


A risk–benefit assessment strategy to exclude cervical artery dissection in spinal manual-therapy: a comprehensive review

Aleksander Chaibi^{a,b}  and Michael Bjørn Russell^{a,b}

^aHead and Neck Research Group, Research Centre, Akershus University Hospital, Oslo, Norway; ^bInstitute of Clinical Medicine, Akershus University Hospital, University of Oslo, Nordbyhagen, Norway

ABSTRACT

Cervical artery dissection refers to a tear in the internal carotid or the vertebral artery that results in an intramural haematoma and/or an aneurysmal dilatation. Although cervical artery dissection is thought to occur spontaneously, physical trauma to the neck, especially hyperextension and rotation, has been reported as a trigger. Headache and/or neck pain is the most common initial symptom of cervical artery dissection. Other symptoms include Horner's syndrome and lower cranial nerve palsy. Both headache and/or neck pain are common symptoms and leading causes of disability, while cervical artery dissection is rare. Patients often consult their general practitioner for headache and/or neck pain, and because manual-therapy interventions can alleviate headache and/or neck pain, many patients seek manual therapists, such as chiropractors and physiotherapists. Cervical mobilization and manipulation are two interventions that manual therapists use. Both interventions have been suspected of being able to trigger cervical artery dissection as an adverse event. The aim of this review is to provide an updated step-by-step risk–benefit assessment strategy regarding manual therapy and to provide tools for clinicians to exclude cervical artery dissection.

KEY MESSAGES

- Cervical mobilization and/or manipulation have been suspected to be able to trigger cervical artery dissection (CAD). However, these assumptions are based on case studies which are unable to establish direct causality.
- The concern relates to the chicken and the egg discussion, i.e. whether the CAD symptoms lead the patient to seek cervical manual-therapy or whether the cervical manual-therapy provoked CAD along with the non-CAD presenting complaint.
- Thus, instead of proving a nearly impossible causality hypothesis, this study provides clinicians with an updated step-by-step risk–benefit assessment strategy tool to (a) facilitate clinicians' understanding of CAD, (b) appraise the risk and applicability of cervical manual-therapy, and (c) provide clinicians with adequate tools to better detect and exclude CAD in clinical settings.

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Introduction

Cervical artery dissection (CAD) refers to a tear in the internal carotid artery (ICA) or the vertebral artery (VA), resulting in an intramural haematoma and/or an aneurysmal dilatation, which can ultimately be detrimental to the individual. The pathophysiology of CAD is not fully understood, but multiple coexisting pathological processes leading to a predisposing weakness of the arterial wall, namely, a large aortic root diameter, increased stiffness of the carotid wall, material and circumferential wall stress, hypertension, endothelial dysfunction, and arterial redundancies, have been proposed to increase the risk of CAD [1].

Fortunately, the incidence rate of CAD is relatively low, estimated at 2.9/100,000 individuals per year in the general population [2]. Internal carotid artery dissections (ICADs) occur approximately 3–5 times more frequently than vertebral artery dissections (VADs) [3,4]. This corresponds to 9476 new American CAD cases and 21,537 new European CAD cases per year. CAD usually only occurs once.

Ischaemic stroke is the most common clinical symptom in CAD, and the risk of subarachnoid haemorrhage (SAH) is greater in intracranial artery dissection than in CAD [5]. However, there is also a selection bias towards those with CAD without subarachnoid

CONTACT Aleksander Chaibi  aleksander.chaibi@medisin.uio.no  Head and Neck Research Group, Research Centre, Akershus University Hospital, 1478 Lørenskog, Oslo, Norway

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haemorrhage being recruited through neurology departments, whereas recruitment through departments of neurosurgery or interventional neuroradiology is biased towards CAD with SAH [5]. A French prospectively neurological department study in tertiary health care found clinical symptoms to occur in 156 (92%) of 169 patients with spontaneous VAD, i.e. stroke in 114 (67%), TIA in 17 (10%), and occipital head and/or neck pain alone in 21 (12%) patients, SAH without ischaemia were found in three (2%) patients, and sensorimotor cervical radiculopathy C5/C6 in one patient (1%). Three of the patients with ischemic stroke also showed signs of SAH on brain imaging [6]. A Swiss prospectively neurological department study in tertiary health care found clinical symptoms to occur in 290 (97%) of 298 patients with spontaneous ICAD, i.e. stroke in 165 (55%), TIA in 37 (12%), amaurosis fugax in 8 (3%), local symptoms, and signs (headache, neck pain, Horner's syndrome and nerve palsy) in 80 (27%), while eight (3%) were asymptomatic [7].

The prognosis of disability after CAD at 3 months is good for 89% of cases, with 91% for ICAD and 88% for VAD, according to the modified Rankin score (mRS 0–2): (0) no symptoms, (1) no significant disability despite symptoms and able to carry out all usual duties and activities, and (2) slight disability, unable to carry out all previous activities, but able to look after own affairs without assistance [2,8]. The mortality rate is less than 4% [1,4]: mean 5.1% (SD 7.2) for ICAD [2,9–21] and mean 1.3% (SD 2.3) for VAD [2,14,16,18,20–22], calculated by the authors. The mean age of CAD patients is 44 years (46 years for men and 41 years for women) [23], with a slight male preponderance (55%) [24]. CAD is extremely rare in children and adults beyond the age of 65 years [25].

Headache and/or neck pain are the most common initial symptoms of CAD [26]. Other symptoms are Horner's syndrome and lower cranial nerve palsy [4]. The headache is often new and unilateral, exhibits sudden onset, and may resemble a migraine or cluster headache [27]. The time from initial symptoms to ischaemic stroke varies from minutes to few weeks [28].

With headaches and/or neck pain as common initial physical symptoms, many patients seek manual therapy to alleviate the pain [29–34]. Headaches and neck pain have also been among the leading global causes of disability within the last decade [35]. Although CAD is thought to occur spontaneously, physical trauma to the neck, especially traumas involving hyperextension and rotation, has been suspected to trigger CAD [4,36,37]. Some case reports have suggested that CAD may be an adverse event (AE) following manual

therapy that includes cervical mobilization and/or manipulation intervention [38–45].

However, although some have argued that the presenting symptoms of headaches and/or neck pain in manual-therapy settings are symptoms that are caused by a CAD in progress, questions remain as to whether the manual technique is directly responsible for CAD or can worsen a CAD in progress and, importantly, whether the diagnosis of CAD is overlooked prior to the manual intervention.

It is paramount that all clinicians, especially manual therapists who utilize cervical mobilization and/or manipulation techniques, are well informed of the possible red flags and are capable of referring patients to essential medical examinations and treatments (anticoagulants or antiplatelet drugs) before initiating manual-therapy interventions, as recommended by the American Heart and Stroke Association [46].

The objective of this review is to present an updated step-by-step risk–benefit assessment strategy tool to (a) provide clinicians with knowledge and adequate tools to better exclude CAD and (b) appraise the risk and applicability of cervical manual therapy.

Manual therapy does not result in an increased risk of CAD

The World Health Organization regards manual mobilization and/or spinal manipulative treatment conducted by chiropractors to be a safe and effective treatment with few, mild, transient AEs [47], such as local soft tissue tenderness and tiredness on the treatment day [48–55]. A few case studies have reported serious AEs following cervical spinal manipulative therapy (SMT) [56–64], but whether there is a causal relationship between cervical SMT and CAD has not been determined because of the methodological design, low level of evidence and low prevalence [40,42,43].

The lack of established causality relates to the chicken and egg discussion, i.e. whether the CAD symptoms lead the patient to seek cervical SMT or whether the cervical SMT provokes CAD along with the non-CAD presenting headache and/or neck complaint. The infrequent reporting of serious AEs in prospective manual-therapy randomized controlled trials might be a true figure or an underestimation [39,42,44,48–55,65–67]. The rarity of CAD also makes the provision of epidemiological evidence challenging. However, several extensive cohort studies and meta-analyses have found no excess risk of CAD resulting in secondary ischaemic stroke for chiropractic SMT compared to primary care follow-up [39,44,68]. Similarly,

retrospective cohort studies have reported no association with traumatic injury to the head or neck after SMT for neuromusculoskeletal pain [69]. Invasive studies have further disproven any misconception as to whether VA strains during head movements, including SMT, exceed failure strains [70,71]. No changes in blood flow or velocity in the VA of healthy young male adults were found in various head positions and during a cervical SMT [72]. Thus, these studies support the evidence of spontaneous causality or minimally suggest a very low risk for serious AEs following SMT [41,73,74].

Thus, there is no strong evidence in the literature that manual therapy provokes CAD. However, to provide evidence-based knowledge on AEs, all health personnel must record AEs observed in all their patients in relation to the treatments they provide.

Internal carotid artery

The ICA is a terminal branch of the common carotid artery and arises around the level of the fourth cervical vertebra, where it continues intracranially to join the circle of Willis (Figure 1). The ICA moves freely within the cervical pathway and enters the carotid canal first above the first cervical vertebrae, where it

becomes fixed [75]. The ICA provides the most significant proportion of blood to the brain, specifically the anterior portion that includes the retina, while the external carotid artery supplies the face, scalp, skull, and meninges. Any disruption to the anterior circulation can cause retinal and/or cerebral ischaemic symptoms, namely, hemiparesis, hemisensory loss, neglect, aphasia, gaze deviation, dysarthria, and monocular visual loss. The location of pain symptoms from an ICAD can vary, but neck pain commonly involves the periorbital, frontal, or upper anterior cervical region and is unilateral and ipsilateral to the affected cervical artery (Figure 2). The headache can resemble migraine or cluster headaches with its unilateral pain location [25]. However, neither a migraine nor cluster headache are characterized by pain in the upper cervical region, with migraines often presenting with accompanying symptoms such as nausea, vomiting, and photo- and phonophobia, while cluster headaches have one or more associated symptoms such as ipsilateral tearing, injection, rhinorrhoea, nasal stenosis, miosis, and/or ptosis [27]. Symptoms of ICAD can also be mild and, thus, may only be detected by coincidence, while asymptomatic cases are not diagnosed. When local symptoms are due to compression of adjacent structures, such as by aneurysm formation, peripheral

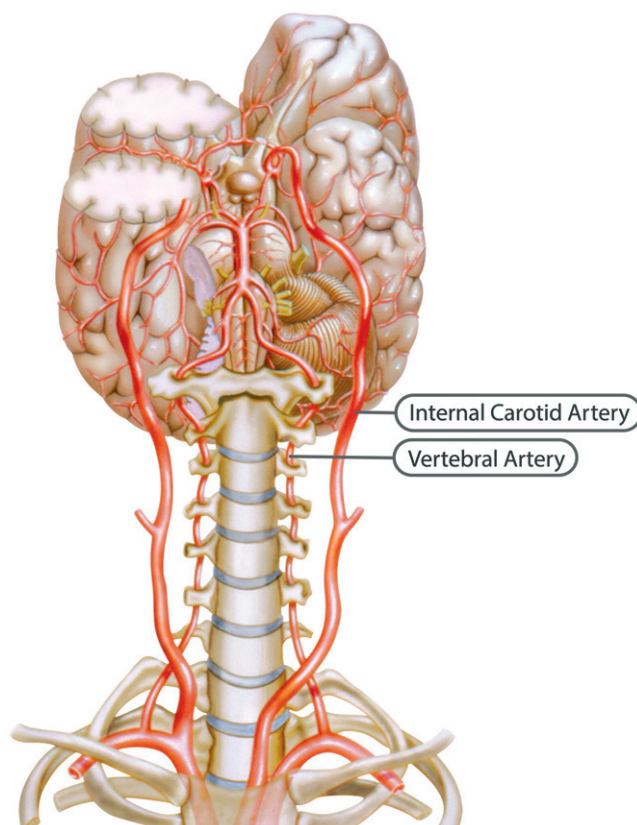


Figure 1. Vertebral and internal carotid arteries. Reprinted with permission by Jose Falcetti. josefalcetti@gmail.com.

cranial nerve involvement becomes apparent, commonly as N. hypoglossus and less commonly as N. accessories, N. vagus, or N. glossopharyngeus, as these cranial nerves are in close proximity to the carotid artery in the cervical region. An intracranial ICA rupture can cause subarachnoid haemorrhage, which causes a sudden onset of a severe headache. Thus, based on the ICA location, it is highly unlikely that mobilization and manipulative techniques that tend to be specific with minimal force and amplitude affect the ICAs.

Vertebral artery

The VAs supply blood to the posterior portion of the brain. Once the VAs project into the skull, the two VAs merge to form the basilar artery, which in turn feeds into the circle of Willis as the a. cerebri posteriors (Figure 1). Any disruption to the posterior circulation might, therefore, produce brainstem ischaemic symptoms, namely, ipsilateral loss of pain and contralateral temperature sensation in the body, ipsilateral hemiparesis, nausea, vomiting, vertigo, nystagmus, diplopia, dysphagia, dysarthria, dysphonia, and/or cerebellar ischaemic symptoms, such as ataxia, vertigo, and/or nystagmus. The location of pain symptoms in VAD varies. However, neck pain commonly involves the unilateral suboccipital region and is ipsilateral to the affected artery (Figure 2), while the character of the new and sudden onset headache is similar to that of ICAD but with a unilateral and suboccipital location [25,27]. As the VA runs through the intervertebral foramen of the six cervical vertebrae (C1–C6), the VA is more vulnerable to mechanical stress than the ICA. The VA is thought to be most susceptible to injury due to extreme rotatory head movements, especially in the transverse foramen in the first cervical vertebrae, as the VA abruptly transitions from a vertical path to a horizontal orientation (Figure 1) [76]. Previous neck trauma has also been more commonly reported in VAD than in ICAD, which probably also relates to the vulnerable location of the artery. However, from a pragmatic view, all people execute several different head and neck movements every day, including side-to-side neck rotations that consequently stretch the VA. Fortunately, this usually does not trigger CAD.

Neck pain and CAD

Neck pain is often not specified in the CAD literature. By definition, neck pain is a subjective and personal

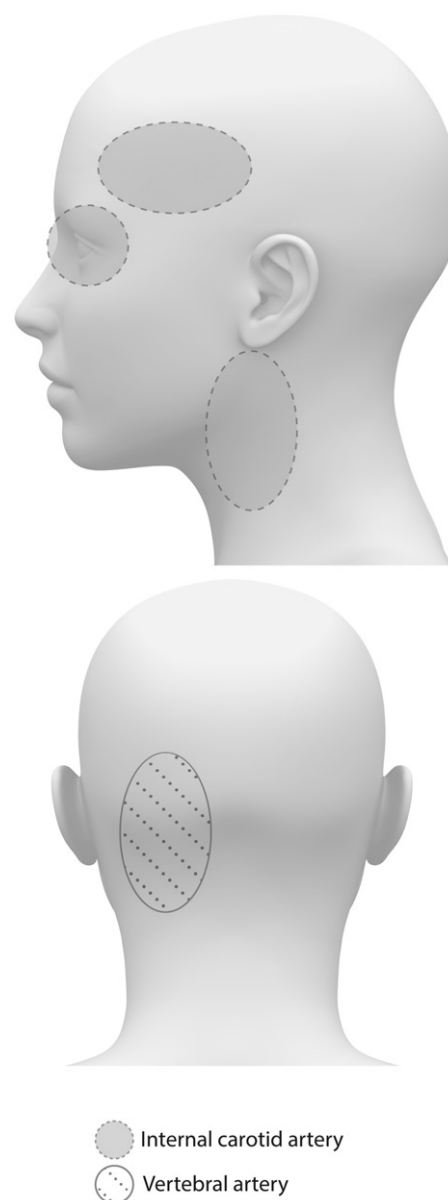


Figure 2. Typical pain distribution due to vertebral artery and internal carotid artery dissections.

experience, and in contrast to CAD, the first experience with neck pain often occurs early in life [77]. The 1-year prevalence of neck pain is up to 50% in the adult population, and up to 40% of the general population report having experienced neck pain in the past month [78]. Usually, neck pain presents in episodes during a lifetime with variable degrees of recovery between episodes [77]. However, when coexisting CAD is responsible for neck pain, the pain is often sudden, sharp, severe, steady and different from previously experienced neck pain [79,80]. In general, pain due to a vascular condition tends to present as throbbing, pounding, pulsing, and/or beating, while musculoskeletal pain conditions usually have an aching, sore, heavy, hurting, deep, cramping, and/or dull character [81].

The Bone and Joint Decade 2000–2010 Task Force on neck pain presented evidence-based guidelines for primary care clinicians to inform their assessments of neck pain [78]: For grade I, complaints of neck pain may be associated with stiffness or tenderness but no significant neurological complaints; for grade II, neck pain interferes with daily activities, but no signs or symptoms are evident to suggest major structural pathology or significant nerve root compression; for grade III, complaints of neck pain are associated with significant neurological signs; and for grade IV, neck pain includes complaints of neck pain and/or its associated disorders, and the examining clinician detects signs or symptoms suggestive of major structural pathology. A similar classification was proposed by the Quebec Task Force on whiplash-associated disorders but with a grading system from 0 to 4: For grade 0, no complaint of neck problems and no physical sign(s); for grade 1, neck pain, stiffness, or tenderness, with no physical sign(s); for grade 2, neck pain, stiffness, or tenderness, with musculoskeletal sign(s); for grade 3, neck pain, stiffness, or tenderness, with neurological signs; and for grade 4, neck fracture or dislocation [82]. Thus, for both classifications, grades 3 and 4 should warrant alertness by the clinician regarding possible CAD, and a careful history and thorough examination for other neurological signs should be obtained and performed as outlined in Figure 3.

Unfortunately, most clinical examinations have little or no proven usefulness, unless radiculopathy or serious structural disease is strongly suspected [83]. Musculoskeletal pain is often reproducible, namely, the pain can be provoked by active or passive provocative movements and relieved by certain movements that diminish the muscle tension, which is not the case if the pain is of vascular origin. Furthermore, vascular pain is not typically relieved by analgesics, but in VAD, the pain progresses around its known location, which is often occipital and medially along the nuchal line (Figure 2) [84]. Musculoskeletal neck stiffness often presents with a reduced rotational and/or lateral flexion range of motion with sharp, stabbing and/or stinging pain characteristics. A recent study of patients with acute neck pain investigated 1235 distinct cervical SMTs conducted by chiropractors and found that 74% of the cervical SMTs were conducted in the lower cervical spine [85]. Thus, although the literature is sparse on specific locations of mechanical musculoskeletal pain, mechanical neck pain appears to usually present in the lower cervical spine.

Thus, with common symptoms such as neck pain, stiffness, and/or tenderness, without a change in

response to mechanical provocation manoeuvres, the clinician should be alerted to a possible red flag. In situations where neurological deficits are also present along with the history of the musculoskeletal complaint, CAD should be suspected until proven otherwise (Figure 3).

Risk–benefit identification strategy assessment tool

The initial signs of CAD can be very difficult to detect. Therefore, a multifactorial approach must be considered when evaluating the risk–benefit ratio of any manual intervention, including mobilization and/or manipulation, with specific emphasis on history taking and the physical examination, in relation to a possible latent CAD. As there are known important risk factors for CAD that have been shown to increase the incidence rate, clinicians and, especially, manual therapists should specifically be aware of the importance of history taking (Figure 3). That is, environmental risk factors such as recent acute respiratory infection [1,4]; hyperhomocysteinaemia, namely, B-6, -9, and 12 vitamin deficiency [1,4]; a low body mass index and low cholesterol [1,4]; smoking [1]; and pulsating tinnitus [4]. While inherited risk factors include medical and/or family history of arterial anomalies and/or CAD, respectively [1,4], and connective tissue disorders, i.e. Ehlers–Danlos syndrome type IV, Marfan’s syndrome, Osteogenesis Imperfecta, or Loeys–Dietz syndrome [1,4] (Figure 3).

A significant amount of information is available to clinicians to help them understand and evaluate the risk–benefit ratio for any cervical manual intervention and the exclusion of CAD. Thus, Figure 3 outlines a risk–benefit assessment strategy that should provide additional knowledge and improve the vigilance of all clinicians to enable them to exclude CAD, refer patients with suspected CAD to appropriate care, and consequently prevent CAD from progressing. One report has argued that most patients present with at least two physical symptoms [86]. The clinical characteristics and recommendations in Figure 3 follow this assumption. This figure is intended to function as a knowledge base that should be implemented in preliminary screening and be part of good clinical practice. This knowledge base will likely contribute to sharpening the attention of the clinician and alert him or her as to whether the presenting complaint, combined with a collection of warning signs listed in Figure 3, deviates from what he or she considers to be a usual musculoskeletal presentation.

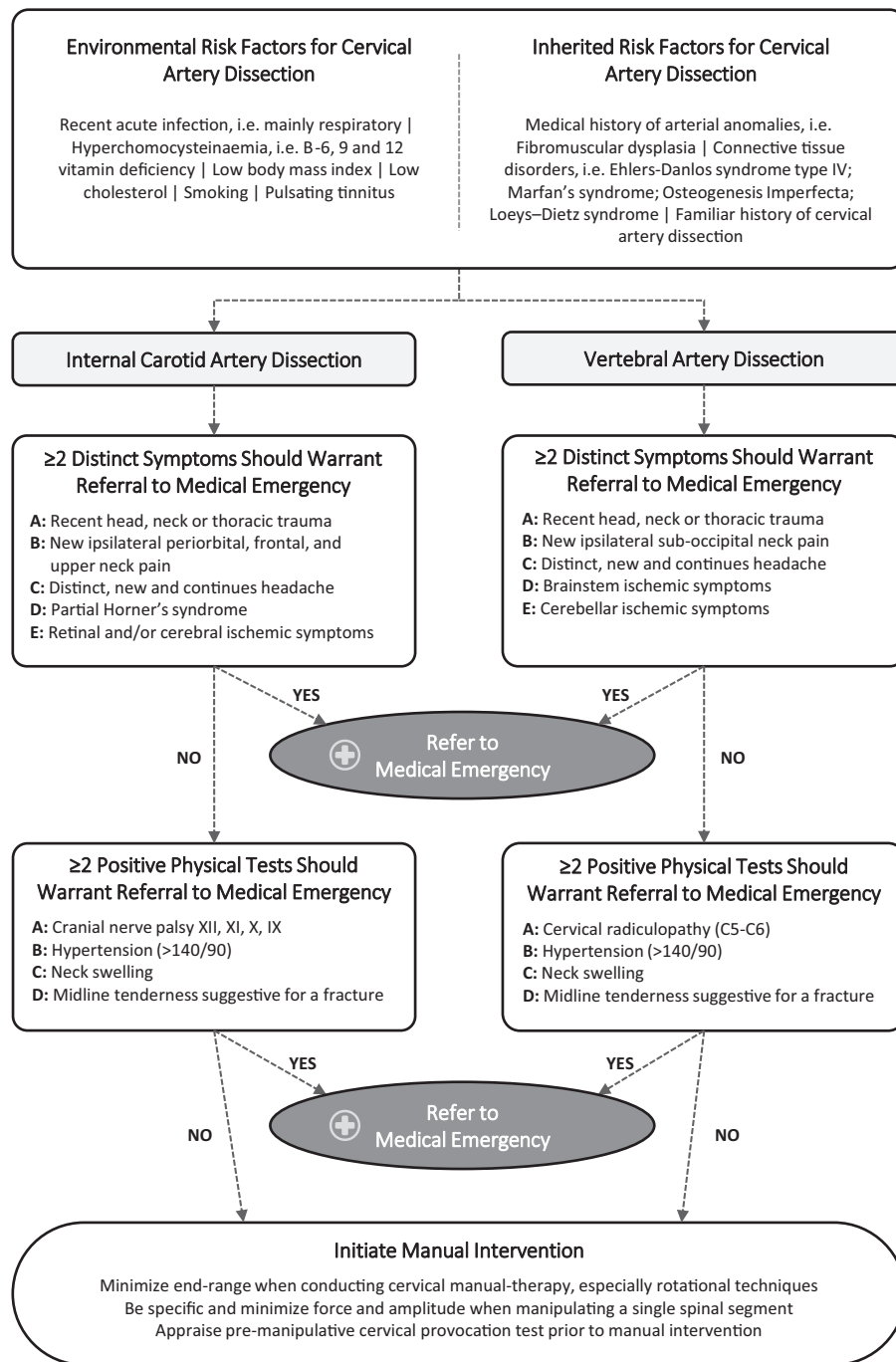


Figure 3. Step-by-step risk-benefit assessment strategy tool to exclude cervical artery dissection.

Discussion

This review outlines a systematic approach to exclude a serious and potential life-threatening disorder, such as CAD, within primary care and, especially, the manual-therapy clinical settings. The risk-benefit analysis tool is based on the most recent evidence and should benefit clinicians to help them better understand the many warning signs, especially if the presenting complaint deviates from what they consider to be the usual musculoskeletal presentation. Thus, this approach should

help clinicians refer patients to medical examinations and treatment immediately upon a suspicion of CAD.

Considering the rarity of CAD, which reportedly constitutes as few as 1 per 8.1 million chiropractic office visits and 1 per 5.9 million cervical manipulations by practising chiropractors in Canada [38], conducting sufficiently powered clinical manual-therapy randomized controlled trials to evaluate causality is nearly impossible. Naturally, one can suggest that to scientifically establish the prevalence of CAD as a

direct trigger of cervical mobilization and/or manipulation intervention, a prospective study would need to include 1000 manual therapists treating the cervical spine 100 times per week for 52 weeks. As a consequence, most manual-therapy randomized controlled trials have abundant type II errors.

The assumption that the cervical manual-therapy intervention triggers CAD in rare cases has been dominated by single-case reports and retrospective case series or surveys from neurologists who naturally lack substantial methodological quality to establish definitive causality [87]. These neurological case reports have probably contributed to an over-reporting of serious and catastrophic AEs compared to minor and moderate AEs, which are likely to occur more frequently [55,88]. In light of the evidence provided in this comprehensive review, the reality is (a) that there is no firm scientific basis for direct causality between cervical SMT and CAD; (b) that the ICA moves freely within the cervical pathway, while 74% of cervical SMTs are conducted in the lower cervical spine where the VA also moves freely; (c) that active daily life consists of multiple cervical movements including rotations that do not trigger CAD, as is true for a range of physical activities; and (d) that a cervical manipulation and/or grade C cervical mobilization goes beyond the physiological limit but remains within the anatomical range, which theoretically means that the artery should not exceed failure strain. These factors underscore the fact that no serious AE was reported in a large prospective national survey conducted in the UK that assessed all AEs in 28,807 chiropractic treatment consultations, which included 50,276 cervical spine manipulations [50].

While no mechanical event is reported in one-third of patients, spontaneous CAD has been reported to be caused by minor traumas to the neck from various activities, namely, skating, tennis, basketball, volleyball, swimming, scuba diving, weight lifting, dancing, yoga, jumping on a trampoline, roller coaster rides, sexual intercourse, coughing or sneezing and dental procedures, while traumatic CAD, a major trauma is present, namely, neck fractures, spinal cord injuries, and muscular tears [36,37,89]. Minor traumas together with a recent infection may contribute to the hypothesized direct injury or weakness in the vessel wall, respectively, while increased systolic blood pressure can contribute to arterial stiffness [90]. Thus, these factors must be incorporated in the risk–benefit assessment and in the evaluation of the true musculoskeletal problem presentation versus a latent CAD.

An intervention with a proven effect for a range of musculoskeletal disorders cannot be without risk. However, instead of proving a nearly impossible causality hypothesis that today is based on insufficient and poorly descriptive case studies, focus should be directed to the early detection and exclusion of CAD, and questions should be raised on how to minimize the risk.

History taking, especially regarding the time of symptom onset, is the single most important factor for detecting subtle symptoms of CAD; thus, primary care clinicians and, especially, manual therapists should dedicate enough time during the first consultation to allow for thorough history taking and physical examination. During history taking, follow-up of the patient's answers in relation to his or her (new) neck pain and/or headache is extremely important to obtain sufficient knowledge and understanding, and one must not accept a simple yes or no answer. In cases with suspicion of high-risk CAD, which contain a combination of several warning signs, there should be an immediate referral to the medical emergency department. If time allows, this referral can include a short description of the clinician's report of his or her findings. In time, this vigilant act by a professional may contribute to closer cooperation and mutual respect between physicians and manual therapists, which is highly important for improving the efficiency of today's healthcare and ultimately benefits patients.

There is no sufficient evidence to support cervical VA tests to identify patients with a higher risk, and the validity and reliability of these tests are low [91]. A recent guideline by the Australian Physiotherapy Association suggests that sustained cervical rotation might be an alternative test to assess for blood flow insufficiency in a controlled way [92]. However, the validity and reliability of this new test conforms to the same uncertainties as previous tests for vascular insufficiency [91]. Thus, in the absence of a physical vascular screening test, manual therapists would need to rely on a thorough history and clinical reasoning to follow the principles of do-no-harm.

Although the chiropractic profession evolved in the early nineteenth hundreds as an art, philosophy, and science, neck manipulation should not resemble a martial art. Thus, when cervical manipulation techniques are being conducted, one must be specific when manipulating a single spinal segment, minimizing the end range in cervical techniques, especially rotational techniques, and minimizing force, all of which have been recommended to reduce the risk of serious AEs [93].

We propose that considering the risk–benefit assessment tool outlined in [Figure 3](#), clinicians will consequently enhance decision-making with respect to differential diagnoses and enable the detection of a larger number of latent and possible progressive CADs, regardless of the actual manual intervention.

Disclosure statement

The authors have completed the ICMJE uniform disclosure form and declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

The first and lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies in the study as originally planned have been explained.

ORCID

Aleksander Chaibi  <http://orcid.org/0000-0003-2566-5984>

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