artery dissection. J Neurol Neurosurg Psychiatry 2006;77:1021–4.

Arnold M, Pannier B, Chabriat H, Nedeltchev K, Stapf C, Buffon F, et al. Vascular risk factors and morphometric data in cervical artery dissection: a case -control study. J Neurol Neurosurg Psychiatry 2009;80:232–4.

Baumgartner RW, Bogousslavsky J. Clinical manifestations of carotid dissection. In: Baumgartner RW, Bogousslavsky J, Caso V, Paciaroni M, editors. Handbook on cerebral artery dissection. Basel: Karger; 2005. p. 70–6.

Biller J, Sacco R, Alberquerque F, Demaerschalk B, Fayad P, Long P, et al. Cervical arterial dissections and association with cervical manipulative therapy. A statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2014;45:3155–74.

Biousse V, D'Anglejan-Chatillon J, Massiou H, Bousser M-G. Head pain in non-traumatic carotid dissections: a series of 65 patients. Cephalalgia 1994;14:33–6.

Biousse V, D'Anglejan-Chatillon J, Touboul P, Amarenco P, Bousser M. Time course of symptoms in extracranial carotid artery dissections. Stroke 1995;26:235–9.
Bogduk N, Mercer S. Biomechanics of the cervical spine. I: normal kinematics. Clin Biomech 2000;15:633–48.
Brandt T, Hausser I, Orberk E, Grau P, Hartschuh W, Anton-Lamprecht I, et al. Ultrastructural connective tissue abnormalities in patients with spontaneous cervicocerebral artery dissections. Ann Neurol 1998;44:281–5.
Calvet D, Boutouyrie P, Touze E, Laloux B, Mas JL, laurent S. Increased stiffness of the carotid wall material in patients with spontaneous cervical artery dissection. Stroke 2004;35:2078–82.
Caso V, Paciaroni M, Bogousslavsky J. Environmental factors and cervical artery dissection. In: Baumgartner RW, Bogousslavsky J, Caso V, Paciaroni M, editors. Handbook on cerebral artery dissection. Basel: Karger; 2005. p. 44–53.
Cassidy D, Boyle E, Cote P, He Y, Hogg-Johnson S, Silver FL, et al. Risk of vertebrobasilar stroke and Chiropractic Care. Results of a population-based case-control and case-crossover study. Spine 2008;33:S176–83.
Debette S. Pathophysiology and risk factors of cervical artery dissection: what have we learnt from large hospital-based cohorts? Curr Opin Neurology 2014;27:20–8.
Debette S, Leys D. Cervical-artery dissections: predisposing factors, diagnosis and outcome. Lancet Neurol 2009;8:668–78.
Debette S, Markus G. The genetics of cervical artery dissection. A systematic review. Stroke 2009;40:e459–66.
Dittrich R, Rohsbach D, Heidbreder A, Heuschmann P, Nassenstein I, Bachmann R, et al. Mild mechanical traumas are possible risk factors for cervical artery dissection. Cerebrovasc Dis 2007;23:275–81.
Engelter S, Grond-Ginsbach C, Metso A, Kloss M, Debette S, Leys D, et al. Cervical artery dissection: trauma and other potential mechanical trigger events. Neurology 2013;80:1950–7.
Grau AJ, Brandt T, Buggle F, Orberk E, Mytilineos J, Werle E, et al. Association of cervical artery dissection with recent infection. Archives Neurol 1999;52:851–6.
Grond-Ginsbach C, Giossi A, Aksay SS, Engelter ST, Lyrer PA, Metso TM, et al. Elevated peripheral leukocyte counts in acute cervical artery dissection. Eur J Neurol Off J Eur Fed Neurol Soc 2013a;20:1405–10.
Grond-Ginsbach C, Metso A, Metso T, Pezzini A, Tatlisumak T, Hakimi M, et al. Cervical artery dissection goes frequently undiagnosed. Med Hypotheses 2013b;80:787–90.
Guillon B, Berthet K, Benslamia L, Bertrand M, Bousser M, Tzourio C. Infection and the risk of spontaneous cervical artery dissection. Stroke 2003;34:e79–81.
Guillon B, Tzourio C, Biousse V, Bousser M. Arterial wall properties in cartid artery dissection: an ultrasound study. Neurology 2000;55:663–6.
Haldeman S, Kohlbeck FJ, McGregor M. Risk factors and precipitating neck movements causing vertebrobasilar artery dissection after cervical trauma and spinal manipulation. Spine 1999;24:785–94.
Haldeman S, Kohlbeck FJ, McGregor M. Unpredictability of cerebrovascular ischemia associated with cervical spine manipulation therapy. Spine 2002;27:49–55.
Haneline M, Triano J. Cervical artery dissection. A comparison of highly dynamic mechanisms: manipulation versus motor vehicle collision. J Manip Physiol Ther 2005;28:57–63.
Haneline MT, Lewkovich GN. An analysis of the etiology of cervical artery dissection: 1994 to 2003. J Manip Physiol Ther 2005;28:617–22.
Haynes M, Cala LA, Melsom A, Mastaglia F, Milne N, McGeachie J. Vertebral arteries and cervical rotation: modelling and magnetic resonance angiography studies. J Manip Physiol Ther 2002;25:370–83.
Haynes M, Hart R, McGeachie J. Vertebral arteries and neck rotation: Doppler Velocimeter interexaminer reliability. Ultrasound Med Biol 2000;26:1363–7.
Johnson C, Grant R, Dansie B, Spyropolous P. Measurement of blood flow in the vertebral artery using colour duplex Doppler ultrasound: establishment of the reliability of selected parameters. Man Ther 2000;5:21–9.
Kathuria S, Chen J, Gregg L, Parmar HA, Gandhi D. Congenital arterial and venous anomalies of the brain and skull base. Neuroimaging Clin N. Am 2011;21:545–62. vii.
Kawchuk G, Jhangri G, Hurwitz E, Wynd S, Haldeman S, Hill MD. The relation between the spatial distribution of vertebral artery compromise and exposure to spinal manipulation. J Neurol 2008;255:371–7.
Kerry R, Taylor A, Mitchell J, McCarthy C. Cervical arterial dysfunction and manual therapy: a critical literature review to inform professional practice. Man Ther 2008;13:278–88.
Kloss M, Metso A, Pezzini A, Leys D, Giroud M, Metso TM, et al. Towards understanding seasonal variability in cervical artery dissection (CeAD). J Neurol 2012;259:1662–7.
Lee K, Carlini WG, McCormick GF, Albers GW. Neurologic complications following chiropractic manipulation: a survey of California neurologists. Neurology 1995;45:1213–5.
Li Y-K, Zhang Y-K, Lu C-M, Zhong S-Z. Changes and implications of blood flow velocity of the vertebral artery during rotation and extension of the head. J Manip Physiol Ther 1999;22:91–5.
Licht PB, Christensen HW, Hojgaard P, Hiolund-Carlson PF. Triplex ultrasound of vertebral artery flow during cervical rotation. J Manip Physiol Ther 1998;21:27–31.
Licht PB, Christensen HW, Svendsen P, Hoilund-Carlsen PF. Vertebral artery flow and cervical manipulation: an experimental study. J Manip Physiol Ther 1999;22:431–5.
Lichy C, Metso A, Pezzini A, Leys D, Metso T, Lyrer P, et al. Predictors of delayed stroke in patients with cervical artery dissection. Int J Stroke Off J Int Stroke Soc 2015;10(3):360–3.
Lindsberg PJ, Grau AJ. Inflammation and infections as risk factors for ischemic stroke. Stroke 2003;34:2518–32.
Lleva P, Ahluwalia B, Marks S, Sahni R, Tenner M, Risucci D, et al. Traumatic and spontaneous carotid and vertebral artery dissection in a level 1 trauma center. J Clin Neurosci 2012;19:1112–4.
Mann T, Refshauge KM. Causes of complications from cervical manipulation. Aust J Physiother 2001;47:255–66.
Metso TM, Tatlisumak T, Debette S, Dallongeville J, Engelter ST, Lyrer PA, et al. Migraine in cervical artery dissection and ischemic stroke patients. Neurology 2012;78:1221–8.
Micheli S, Paciaroni M, Corea F, Agnelli G, Zampolini M, Caso V. Cervical artery dissection: emerging risk factors. Open Neurol J 2010;4:50–5.
Mitchell J. Vertebral artery blood flow velocity changes associated with cervical spine rotation: a meta-analysis of the evidence with implications for professional practice. J Man Manip Ther 2009;17:46–57.
Mitchell J, Kramschuster K. Real-time ultrasound measurements of changes in suboccipital vertebral artery diameter and blood flow associated with cervical spine rotation. Physiother Res Int 2008;13:241–54.
Mitchell JA. Changes in vertebral artery blood flow following normal rotation of the cervical spine. J Manip Physiol Ther 2003;26:347–51.
Norris JW, Beletsky V, Nadareishvili Z. Sudden neck movement and cervical artery dissection. Can Med Assoc J 2000;163:38–40.
Pfefferkorn T, Saam T, Rominger A, Habs M, Gerdes L-A, Schmidt C, et al. Vessel wall inflammation in spontaneous cervical artery dissection: a prospective, observational positron emission tomography, computed tomography, and magnetic resonance imaging study. Stroke 2011;42:1563–8.
Puentedura E, March J, Anders J, Perez A, Landers M, Wallmann H, et al. Safety of cervical spine manipulation: are adverse events preventable and are manipulations being performed appropriately? A review of 134 case reports. J Man Manip Ther 2012;20:66–74.
Refshauge KM. Rotation: a valid premanipulative dizziness test? Does it predict safe manipulation? J Manip Physiol Ther 1994;17:15–9.
Rivett D. Vertebral artery blood flow during pre-manipulative testing of the cervical spine. Dunedin: University of Otago; 2000 [PhD thesis].
Rothwell DM. Chiropractic manipulation and stroke: a population-based case-control study. Stroke 2001;32:1054–60.
Rubinstein S, Peerdeman S, van Tulder M, Riphagen I, Haldeman S. A systematic review of the risk factors for cervical artery disection. Stroke 2005;36:1575–80.
Rushton A, Rivett D, Carlesso L, Flynn T, Hing W, Kern R. International framework for examining of the cervical region for cervical arterial dysfunction prior to Orthopaedic manual therapy intervention. Man Ther 2014;19:222–8.
Rushton A, Rivett D, Carlesso L, Flynn T, Hing W, Kerry R. International framework for examination of the cervical region for potential of cervical arterial dysfunction prior to Orthopaedic manual therapy intervention. In: Therapists IFoOMP. International Federation of Orthopaedic Manipulative Physical Therapists; 2012.
Schievinck WI. Spontaneous dissection of the carotid and vertebral arteries. N. Engl J Med 2001;344:898–906.
Schievink WI, Debette S. Etiology of cervical artery dissections: the writing is in the wall. Neurology 2011;76:1452–3.
Silbert P, Mokri B, Schievinck W. Headache and neck pain in spontaneous internal carotid artery dissection. Neurology 1995;45:1517–22.
Stevens A. Functional Doppler sonography of the vertebral artery and some considerations about manual techniques. J Man Med 1991;6:102–5.
Thanvi B, Munshi SK, Dawson SL, Robinson TG. Carotid and vertebral artery dissection syndromes. Postgrad Med J 2005;81:383–8.
Thiel H, Bolton JE, Docherty S, Portlock JC. Safety of chiropractic manipulation of the cervical spine. A prospective National survey. Spine 2007;32:2375–8.
Thiel H, Wallace K, Donat J, Yong-Hing K. Effect of various head and neck positions on vertebral artery blood flow. Clin Biomech 1994;9:105–10.
Thomas L, McLeod L, Osmotherly P, Rivett D. The effect of end-range cervical rotation on vertebral and internal carotid arterial blood flow and cerebral inflow: a sub analysis of an MRI study manual therapy. 2014.
Thomas L, Rivett D, Bateman GA, Stanwell P, Levi C. Effect of selected manual therapy interventions for mechanical neck pain on vertebral and internal carotid arterial blood flow and cerebral inflow. Phys Ther 2013;93:1563–74.
Thomas L, Rivett D, Bolton PS. Pre-manipulative testing and the use of the velocimeter. Man Ther 2008;13:29–36.
Thomas L, Rivett D, Levi C. Risk factors and clinical features of craniocervical arterial dissection. Man Ther 2011;16:351–6.
Thomas LC, Rivett DR, Attia JR, Levi C. Risk factors and clinical presentation of cervical arterial dissection: preliminary results of a prospective case-control study. J Orthop Sports Phys Ther 2015;45(7):503–11.
Volker W, Besselman M, Dittrich R, Nabavi DG, Konrad C, Dziewas R, et al. Generalised arteriopathy in patients with cervical artery dissection. Neurology 2005;64:1508–13.
Volker W, Dittrich R, Grewe S, Nassenstein I, Csiba L, Herczeg L, et al. The outer arterial wall layers are primarily affected in spontaneous cervical artery dissection. Neurology 2011;76:1463–71.
Wand B, Heine P, O'Connell N. Should we abandon neck manipulation for mechanical neck pain? Yes Br Med J 2012;345. e3679-e.

Weingart JR, Bischoff HP. Doppler sonography of the vertebral artery with regard to head positions appropriate to manual medicine. Man Med 1992;30:62–5.
Wuest S, Symons B, Leonard T, Herzog W. Preliminary report: biomechanics of vertebral artery segments C1-6 during cervical spinal manipulation. J Manip Physiol Ther 2010;33:273–8.
Wynd S, Anderson T, Kawchuk GN. Effect of cervical spine manipulation on a pre-existing vascular lesion within the canine vertebral artery. Cerebrovasc Dis 2008;26:304–9.
Zaina C, Grant R, Johnson C, Dansie B, Taylor J, Spyropolous P. The effect of cervical rotation on blood flow in the contralateral artery. Man Ther 2003;8:103–9.