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Cervical Artery Dissection

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James Demetrious, DC, DABCO

Clinician
- Active Practice >38 years
- Diplomate, American Board of Chiropractic Orthopedists
- Diplomate, International Academy of Neuromusculoskeletal Medicine

Publications
- Over 31 Peer-Reviewed chiropractic journal articles.
- Many Contributions to NCMIC Examiner and Podcast

Educator
- Post-Grad. > 24 years
- NCMIC Speakers' Bureau for>10 years
- Northeast College of Health Sciences
- **PostGradDC**

Editorial
- Editorial Reviewer for journals *Spine*, *Annals of Internal Medicine*, and *Clinical Anatomy*
- Former Managing Editor of *Journal of Chiropractic Orthopedists*

Honors
- Academy of Chiropractic Orthopedists Distinguished Service and Fellow Awards
- American College of Chiropractic Orthopedists Outstanding Achievement Award

Community
- Lower Cape Fear Hospice, Board Member
- Founder, Past-President Wilmington Autism Society
- Optimists Club – Safety Officer

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Purpose...

History taking is the single most important factor for detecting subtle symptoms of CAD.

Chaibi A, Russell MB. A risk-benefit assessment strategy to exclude cervical artery dissection in spinal manual-therapy: a comprehensive review. *Ann Med*. 2019;51(2):118-127.

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Syllabus

- **We will review:**
  - Arterial Dissections and Stenosis
  - The Research
  - Incidence rate of CAD.
  - The rarity of CAD that makes the provision of epidemiological evidence challenging.
  - Bad Science – The Lack of Causality
  - Several extensive cohort studies and meta-analyses have found no excess risk of CAD resulting in secondary ischemic stroke for chiropractic SMT compared to primary care.
  - Retrospective cohort studies have reported no association with traumatic injury to the head or neck after SMT for neuromusculoskeletal pain.
  - Studies that have disproven any misconception about whether SMT strains exceed failure strains.
  - 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.
  - CAD Assessment Tool
  - Cases

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Dissections...

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frontiers | Frontiers in Cardiovascular Medicine

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Arterial dissections: Common features and new perspectives

Monique Bax[1,2], Valentin Romanov[1,2], Keerat Junday[1,2], Eleni Giannoulatou[1,2], Boris Martinac[1,2], Jason C. Kovacic[1,2,3,4], Renjing Liu[1,2], Siiri E. Iismaa[1,2] and Robert M. Graham[1,2,3]*

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- Arterial dissections, which involve an abrupt tear in the wall of a major artery resulting in the intramural accumulation of blood, are a family of catastrophic disorders causing major, potentially fatal sequelae.
- Involving diverse vascular beds, including the aorta or coronary, cervical, pulmonary, and visceral arteries, each type of dissection is devastating in its own way.

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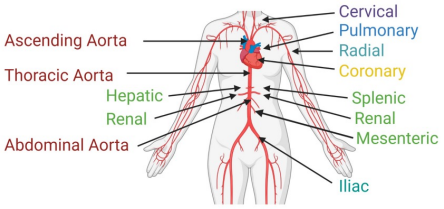

Artery	Intimal Medial Thickness (mm)	Reported Incidence Rates	References
Ascending Aorta	1.48	Most Common 10 cases/100,000 person-years (thoracic); Ascending more common than descending	Bae 2003 Saliba 2015 Roberts 1991
Descending Aorta	1.39		
Abdominal Aorta	1.24	Least Common Aortic Dissection Subtype	Sumbul 2019 Roberts 1991
Coronary Artery	0.75	Less Common 2.7 cases/100,000 person-years	Fayad 2000 Kronzer 2020
Cervical Artery	0.66	Less Common 2.6 cases/100,000 person-years	Eigenbrodt 2007 Lee 2006
Renal Artery	0.50	Rare Estimated 1-2% arterial dissections	Leertouwer 1999 Jha 2020
Pulmonary Artery	0.16	Very Rare ~150 cases reported	Li 2012 Fernando 2019

FIGURE 1
Arterial dissections are reported in large- and medium-sized arteries throughout the body at varying frequencies within the population. The risk of dissection varies with sex and age. Reported incidences correlate with average intimal medial thickness. Created with BioRender.com.

Bax M, et al. (2022) Arterial dissections: Common features and new perspectives. Front. Cardiovasc. Med. 9:1055862.

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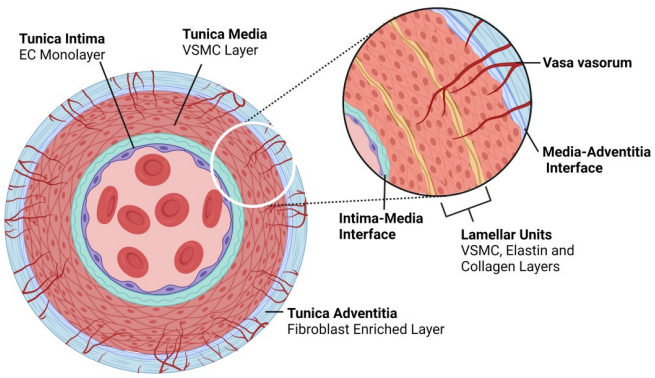

FIGURE 2
Typical architecture of medium to large, elastic and muscular arteries. Arteries comprise of three layers – the tunica intima is the innermost layer consisting of an endothelial monolayer; abluminal this monolayer is an ECM membrane located between the intima and the media, the latter being the second layer of the artery. The tunica media is concentrically layered with lamellar units of VSMCs bounded by elastin- and collagen-rich fibers. In larger arteries, the media is perfused by capillaries known as vasa vasorum, which enter the media through the outermost layer, the tunica adventitia; an ECM and fibroblast-rich layer. Created with BioRender.com.

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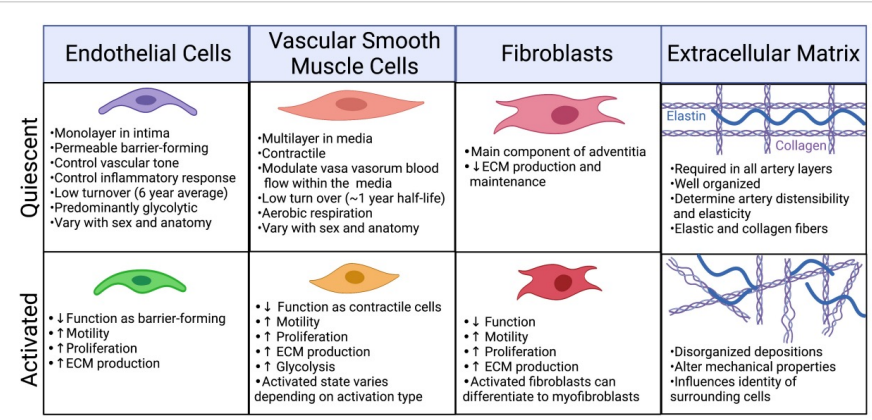

FIGURE 3
Phenotypic changes in the cellular and extracellular components of the artery in response to injury/infection. Created with BioRender.com.

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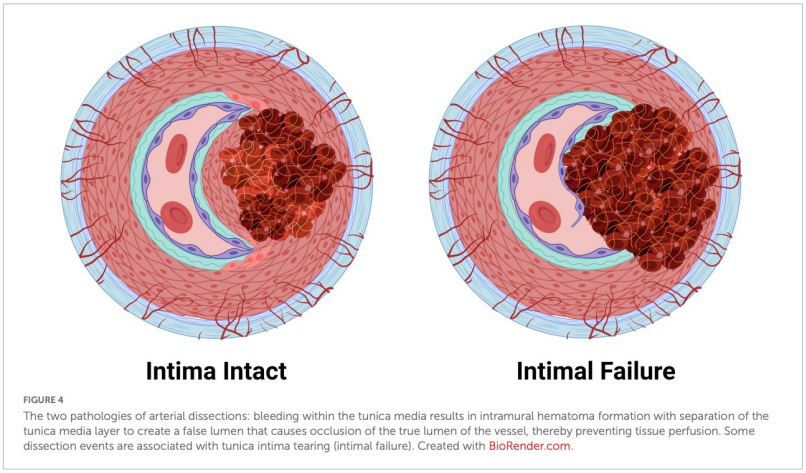

FIGURE 4
The two pathologies of arterial dissections: bleeding within the tunica media results in intramural hematoma formation with separation of the tunica media layer to create a false lumen that causes occlusion of the true lumen of the vessel, thereby preventing tissue perfusion. Some dissection events are associated with tunica intima tearing (intimal failure). Created with BioRender.com.

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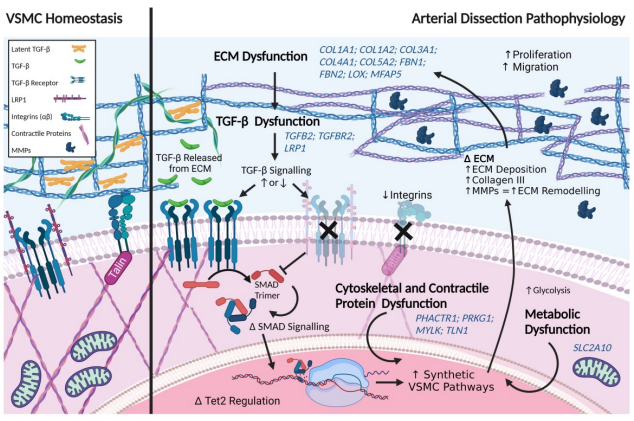

FIGURE 6
Pathways perturbed in arterial dissections include the extracellular matrix (ECM), TGF-β, signaling, cellular contraction/cytoskeleton, and metabolism. Dysregulation in any number of these pathways can drive vascular smooth muscle cells (VSMCs) toward a more synthetic phenotype. Variants in the same genes (italicized in blue) belonging to these pathways have been commonly identified in at least two types of arterial dissections. Created with BioRender.com.

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Innovation

Solution

CAT-7 is a simple blood-based diagnostic test for cerebral aneurysm detection and monitoring. Testing with CAT-7 begins with collection of blood from a patient. The collected blood is then transferred onto a proprietary membrane utilizing industry standard enzyme-linked immunosorbent assay (ELISA) technology. This membrane has 7 antibody spots that correspond to the 7 biomarkers we are measuring. The membrane is imaged using an ELISA reader, which are common in most hospital laboratories and used for a variety of other blood-based tests.

The measurements for the biomarkers from the ELISA reader are then input into our algorithm. The algorithm then provides a patient's probability of having an aneurysm and their risk of rupture metric.

Over 233 unique samples from patients with and without cerebral aneurysms were collected for our study and helped validate our technology. **Our test reports accuracy of 90%, with a sensitivity of 95%, specificity of 70%, PPV 84%, NPV 90%, and p-value 0.0027**. In addition, we report 90.9% accuracy (100% sensitivity and 90% specificity) in identifying inflammatory profiles at high-risk for rupture. We estimate CAT-7 can be performed at 1/100th of the cost of the current standard of care, opening the door for screening and regular monitoring.

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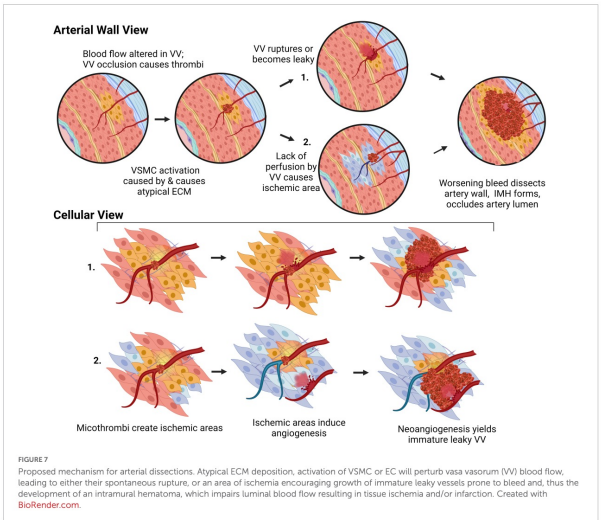

FIGURE 7
Proposed mechanism for arterial dissections. Atypical ECM deposition, activation of VSMC or EC will perturb vasa vasorum (VV) blood flow, leading to either their spontaneous rupture, or an area of ischemia encouraging growth of immature leaky vessels prone to bleed and, thus the development of an intramural hematoma, which impairs luminal blood flow resulting in tissue ischemia and/or infarction. Created with BioRender.com.

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TABLE 1 Arterial dissection associated conditions.

Condition	Description	Genes with pathogenic variants	Prevalence	Sexual dimorphism	Dissection associated	References
Ehlers–Danlos (EDS)	CTD; hyperextendable joints, hyperextensible skin, easy bruising, abnormal scarring; vascular EDS subtype, and in 17% 13 non-vascular EDS have vascular involvement	*COL1A1, COL1A2, COL5A1, COL5A2, COL3A1, COL12A, ADAMTS2, PLOD1, FKBP14, TNXB, CHST14, DSE, B4GALT7, B3GALT6, SLC39A13, ZNF469, PRDM5, C1R, C1S, AEBP1*	1:5,000	Dissection types vary by gender	CeAD, aortic, SCAD	(98, 264–268)
Marfan syndrome	CTD; affects the ocular, skeletal, and cardiovascular systems with varying severity	*FBN1*	1:5,000–1:10,000	Sex related burden (pregnancy increases aortic root dilation)	CeAD, aortic, SCAD, PA	(109, 157, 220, 269–272)
Loeys-Dietz syndrome	CTD; affects the skin, skeletal and cardiovascular system	*TGFBR1, TGFBR2, SMAD3, TGFB2*	Less than 1:10,000	NA	CeAD, aortic, SCAD	(273–275)
Alport syndrome	Affects the renal, auditory and ocular systems. Hypertension increases risk of cardiovascular events 1000 fold.	*COL4A3, COL4A4, COL4A5*	1:10,000	X-linked in 85% cases	Aortic, SCAD	(276–279)
Fibromuscular dysplasia	Abnormal (dysplastic) cell growth in medium-sized arteries causing tortuosity	*PHACTR1*	Up to 6.6% population (potential kidney donors)	90% patients female; male patients significantly associated with CeAD	CeAD, SCAD	(157, 166, 171, 280, 281)
Polycystic kidney disease	Kidney cyst formation, cardiovascular	*PKD1, PKD2*	10M people globally	NA	CeAD, Aortic, SCAD, iliac	(34, 175, 282–284)
Osteogenesis imperfecta	Brittle bones disease	*COL1A1, COL1A2, BMP1, CRTAP, LEPRE1, PPIB, TMEM38B, SERPINH1, FKBP10, PLOD2, WNT1, CREB3L1*	1:20,000	NA	CeAD, aortic, SCAD	(229, 285–289)

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Cureus
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DOI: 10.7759/cureus.28068

Vertebral Artery Stenosis: A Narrative Review

Venkata Sathya Burle [1], Amelia Panjwani [2], Kesava Mandalaneni [3], Sunitha Kollu [4], Vasavi Rakesh Gorantla [5]

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Review began 08/08/2022
Review ended 08/12/2022
Published 08/16/2022

- The true incidence of vertebral artery stenosis is not known due to the cases of asymptomatic stenosis of the vertebral artery.
- In a study conducted with 3,717 patients, 7.6% (6.8% to 8.5%, CI of 95%) of patients, who exhibited symptoms of atherosclerotic arterial disease, had asymptomatic vertebral artery stenosis or occlusion [40].
- Therefore, it was concluded that there is a low risk of posterior circulation stroke in patients with asymptomatic vertebral artery stenosis [40].

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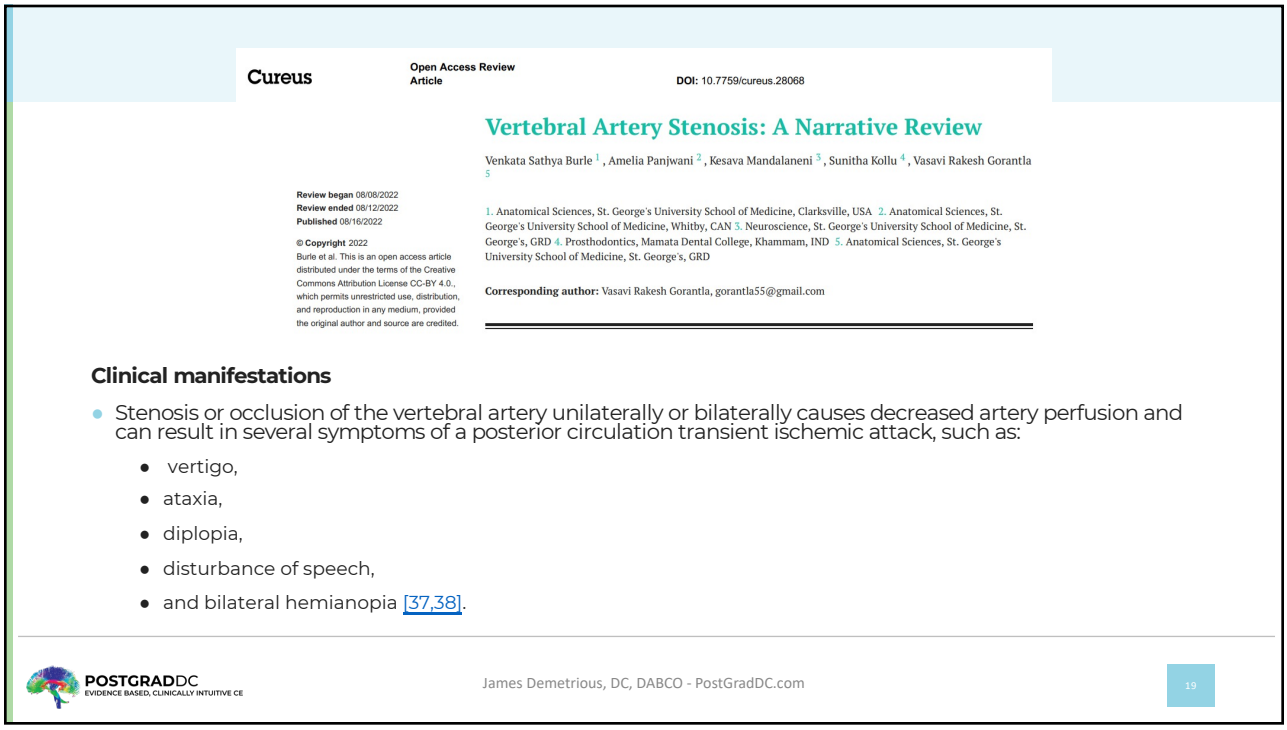

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Clinical manifestations

- Stenosis or occlusion of the vertebral artery unilaterally or bilaterally causes decreased artery perfusion and can result in several symptoms of a posterior circulation transient ischemic attack, such as:
  - vertigo,
  - ataxia,
  - diplopia,
  - disturbance of speech,
  - and bilateral hemianopia [37,38].

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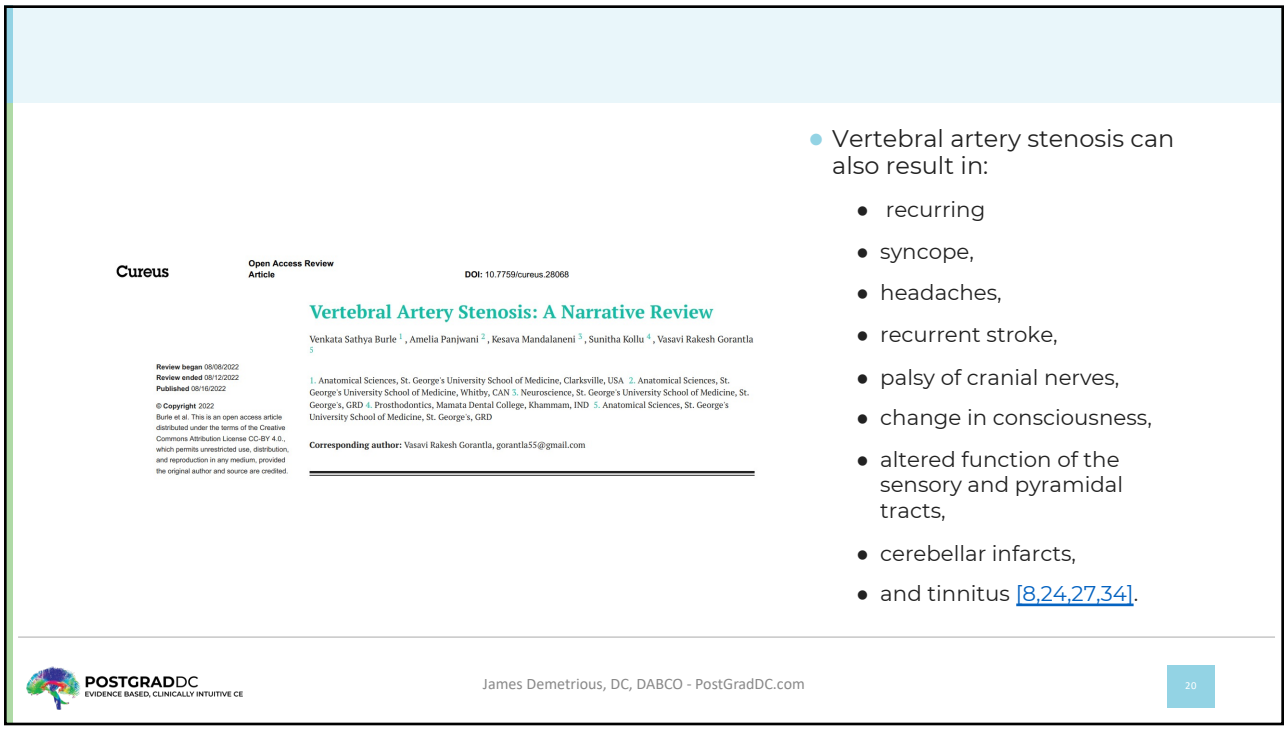

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- Vertebral artery stenosis can also result in:
  - recurring
  - syncope,
  - headaches,
  - recurrent stroke,
  - palsy of cranial nerves,
  - change in consciousness,
  - altered function of the sensory and pyramidal tracts,
  - cerebellar infarcts,
  - and tinnitus [8,24,27,34].

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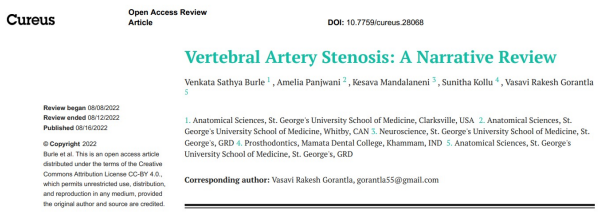

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- Vertebral artery stenosis can also result in decreased perfusion to the basilar artery and cause several symptoms, including:
  - vertigo,
  - dizziness,
  - diplopia,
  - ataxia,
  - dysarthria,
  - nausea,
  - nystagmus,
  - drop attacks,
  - loss of consciousness,
  - motor symptoms,
  - sensory symptoms such as numbness,
  - and an increased risk of experiencing strokes or transient ischemic attacks [6,16,30,32,39].
  - These symptoms are typically observed when there is stenosis or occlusion of both vertebral arteries [16].

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The Research...

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HEAD TO HEAD

Should we abandon cervical spine manipulation for mechanical neck pain? No

Benedict Wand and colleagues (doi:10.1136/bmj.e3679) argue that the risks of cervical spine manipulation are not justified, but **David Cassidy and colleagues** think it is a valuable addition to patient care

J David Cassidy *professor* [1], Gert Bronfort *professor*[2], Jan Hartvigsen *professor*[3]

[1]Division of Epidemiology, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada; [2]Department of Research, Northwestern Health Sciences University, Bloomington, Minnesota, USA; [3]Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark

BMJ 2012;344:e3680

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- The most recent study, by Cassidy et al, replicated the results of the two previous studies using the Ontario population over nine years—that is, over 100 million person years at risk.9
- They confirmed a strong association between chiropractic care and subsequent vertebrobasilar stroke in people under 45 years old using both case-control and case-crossover designs (odds ratio 3.60, 1.46 to 10.84) for those consulting a chiropractor in the previous month.
- However, they found a similar association between family physician care and vertebrobasilar strokes.

BMJ 2012;344:e3680

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The Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders

Executive Summary

Vertebrobasilar Stroke Study Findings

- There was an association between chiropractic services and subsequent vertebrobasilar artery stroke in persons under 45 years of age, but a similar association was also observed among patients receiving general practitioner services.
- This is likely explained by patients with vertebrobasilar artery dissection-related neck pain or headache seeking care before having their stroke.

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The Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders

Executive Summary

- The Task Force consisted of committee members originated from 9 countries and represented 19 clinical and scientific disciplines or specialties.
- The Task Force was affiliated with 8 collaborating universities and research institutes in 4 countries, and 11 professional organizations agreed to become non-financial sponsors.

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The Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders

Executive Summary

- A total of 31,878 citations were screened, and 1203 relevant articles were accepted for review.
- Ultimately, some 552 scientific papers were deemed to be scientifically admissible for the best evidence synthesis.
- In addition, a number of original research projects were conducted within the Task Force mandate.

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AHA/ASA Scientific Statement

Cervical Arterial Dissections and Association With Cervical Manipulative Therapy

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

- Although the incidence of CD in CMT patients is probably low, **[???]** and causality difficult to prove, **[???]** practitioners should both strongly consider the possibility of CD **[???]** and inform patients of the statistical association **[???]** between CD and CMT, prior to performing manipulation of the cervical spine.

Stroke. 2014;45:3155-3174.

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To DX the Developing CAD, We Must Consider…

- Risk Factors
- Symptoms
- Signs

Extraordinarily difficult. CADs are rare. Most doctors will never see this problem. Patients often do not provide detailed histories despite our best efforts.

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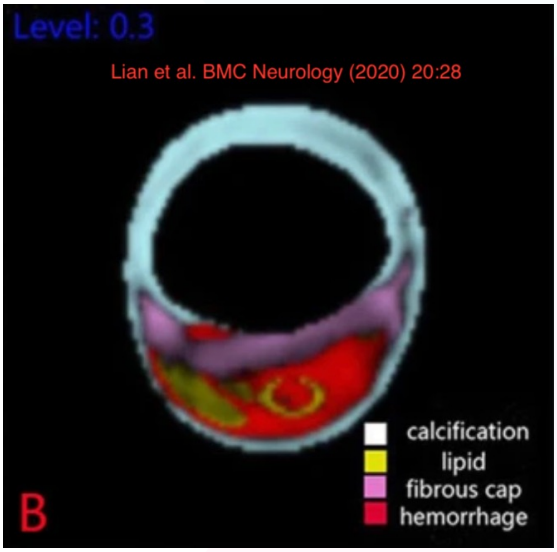
Manual therapy does not result in an increased risk of CAD

The World Health Organization regards manual mobiization 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].

Chaibi and Russell. ANNALS OF MEDICINE. 2019, VOL. 51, NO. 2, 118–127.



30

Mild, Transient AEs

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Chaibi and Russell. ANNALS OF MEDICINE. 2019, VOL. 51, NO. 2, 118–127.

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> J Manipulative Physiol Ther. 2008 Jul-Aug;31(6):461-4. doi: 10.1016/j.jmpt.2008.06.001.

Adverse events following chiropractic care for subjects with neck or low-back pain: do the benefits outweigh the risks?

Sidney M Rubinstein [1]

Affiliations – collapse

Affiliation

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PMID: 18722202 DOI: 10.1016/j.jmpt.2008.06.001

- Most adverse events associated with spinal manipulation are benign and self-limiting.
- The incidence of severe complications following chiropractic care and manipulation is extremely low.
- The best evidence suggests that chiropractic care is a useful therapy for subjects with neck or low-back pain for which the risks of serious adverse events should be considered negligible.

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Incidence Rates and Rarity of CAD

- Fortunately, the incidence rate of CAD is relatively low, estimated at 2.9/100,000 individuals per year in the general population.
  - Bejot Y, Daubail B, Debette S, et al. Incidence and outcome of cerebrovascular events related to cervical artery dissection: the Dijon Stroke Registry. Int J Stroke. 2014;9:879–882.
- Internal carotid artery dissections (ICADs) occur approximately 3–5 times more frequently than vertebral artery dissections (VADs).
  - Hart RG, Easton JD. Dissections of cervical and cerebral arteries. Neurol Clin. 1983;1:155–182.
  - Debette S, Leys D. Cervical-artery dissections: predisposing factors, diagnosis, and outcome. Lancet Neurol. 2009;8:668–678.

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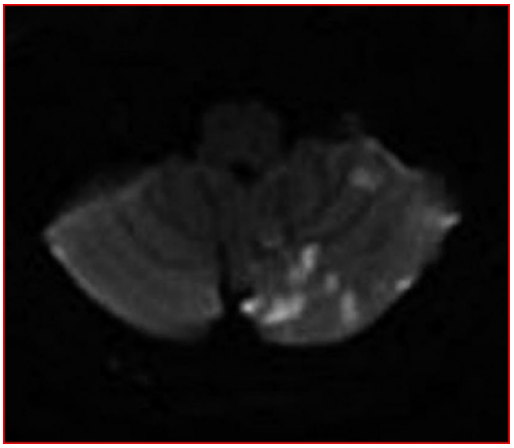
Bad Science – A Lack of Causality

Chiropractic Manipulation of the Neck and Cervical Artery Dissection

Background: Chiropractic manipulation of the neck can cause cervical artery dissection and stroke, although the incidence of these complications is unknown (1–4). Patients younger than 45 years with vertebral artery dissection and stroke are 5 times more likely to have visited a chiropractor in the previous 30 days than an age-matched control group (1).

Case Report: In mid-March 2012, a 37-year-old registered nurse with a history of chronic neck pain went to her chiropractor. She had seen the same chiropractor for 12 to 15 years, usually going once a month for cervical spine manipulation. Because of a new symptom (pain when turning her head up and to the right), the current visit had been the fourth in a week. From the patient's perspective, the manipulation done during the current visit was similar to past procedures.



17 July 2012 | Annals of Internal Medicine | Volume 157 • Number 2 | 151

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Bad Science – A Lack of Causality

Conclusion: Although incidence of cervical artery dissection precipitated by chiropractic neck manipulation is unknown, it is an important risk (3, 4). Given that risk, physical therapy exercises may be a safer option than spinal manipulation for treating patients with neck pain.

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17 July 2012 | Annals of Internal Medicine | Volume 157 • Number 2 | 151

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Bad Science – A Lack of Causality

Case report

A near-fatal consequence of chiropractor massage: massive stroke from carotid arterial dissection and bilateral vertebral arterial oedema

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[1]Curtin Medical School, Faculty of Health Sciences, Curtin University, Perth, Western Australia, Australia
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Accepted 27 July 2021

SUMMARY
A 35-year-old Chinese man with no risk factors for stroke presented with a 2-day history of expressive dysphasia and a 1-day history of right-sided weakness. The presentation was preceded by multiple sessions of neck, shoulder girdle and upper back massage for pain relief in the prior 2 weeks. CT of the brain demonstrated an acute left middle cerebral artery infarct and left internal carotid artery dissection. MRI cerebral angiogram confirmed left carotid arterial dissection and intimal oedema of bilateral vertebral arteries. In the absence of other vascular comorbidities and risk factors, massage-induced internal carotid arterial dissection will most likely precipitate the near-fatal cerebrovascular event. The differential diagnosis of stroke in a younger population was consequently reviewed and discussed.

BACKGROUND
Internal carotid artery dissection, the separation of the tunica media and tunica intima of the internal carotid artery, can lead to cerebral infarction in up to two-thirds of patients,[1] accounting for up to in a healthy man, in which symptom onset coincided solely with massage and neck manipulation. We propose that massage and neck manipulation is an independent risk factor for developing internal carotid artery dissection in healthy individuals. Furthermore, our case highlights the importance of including internal carotid artery dissection in the differential diagnosis of cerebral vascular events in younger patients.

CASE PRESENTATION
A 35-year-old Chinese man was brought to the emergency department by a friend, from home alone with a 2-day history of expressive dysphasia and 1 day of right-sided weakness. On collateral history, the presentation was preceded by multiple sessions of neck, shoulder girdle and upper back massage for pain relief in the prior 2 weeks while he was away on a business trip. He denies having any associated fever, headache, nausea, vomiting, palpitations, syncope, incontinence and neck stiffness. His medical history was unremarkable and was not on any medications or herbal remedies.

- This study has demonstrated that the literature infrequently reports useful data toward understanding the association between cSMT, CADs and stroke.
- Improving the quality, completeness, and consistency of reporting adverse events may improve our understanding of this important relation.

36

Refuting Bad Science

Review > J Manipulative Physiol Ther. 2015 Nov-Dec;38(9):672-676.
doi: 10.1016/j.jmpt.2013.09.005. Epub 2014 Jan 3.

The Association Between Cervical Spine Manipulation and Carotid Artery Dissection: A Systematic Review of the Literature

Chadwick L R Chung [1], Pierre Côté [2], Paula Stern [3], Georges L'Espérance [4]
Affiliations + expand
PMID: 24387889 DOI: 10.1016/j.jmpt.2013.09.005

- Although several case reports and case series raise the hypothesis of an association, we found no epidemiologic studies that validate this hypothesis.

37

Bad Science – A Lack of Causality

Review > J R Soc Med. 2007 Jul;100(7):330-8. doi: 10.1177/014107680710000716.

Adverse effects of spinal manipulation: a systematic review

E Ernst [1]
Affiliations – collapse

Affiliation

1 Complementary Medicine, Peninsula Medical School, Universities of Exeter & Plymouth, Exeter, UK. Edzard.Ernst@pms.ac.uk

- In conclusion, spinal manipulation, particularly when performed on the upper spine, has repeatedly been associated with serious adverse events.

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Refuting Bad Science

Tuchin *Chiropractic & Manual Therapies* 2012, **20**:30
http://chiromt.com/content/20/1/30

CHIROPRACTIC & MANUAL THERAPIES

RESEARCH Open Access

A replication of the study 'Adverse effects of spinal manipulation: a systematic review'

Peter Tuchin*

- The number of errors or omissions in the 2007 Ernst paper, reduce the validity of the study and the reported conclusions.
- The omissions of potential risk factors and the timeline between the adverse event and SMT could be significant confounding factors.
- Greater care is also needed to distinguish between chiropractors and other health practitioners when reviewing the application of SMT and related adverse effects.

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Bad Science – A Lack of Causality

AHA/ASA Scientific Statement

Cervical Arterial Dissections and Association With Cervical Manipulative Therapy

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

- Although the incidence of CD in CMT patients is:
  - probably low, [???]
  - and causality difficult to prove, [???]

  practitioners should both strongly consider the possibility of CD [???] and inform patients of the statistical association [???] between CD and CMT, prior to performing manipulation of the cervical spine.

Stroke. 2014;45:3155-3174.

40

OPEN ACCESS Freely available online

PLOS ONE

The Quality of Reports on Cervical Arterial Dissection following Cervical Spinal Manipulation

Shari Wynd[1]*, Michael Westaway[2], Sunita Vohra[3,4], Greg Kawchuk[5]

1 Texas Chiropractic College, Pasadena, Texas, United States of America, 2 Lifemark Health, University of Alberta, Calgary, Alberta, Canada, 3 Department of Pediatrics, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada, 4 Complementary and Alternative Research and Education Program, Pediatric Complementary and Alternative Medicine Research and Education Network, Alberta Innovates Health Solutions, Edmonton, Alberta, Canada, 5 Department of Physical Therapy, University of Alberta, Edmonton, Alberta, Canada

"This study has demonstrated that the literature infrequently reports useful data toward understanding the association between cSMT, CADs and stroke."

41

Refuting Bad Science

- A few case studies have reported serious AEs following cervical spinal manipulative therapy (SMT), 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].
  - [40] Rubinstein SM. Adverse events following chiropractic care for subjects with neck or low-back pain: do the benefits outweigh the risks? J Manipulative Physiol Ther. 2008;31:461–464.
  - [41] Tuchin P. A replication of the study 'Adverse effects of spinal manipulation: a systematic review'. Chiropr Man Ther. 2012;20:30.
  - [42] Wynd S, Westaway M, Vohra S, et al. The quality of reports on cervical arterial dissection following cervical spinal manipulation. PLoS One. 2013;8:e59170.
  - [43] Chung CL, Cote P, Stern P, et al. The association between cervical spine manipulation and carotid artery dissection: a systematic review of the literature. J Manipulative Physiol Ther. 2015;38:672–676.

Chaibi and Russell. ANNALS OF MEDICINE. 2019, VOL. 51, NO. 2, 118–127.

42

Bad Science – A Lack of Causality

PLOS ONE

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RESEARCH ARTICLE

The Quality of Reports on Cervical Arterial Dissection following Cervical Spinal Manipulation

Shari Wynd, Michael Westaway, Sunita Vohra, Greg Kawchuk

Published: March 20, 2013 • https://doi.org/10.1371/journal.pone.0059170

- This study has demonstrated that the literature infrequently reports useful data toward understanding the association between cSMT, CADs and stroke.
- Improving the quality, completeness, and consistency of reporting adverse events may improve our understanding of this important relation.

43

Bad Science – A Lack of Causality

Case Reports › Vasc Endovascular Surg. 2022 Apr;56(3):303-307.

doi: 10.1177/15385744211072660. Epub 2021 Dec 31.

Carotid Artery Dissection and Ischemic Stroke Following Cervical Chiropractic Manipulation: Two Case Reports

Yimin Chen [1], Mohammad Mofatteh [2], Thanh N Nguyen [3], Jack Wellington [4], Wenlong Wei [1], Wenjun Liang [1], Gan Chen [1], Zhaohui Hu [5], Kexun Ouyang [6], Shuiquan Yang [1]

Affiliations + expand

PMID: 34971321 DOI: 10.1177/15385744211072660

- Although there is no direct evidence that chiropractic manipulation causes cervical artery dissection, clinical reports have found that mechanical forces may contribute to cervical artery dissections.

44

No Excess Risk of CAD

- 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].
  - [39] Cassidy JD, Boyle E, Cote P, et al. Risk of vertebrobasilar stroke and chiropractic care: results of a population-based case–control and case-crossover study. Spine (Phila, PA, 1976). 2008;33:S176–S183.
  - [44] Cassidy JD, Boyle E, Cote P, et al. Risk of carotid stroke after chiropractic care: a population-based case-crossover study. J Stroke Cerebrovasc Dis. 2017; 26:842–850.
  - [68] Church EW, Sieg EP, Zalatimo O, et al. Systematic review and meta-analysis of chiropractic care and cervical artery dissection: no evidence for causation. Cureus. 2016;8:e498.

45

ANNALS OF MEDICINE
2019, VOL. 51, NO. 2, 118–127
https://doi.org/10.1080/07853890.2019.1590627
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REVIEW ARTICLE
OPEN ACCESS Check for updates

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]

[a]Head and Neck Research Group, Research Centre, Akershus University Hospital, Oslo, Norway; [b]Institute of Clinical Medicine, Akershus University Hospital, University of Oslo, Nordbyhagen, Norway

Manual therapy does not result in an increased risk of CAD.

- Cassidy et al. Risk of vertebrobasilar stroke and chiropractic care: results of a population-based case-control and case-crossover study. Spine. 2008;33(4 Suppl):S176-83.
- Church et al. Systematic review and meta-analysis of chiropractic care and cervical artery dissection: no evidence for causation. Cureus. 2016;8(2):e498.
- Cassidy et al. Risk of carotid stroke after chiropractic care: a population-based case-crossover study. J Stroke Cerebrovasc Dis. 2017;26(4):842-850.

46

Eur Spine J (2008) 17 (Suppl 1): S176-S183
DOI 10.1007/s00586-008-0634-9

Risk of Vertebrobasilar Stroke and Chiropractic Care

Results of a Population-Based Case-Control and Case-Crossover Study

J. David Cassidy, DC, PhD, DrMedSc,*†‡ Eleanor Boyle, PhD,* Pierre Côté, DC, PhD,*†‡§
Yaohua He, MD, PhD,* Sheilah Hogg-Johnson, PhD,†§ Frank L. Silver, MD, FRCPC,¶||
and Susan J. Bondy, PhD†

- The source population included all residents of Ontario (109,020,875 person-years of observation over 9 years) covered by the publicly funded Ontario Health Insurance Plan (OHIP).
- Available utilization data included hospitalizations with diagnostic coding, and practitioner (physician and chiropractic) utilization as documented by fee-for-service billings accompanied by diagnostic coding.

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Eur Spine J (2008) 17 (Suppl 1): S176-S183
DOI 10.1007/s00586-008-0634-9

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Yaohua He, MD, PhD,* Sheilah Hogg-Johnson, PhD,†§ Frank L. Silver, MD, FRCPC,¶||
and Susan J. Bondy, PhD†

- **Conclusion.**
  - VBA stroke is a very rare event in the population.
  - The increased risks of VBA stroke associated with chiropractic and PCP visits is likely due to patients with headache and neck pain from VBA dissection seeking care before their stroke.
  - We found no evidence of excess risk of VBA stroke associated chiropractic care compared to primary care.

48

Eur Spine J (2008) 17 (Suppl 1): S176-S183
DOI 10.1007/s00586-008-0634-9

Risk of Vertebrobasilar Stroke and Chiropractic Care

Results of a Population-Based Case-Control and Case-Crossover Study

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- There is an association between vertebrobasilar artery stroke and chiropractic visits in those under 45 years of age.
- We found no evidence of excess risk of VBA stroke associated chiropractic care.
- The increased risks of vertebrobasilar artery stroke associated with chiropractic and physician visits is likely explained by patients with vertebrobasilar dissection-related neck pain and headache consulting both chiropractors and primary care physicians before their VBA stroke.

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J Stroke Cerebrovasc Dis. 2017 Apr;26(4):842-850.
doi: 10.1016/j.jstrokecerebrovasdis.2016.10.031. Epub 2016 Nov 21.

Risk of Carotid Stroke after Chiropractic Care: A Population-Based Case-Crossover Study

J David Cassidy [1], Eleanor Boyle [2], Pierre Côté [3], Sheilah Hogg-Johnson [4], Susan J Bondy [5], Scott Haldeman [6]

Affiliations + expand

PMID: 27884458 DOI: 10.1016/j.jstrokecerebrovasdis.2016.10.031

- In 2017, Cassidy et al. published the results of a large population-based, case-crossover study in the Journal of Stroke and Cerebrovascular Diseases. The authors found **no excess of carotid artery stroke following chiropractic care and confirmed that patients sought care with early dissection related symptoms before developing strokes.**

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ARTICLE IN PRESS

Risk of Carotid Stroke after Chiropractic Care: A Population-Based Case-Crossover Study

J. David Cassidy, DC, PhD, DrMedSc,*†‡ Eleanor Boyle, PhD,*‡ Pierre Côté, DC, PhD,‡§ Sheilah Hogg-Johnson, PhD,‖¶ Susan J. Bondy, PhD,‡ and Scott Haldeman, MD, PhD#

- Positive associations were found for both chiropractic and PCP visits and subsequent stroke in patients less than 45 years of age.
- There was no significant difference between chiropractic and PCP risk.

Journal of Stroke and Cerebrovascular Diseases, Vol. ■■, No. ■■ (■■), 2016: pp ■■–■■

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No Causal Relationship

52

Cureus

Open Access Original Article

DOI: 10.7759/cureus.498

Systematic Review and Meta-analysis of Chiropractic Care and Cervical Artery Dissection: No Evidence for Causation

Ephraim W. Church [1], Emily P. Sieg [1], Omar Zalatimo [1], Namath S. Hussain [1], Michael Glantz [1], Robert E. Harbaugh [1]

1. Department of Neurosurgery, Penn State Hershey Medical Center

Corresponding author: Ephraim W. Church, echurch@hmc.psu.edu

Disclosures can be found in Additional Information at the end of the article

- In 2016, Church et al. reported, **"There is no convincing evidence to support a causal link between chiropractic manipulation and CAD."** The authors reported an unfounded belief in causation might have dire consequences.

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Open Access Original Article

DOI: 10.7759/cureus.498

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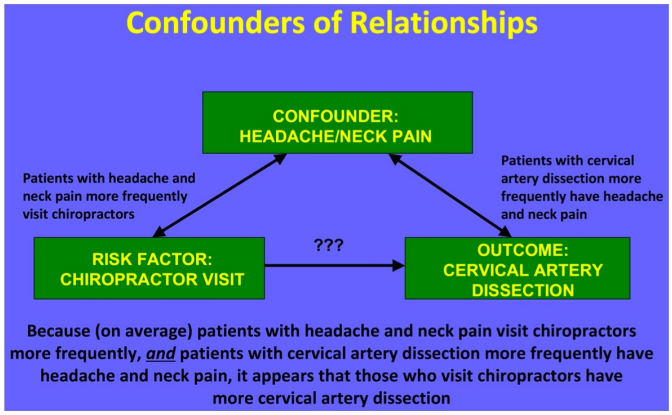

FIGURE 3: The association between a chiropractor visit and dissection may be explained by headache/neck pain, a likely confounder.

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J Stroke Cerebrovasc Dis. 2017 Apr;26(4):842-850.
doi: 10.1016/j.jstrokecerebrovasdis.2016.10.031. Epub 2016 Nov 21.

Risk of Carotid Stroke after Chiropractic Care: A Population-Based Case-Crossover Study

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55

Whedon et al. BMC Geriatrics (2022) 22:917
https://doi.org/10.1186/s12877-022-03495-5

BMC Geriatrics

RESEARCH Open Access

Association between cervical artery dissection and spinal manipulative therapy –a medicare claims analysis

James M Whedon[1*], Curtis L Petersen[2], Zhongze Li[2], William J Schoelkopf[3], Scott Haldeman[4], Todd A MacKenzie[2] and Jon D Lurie[2]

- **Conclusion** Among Medicare beneficiaries aged 65 and older who received cervical spinal manipulation, the risk of cervical artery dissection is no greater than that among control groups.

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Whedon *et al. BMC Geriatrics* (2022) 22:917
https://doi.org/10.1186/s12877-022-03495-5

BMC Geriatrics

RESEARCH Open Access

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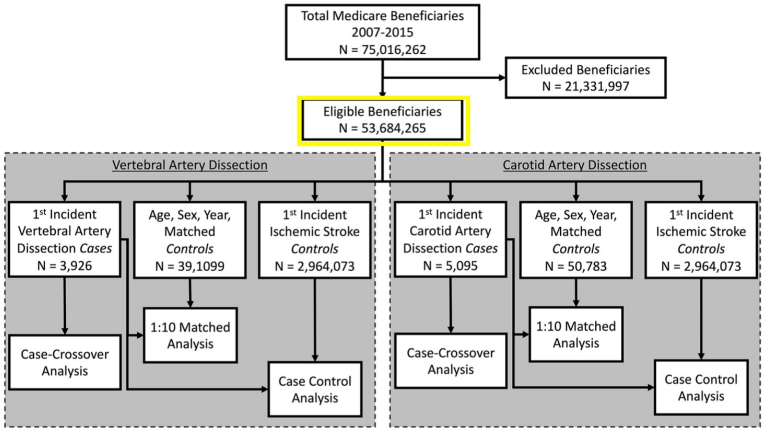

Fig. 1 Definition of Cases and Controls. The design of the study consists of three case-controls drawn from Medicare beneficiaries between 2007 and 2015. It studies VAD and CAD cases and compares each to (i) age-sex-year matched Medicare beneficiaries (10:1), (ii) Ischemic stroke controls and self-controls (cases 6 months before their incident artery dissection). The numbers of each case and control are shown.

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Whedon *et al. BMC Geriatrics* (2022) 22:917
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BMC Geriatrics

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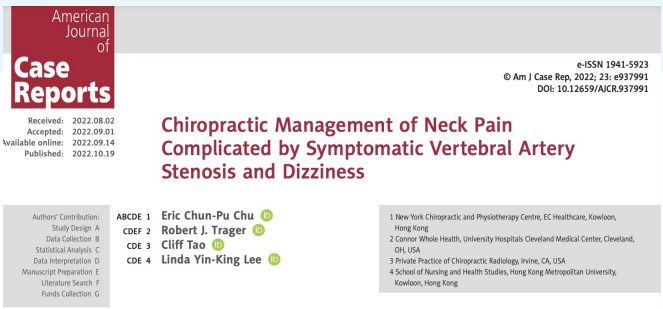
- CSM does not appear to be a significant risk factor for CeAD in this population group.

58

SMT is Safe

- Thus, these studies support the evidence of spontaneous causality or minimally suggest a very low risk for serious AEs following SMT [41,73,74].
  - [41] Tuchin P. A replication of the study 'Adverse effects of spinal manipulation: a systematic review'. Chiropr Man Ther. 2012;20:30.
  - [73] Gouveia LO, Castanho P, Ferreira JJ. Safety of chiro- practic interventions: a systematic review. Spine (Phila, PA, 1976). 2009;34:E405–E413.
  - [74] Whedon JM, Song Y, Mackenzie TA, et al. Risk of stroke after chiropractic spinal manipulation in medi- care B beneficiaries aged 66 to 99 years with neck pain. J Manipulative Physiol Ther. 2015;38:93–101.
- There is no strong evidence in the literature that manual therapy provokes CAD.

59



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Chiropractic Management of Neck Pain Complicated by Symptomatic Vertebral Artery Stenosis and Dizziness

Authors' Contribution: Study Design A, Data Collection B, Statistical Analysis C, Data Interpretation D, Manuscript Preparation E, Literature Search F, Funds Collection G

ABCDE 1 Eric Chun-Pu Chu
CDEF 2 Robert J. Trager
CDE 3 Cliff Tao
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3 Private Practice of Chiropractic Radiology, Irvine, CA, USA
4 School of Nursing and Health Studies, Hong Kong Metropolitan University, Kowloon, Hong Kong

- The present and previous cases provide limited evidence that some carefully considered chiropractic manual therapies can afford patients with VBI relief from concurrent neck pain and possibly dizziness.
- Given the paucity of research, cervical SMT cannot be recommended in such patients. These findings do not apply to vertebral artery dissection, for which SMT is an absolute contraindication.
- **Limitations**
  - **First, as a single case, the demonstrated results are not generalizable.**

60

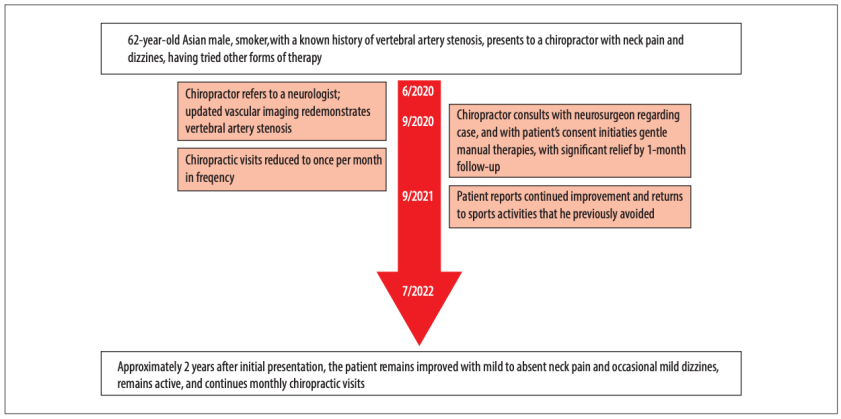

Figure 1. Timeline of care.

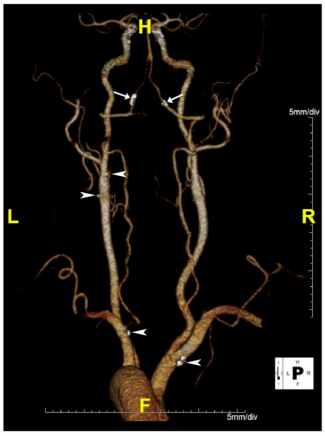

Figure 3. Computed tomography angiogram of neck, 3D volume-rendered image. Orientation: left (L), right (R), head (H), feet (F). Calcified plaques of the vertebral arteries are evident bilaterally (arrows), more prominently on the left than right. From superior to inferior, additional smaller calcified plaques are easily visible at the left carotid bulb (×2), left subclavian artery, and right brachiocephalic trunk (arrowheads).

Chu et al. Am J Case Rep, 2022; 23: e937991.

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Table 1. Patients with vertebrobasilar insufficiency treated by a chiropractor.

Author	Year	Patient age	Sex	Symptoms	VBI diagnosis and testing	Treatment
Current case	2022	62	M	Neck pain, headaches, dizziness	Calcified plaques in VA, MRA, CTA	Thoracic SMT, no cervical rotation, IASTM
Jensen [54]	2003	40	F	Neck and interscapular pain, lightheadedness, tremor	Decreased VA blood flow via Doppler	Cervical SMT with <45° rotation
Jensen [54]	2003	42	M	Neck pain, tremor, left hand numbness	Decreased VA flow via Doppler	Cervical SMT with <45° rotation
Rectenwald [53]	2018	39	F	Neck pain, upper extremity numbness	Bow hunter's syndrome, C1-2 stenosis via dynamic angiography	Instrument-assisted cervical SMT (cervical spine in neutral position)
Terenzi [41]	2002	28	F	Neck and arm pain, headaches, dizziness	Perfusion deficit on transcranial Doppler, VA compression and anomaly	Cervical SMT with flexion and no rotation

CTA – computed tomography angiography; F – female; IASTM – instrument assisted soft tissue manipulation; MRA – magnetic resonance angiography; M – male; NR – not reported; SMT – spinal manipulative therapy; VA – vertebral artery; VBI – vertebrobasilar insufficiency.

Chu et al. Am J Case Rep, 2022; 23: e937991.

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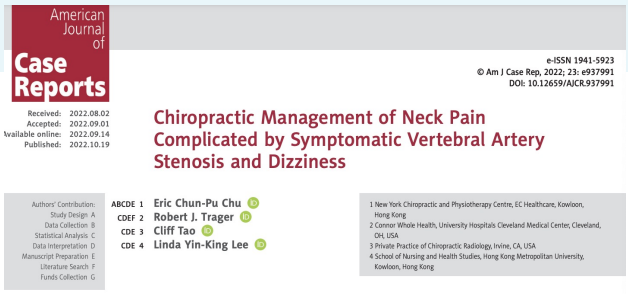

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Chiropractic Management of Neck Pain Complicated by Symptomatic Vertebral Artery Stenosis and Dizziness

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDE 1 Eric Chun-Pu Chu
CDEF 2 Robert J. Trager
CDE 3 Cliff Tao
CDE 4 Linda Yin-King Lee

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2 Connor Whole Health, University Hospitals Cleveland Medical Center, Cleveland, OH, USA
3 Private Practice of Chiropractic Radiology, Irvine, CA, USA
4 School of Nursing and Health Studies, Hong Kong Metropolitan University, Kowloon, Hong Kong

- This case highlights a patient with neck pain and concurrent VBI, with confirmed VBI on imaging related to vertebral artery stenosis that responded positively to thoracic SMT and soft tissue manipulation.
- Four cases were reported in the literature in which chiropractors either avoided manual cervical SMT altogether or modified it to reduce or avoid cervical rotation as a safety precaution when treating neck pain among patients with VBI, yielding a positive outcome.
- However, as there is insufficient evidence that cervical SMT is safe for patients with VBI, this therapy should be avoided in these patients.
- As illustrated in the present case and supported by recent research, thoracic SMT or soft tissue manipulation may provide alternative means of alleviating neck pain in those with VBI.
- Practitioners considering these treatments should do so in collaboration with medical specialists and on a case-by-case basis.

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Kosloff *et al. Chiropractic & Manual Therapies* (2015) 23:19
DOI 10.1186/s12998-015-0063-x

CHIROPRACTIC & MANUAL THERAPIES

RESEARCH Open Access

Chiropractic care and the risk of vertebrobasilar stroke: results of a case–control study in U.S. commercial and Medicare Advantage populations

Thomas M Kosloff[1*†], David Elton[1†], Jiang Tao[2†] and Wade M Bannister[2†]

- We found no significant association between exposure to chiropractic care and the risk of VBA stroke.
- We conclude that manipulation is an unlikely cause of VBA stroke.

64

No Association with Traumatic Injury

- Retrospective cohort studies have reported no association with traumatic injury to the head or neck after SMT for neuromusculoskeletal pain [69].
  - [69] Whedon JM, Mackenzie TA, Phillips RB, et al. Risk of traumatic injury associated with chiropractic spinal manipulation in Medicare Part B beneficiaries aged 66 to 99 years. Spine. 2015;40:264–270.

65

SMT Strains Do Not Exceed Failure Strains

- Invasive studies have further disproven any misconception as to whether VA strains during head movements, including SMT, exceed failure strains [70,71].
  - [70] Herzog W, Leonard TR, Symons B, et al. Vertebral artery strains during high-speed, low amplitude cervical spinal manipulation. J Electromyogr Kinesiol. 2012;22:740–746.
  - [71] Piper SL, Howarth SJ, Triano J, et al. Quantifying strain in the vertebral artery with simultaneous motion analysis of the head and neck: a preliminary investigation. Clin Biomech (Bristol, Avon). 2014;29:1099–1107.

66

Gorrell et al. Chiropractic & Manual Therapies (2022) 30:28
https://doi.org/10.1186/s12998-022-00438-0

Chiropractic & Manual Therapies

RESEARCH Open Access

Kinematics of the head and associated vertebral artery length changes during high-velocity, low-amplitude cervical spine manipulation

Lindsay M. Gorrell[1,2*], Gregor Kuntze[3], Janet L. Ronsky[1,4], Ryan Carter[5], Bruce Symons[5], John J. Triano[6] and Walter Herzog[1]

Conclusions: Mean head angular displacements and VA length changes were small during CSM thrusts. Of the four different CSM measured, mean VA length changes were largest during rotation procedures. This suggests that if clinicians wish to limit VA length changes during the thrust phase of CSM, consideration should be given to the type of CSM used.

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Gorrell et al. Chiropractic & Manual Therapies (2022) 30:28
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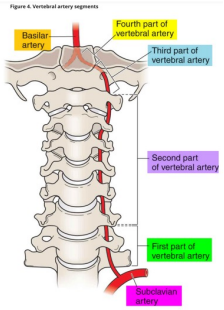

Table 2 Angular displacement (degrees) of the head relative to the sternum and VA length change (%) combining data from all donors and clinicians during ipsilateral CSM thrusts

		Rotation					Lateral flexion				
		X	Y	Z	Whole	V3	X	Y	Z	Whole	V3
C1	Mean	2.5	8.1	−11.5	1.1	3.7	−3.0	4.9	−4.4	0.9	2.6
	SD	2.6	2.8	3.8	0.9	4.4	1.7	4.3	7.8	1.5	4.3
	Minimum	0.2	5.9	−15.0	0.0	−0.3	−5.3	0.4	−20.0	−1.1	0.0
	Maximum	6.5	12.5	−5.8	2.3	10.0	−0.9	10.7	0.7	3.2	10.4
C2	Mean	2.1	10.0	−12.6	1.6	−0.1	−5.3	5.6	−6.4	1.1	2.3
	SD	4.4	3.5	4.5	1.3	5.3	4.2	3.2	8.9	0.8	3.6
	Minimum	−3.8	−5.0	−16.1	0.1	−9.3	−13.0	1.0	−19.3	0.2	−0.3
	Maximum	7.6	13.9	−3.7	3.2	7.1	−1.6	9.8	7.9	2.1	8.9
C3	Mean	−0.3	7.2	−11.0	1.9	4.5	−3.6	4.7	−4.1	0.7	1.7
	SD	2.1	2.3	2.6	0.7	5.4	2.2	3.2	3.0	0.5	2.6
	Minimum	−1.9	4.4	−13.7	0.8	0.0	−7.0	1.1	−8.9	0.2	0.0
	Maximum	2.8	10.1	−7.5	2.4	10.8	−1.4	9.4	−0.9	1.3	6.7
C4	Mean	1.5	8.9	−9.8	1.4	2.8	−3.9	6.3	−5.1	0.6	2.1
	SD	2.6	4.5	3.7	1.0	4.0	3.1	2.5	5.1	1.0	2.6
	Minimum	−2.8	2.5	−14.5	0.2	0.0	−9.1	2.2	−10.7	−0.6	0.0
	Maximum	5.0	13.2	−5.6	2.7	8.6	−1.7	9.1	2.0	2.1	5.6
C5	Mean	1.4	9.6	−10.7	1.8	2.5	−3.9	5.7	−2.1	1.2	2.5
	SD	4.7	2.7	3.1	1.2	3.1	3.0	3.8	4.2	1.0	2.6
	Minimum	−6.1	5.7	−15.5	−0.1	0.0	−7.6	1.3	−6.0	0.2	0.0
	Maximum	5.1	12.6	−7.4	3.1	6.6	−0.9	12.6	5.5	2.6	6.4
C6	Mean	1.3	8.9	−8.0	1.0	1.8	−4.2	4.6	−5.4	1.3	2.4
	SD	3.2	3.0	2.6	1.2	3.7	3.2	2.0	6.3	0.7	2.4
	Minimum	−3.9	5.0	−12.0	−0.4	−0.4	−9.4	1.5	−10.6	0.7	0.0
	Maximum	5.5	14.1	−4.6	3.1	11.6	−1.1	6.5	5.1	2.1	5.8
C7	Mean	−0.8	8.7	−9.5	1.3	2.0	−3.5	5.4	−3.3	1.2	2.0
	SD	4.3	2.6	3.0	1.1	2.8	3.5	2.6	4.1	1.0	3.6
	Minimum	−6.6	6.0	−15.3	0.3	−0.1	−8.8	2.3	−7.7	−0.3	−1.1
	Maximum	3.9	12.3	−7.0	3.3	6.8	0.8	7.9	2.5	2.3	7.1

Ipsilateral manipulations involve contralateral head rotation; positive kinematic values indicate flexion, left lateral flexion and left rotation; positive VA length changes indicate elongation of the vessel

X, coronal axis; Y, sagittal axis; Z, transverse axis; SD, standard deviation; whole, whole VA; V3, V3 segment of VA

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Gorrell et al. Chiropractic & Manual Therapies (2022) 30:28
https://doi.org/10.1186/s12998-022-00438-0

Chiropractic & Manual Therapies

RESEARCH Open Access

Kinematics of the head and associated vertebral artery length changes during high-velocity, low-amplitude cervical spine manipulation

Lindsay M. Gorrell[1,2*], Gregor Kuntze[3], Janet L. Ronsky[1,4], Ryan Carter[5], Bruce Symons[5], John J. Triano[6] and Walter Herzog[1]

Table 3 Angular displacement (degrees) of the head relative to the sternum and VA length change (%) combining data from all donors and clinicians during contralateral CSM thrusts

		Rotation					Lateral flexion				
		X	Y	Z	Whole	V3	X	Y	Z	Whole	V3
C1	Mean	1.0	−8.8	9.7	0.9	1.8	−2.0	−5.9	0.1	0.8	1.8
	SD	3.4	2.0	3.3	0.8	1.4	1.6	3.0	4.1	1.2	1.8
	Minimum	−2.9	−11.8	6.2	0.2	0.0	−5.0	−10.1	−3.9	−1.3	0.0
	Maximum	5.2	−6.5	14.6	2.2	3.1	−0.5	−2.8	7.6	1.9	3.7
C2	Mean	0.9	−7.0	9.7	0.6	0.9	−2.3	−5.6	−0.3	1.6	2.0
	SD	2.8	3.0	3.2	0.4	1.0	3.3	5.7	2.2	1.2	2.6
	Minimum	−2.6	−10.3	5.4	0.2	0.0	−7.3	−11.5	−4.0	0.1	0.0
	Maximum	4.2	−2.6	13.6	1.1	2.2	1.8	4.4	2.3	3.6	6.0
C3	Mean	0.5	−9.1	8.3	1.4	2.2	−3.8	−7.4	1.6	1.4	1.1
	SD	4.5	5.7	2.7	0.7	2.7	2.9	4.2	4.3	2.0	1.9
	Minimum	−3.6	−19.3	3.9	0.2	0.0	−7.1	−15.1	−3.1	−1.4	−1.3
	Maximum	9.1	−3.7	11.0	2.3	5.8	−0.3	−4.3	8.8	4.2	4.2
C4	Mean	0.1	−8.2	7.4	1.0	1.3	−4.3	−6.0	1.8	1.8	0.7
	SD	2.0	3.9	2.5	0.7	1.8	4.5	2.3	6.8	1.7	2.1
	Minimum	−2.5	−14.5	5.1	−0.3	−0.7	−10.1	−10.1	−7.8	0.0	−1.3
	Maximum	3.5	−3.8	11.6	1.6	3.5	1.0	−3.6	12.9	4.4	3.9
C5	Mean	−1.3	−5.4	4.5	1.1	1.0	−3.7	−6.3	3.6	0.9	1.8
	SD	1.0	2.6	1.9	0.6	1.3	1.7	2.6	6.1	1.7	2.4
	Minimum	−3.2	−8.5	2.2	0.3	0.0	−6.6	−9.0	−2.8	−2.0	−0.2
	Maximum	−0.2	−1.9	7.0	1.8	3.3	−1.8	−3.2	11.9	2.5	5.8
C6	Mean	−0.7	−8.3	7.5	1.2	1.4	−4.6	−5.2	0.8	1.5	1.7
	SD	3.5	1.6	2.6	0.2	1.5	2.3	3.2	6.4	0.7	2.0
	Minimum	−7.7	−10.9	3.3	1.0	0.0	−6.1	−8.8	−4.9	0.6	0.0
	Maximum	1.7	−6.3	10.4	1.5	4.0	−1.2	−1.3	9.9	2.3	3.9
C7	Mean	−0.3	−8.4	6.1	0.9	1.3	−2.8	−5.7	0.7	0.7	0.5
	SD	2.7	2.4	3.1	0.5	2.4	3.1	1.5	5.8	0.7	1.1
	Minimum	−4.3	−12.3	2.7	0.2	−1.1	−6.7	−7.9	−6.5	0.0	−0.8
	Maximum	2.8	−6.3	10.4	1.6	4.4	1.4	−3.7	10.6	1.9	2.3

Contralateral manipulations involve ipsilateral head rotation; positive kinematic values indicate flexion, left lateral flexion and left rotation; positive VA length changes indicate elongation of the vessel

X, coronal axis; Y, sagittal axis; Z, transverse axis; SD, standard deviation; whole, whole VA; V3, V3 segment of VA

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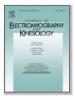
ELSEVIER

Journal of Electromyography and Kinesiology
Volume 22, Issue 5, October 2012, Pages 740-746



Vertebral artery strains during high-speed, low amplitude cervical spinal manipulation

W. Herzog, T.R. Leonard, B. Symons, C. Tang, S. Wuest

- VA strains obtained during SMT are significantly smaller than those obtained during diagnostic and range of motion testing, and are much smaller than failure strains.
- We conclude from this work that cervical SMT performed by trained clinicians does not appear to place undue strain on VA, and thus does not seem to be a factor in vertebro-basilar injuries.

70

J Man Manip Ther. 2022 Nov 15;1-9. doi: 10.1080/10669817.2022.2148048.
Online ahead of print.

Vertebral arteries do not experience tensile force during manual cervical spine manipulation applied to human cadavers

Lindsay M Gorrell [1 2], Andrew Sawatsky [2], W Brent Edwards [2], Walter Herzog [2]

Affiliations – collapse

Affiliations

1 Integrative Spinal Research Group, Department of Chiropractic Medicine, University Hospital Balgrist and University of Zürich, Zürich ,Switzerland.
2 Human Performance Laboratory, Faculty of Kinesiology, University of Calgary, Calgary, Canada.

- During cervical spine manipulations (using cervical spine extension and rotation), arterial length changes remained below that slack length, suggesting that VA elongated but were not stretched during the manipulation.

71

Am J Physiol Heart Circ Physiol 300: H1451–H1458, 2011.
First published February 4, 2011; doi:10.1152/ajpheart.00871.2010.

Wall stress of the cervical carotid artery in patients with carotid dissection: a case-control study

Fraser M. Callaghan,[1] Roger Luechinger,[2] Vartan Kurtcuoglu,[1] Hakan Sarikaya,[3] Dimos Poulikakos,[1] and Ralf W. Baumgartner[3]

[1]*Laboratory of Thermodynamics in Emerging Technologies, Department of Mechanical and Process Engineering, ETH Zurich,* [2]*Institute for Biomedical Engineering, University and ETH Zurich, and* [3]*Department of Neurology, University Hospital Zurich, Zurich, Switzerland*

Submitted 30 August 2010; accepted in final form 27 January 2011

- The present findings suggest that wall stress increases at the intimal side of the artery wall surrounding the distal edge of the carotid bulb after head movements may be important for the development of carotid dissection.
- The lack of wall stress difference between the two groups indicates that the carotid arteries of patients with carotid dissection have either distinct functional or anatomical properties or endured unusually heavy wall stresses to initiate dissection.

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Am J Physiol Heart Circ Physiol 300: H1451–H1458, 2011.
First published February 4, 2011; doi:10.1152/ajpheart.00871.2010.

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[1]*Laboratory of Thermodynamics in Emerging Technologies, Department of Mechanical and Process Engineering, ETH Zurich,* [2]*Institute for Biomedical Engineering, University and ETH Zurich, and* [3]*Department of Neurology, University Hospital Zurich, Zurich, Switzerland*

Submitted 30 August 2010; accepted in final form 27 January 2011

- Because most events of sICAD are connected with normal head movements, this suggests that the carotid arteries of sICAD patients may have distinct functional or anatomical properties important in the initiation of dissection.
- Patients with sICAD have a higher prevalence of hereditary connective tissue disorders such as Marfan syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta, and, in particular, fibro-muscular dysplasia.

73

Trauma?

frontiers in Neurology
PERSPECTIVE
published: 31 May 2021
doi: 10.3389/fneur.2021.663830

Cervical Artery Dissection and Sports

Stefan T. Engelter[1,2], Christopher Traenka[1,2], Caspar Grond-Ginsbach[2,3], Tobias Brandt[4], Maani Hakimi[5], Bradford B. Worrall[6], Stephanie Debette[7,8], Alessandro Pezzini[9], Didier Leys[10], Turgut Tatlisumak[11], Christian H. Nolte[12] and Philippe Lyrer[1]*

- Approximately 40% of the CeAD patients reported any kind of recent head or neck trauma in the month prior to symptom onset (4), as compared to 10% of the patients with ischemic stroke attributable to a cause other than CeAD and 20% of the healthy controls (4).
- More than 90% of the trauma events recalled by the CeAD patients were trivial and so mild that the individuals did not seek for medical care or advice.
- As a causal relationship with the CeAD is either questionable or unclear, the term *mechanical trigger event* is preferred.

74

Randomized Controlled Trial > J Manipulative Physiol Ther. 2014 Jan;37(1):22-31.
doi: 10.1016/j.jmpt.2013.07.008. Epub 2013 Nov 15.

Changes in vertebral artery blood flow following various head positions and cervical spine manipulation

Jairus J Quesnele [1], John J Triano [2], Michael D Noseworthy [3], Greg D Wells [4]

- There were no significant changes in blood flow or velocity in the vertebral arteries of healthy young male adults after various head positions and cervical spine manipulations.

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Open access Research
BMJ Open

Effect of cervical manipulation on vertebral artery and cerebral haemodynamics in patients with chronic neck pain: a crossover randomised controlled trial

Nicholas Moser,[1] Silvano Mior,[1,2] Michael Noseworthy,[3] Pierre Côté,[4] Greg Wells,[5] Michael Behr,[6] John Triano[1]

- Our work is the first to show that cervical manipulation does not result in brain perfusion changes compared with a neutral neck position or maximal neck rotation.
- The changes observed were found to not be clinically meaningful and suggests that cervical manipulation may not increase the risk of cerebrovascular events through a haemodynamic mechanism.

76

J Manipulative Physiol Ther. 2020 Feb;43(2):144-151. doi: 10.1016/j.jmpt.2019.09.001. Epub 2020 May 30.

Changes in Vertebral Artery Blood Flow in Different Head Positions and Post-Cervical Manipulative Therapy

Christopher Yelverton [1], Jessica Joy Wood [2], Diana Lopes Petersen [2], Cynthia Peterson [2]

- Hemodynamic measurements of the V3 region of the vertebral artery do not show significant changes in the measured head positions or following manipulation of the upper cervical spine in patients **without** pre-existing risk factors.

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MAYO CLINIC

CONCISE REVIEW

Craniocervical Artery Dissections: A Concise Review for Clinicians

Zafer Keser, MD; James F. Meschia, MD; and Giuseppe Lanzino, MD

- Craniocervical artery dissection (CAD) is a sudden tear in the intimal layer with subsequent bleeding into the subintimal space.
- This causes progressive vessel wall incursion into the lumen and narrowing, which at times proceeds to occlusion.1
- The site of dissection becomes thrombogenic because of turbulent blood flow and exposure of thrombogenic factors (Figure 1A).
- Enlargement of the vessel wall can also lead to compression on surrounding structures like cranial nerves.2
- If the intramural hematoma grows into the adventitia, it can lead to pseudoaneurysm formation (Figure 1B).
- Rupture of a pseudoaneurysm can cause subarachnoid hemorrhage (SAH) if the site of dissection extends to the intracranial vasculature.

Mayo Clin Proc. ■ April 2022;97(4):777-783 ■ https://doi.org/10.1016/j.mayocp.2022.02.007
www.mayoclinicproceedings.org ■ © 2022 Mayo Foundation for Medical Education and Research

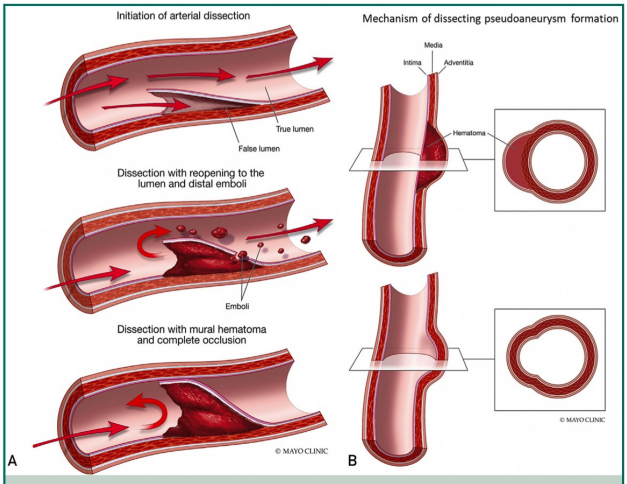

FIGURE 1. Mechanism and evolution of a dissection formation (A) and dissecting pseudoaneurysm (B). (Used with permission of Mayo Foundation for Medical Education and Research, all rights reserved.)

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Chaibi et al. report that history taking is the single most important factor for detecting subtle symptoms of CAD.

Chaibi A, Russell BR. A risk-benefit assessment strategy to exclude cervical artery dissection in spinal-therapy: a comprehensive review. Annals of Medicine. 2019; 51 (2)118-127.

79

Difficult (IF Not Impossible DX)

Peter Tuchin
to me
Tue, Jul 26, 6:19 PM (17 hours ago)

Hi Jim

Many case reports do not supply good clinical info in their history summary, so IMO, to determine clear indications for a potential CAD is very difficult (if not impossible)

FQ could certainly be a significant factor and one which has not previously received strong recognition. Most case reports don't ask about any recent infections or FQ use.

But I suspect there are a multitude of factors, which may be different for almost every case. These factors include things you mentioned (genetics, risk factors such as smoking, migraine, etc), but also include other minor activities (eg sports, or activities involving neck movements) which appear to be the last factor that damages a probably weakened artery.

These other minor activities (eg sports, or activities involving neck movements) are rarely documented in any detail making it very hard to get a clear timeline of symptoms. I have attached 2 recent case reports to highlight this

80

Annals of Medicine

ISSN: 0785-3890 (Print) 1365-2060 (Online) Journal homepage: https://www.tandfonline.com/loi/iann20

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

Aleksander Chaibi & Michael Bjørn Russell

To cite this article: Aleksander Chaibi & Michael Bjørn Russell (2019) A risk–benefit assessment strategy to exclude cervical artery dissection in spinal manual-therapy: a comprehensive review, Annals of Medicine, 51:2, 118-127, DOI: 10.1080/07853890.2019.1590627

- In a comprehensive review of the literature published in the Annals of Medicine, Chaibi and Russell concluded, **"Manual therapy does not result in an increased risk of CAD." Additionally, the authors state, "...there is no firm scientific basis for direct causality between cervical spinal manipulative therapy and CAD."**

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Annals of Medicine

ISSN: 0785-3890 (Print) 1365-2060 (Online) Journal homepage: https://www.tandfonline.com/loi/iann20

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

Aleksander Chaibi & Michael Bjørn Russell

To cite this article: Aleksander Chaibi & Michael Bjørn Russell (2019) A risk–benefit assessment strategy to exclude cervical artery dissection in spinal manual-therapy: a comprehensive review, Annals of Medicine, 51:2, 118-127, DOI: 10.1080/07853890.2019.1590627

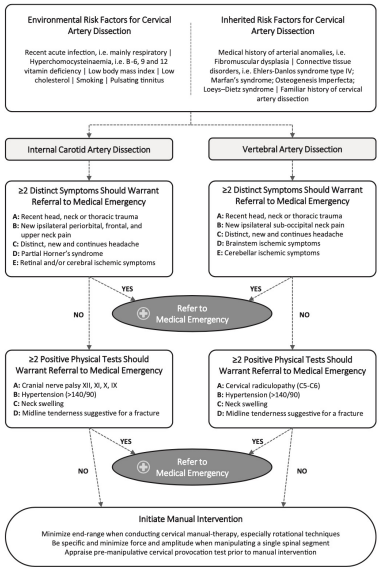

Figure 3. Step-by-step risk–benefit assessment strategy tool to exclude cervical artery dissection.

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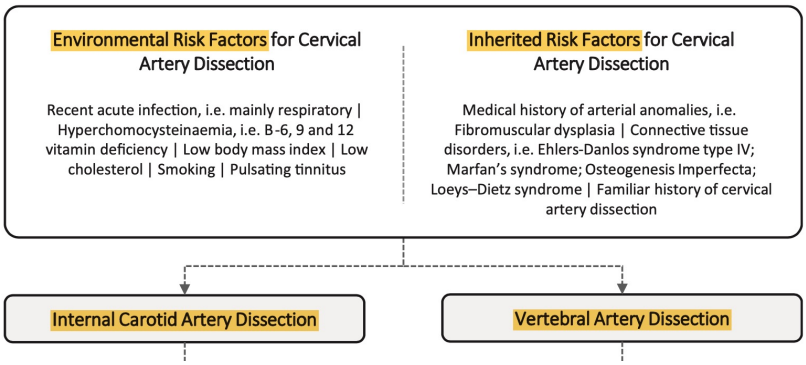
Chaibi and Russell's CAD Assessment Tool



- **Other Risk Factors?:**
  - Age <45
  - Prior incident
  - Fluoroquinolone antibiotics
  - Arteriopathies
  - ?

Chaibi A, Russell BR. Annals of Medicine. 2019; 51 (2)118-127.

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AHA/ASA Scientific Statement

Cervical Arterial Dissections and Association With Cervical Manipulative Therapy

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

Factors Associated With CD:

- Major and minor cervical trauma
- Arterial hypertension
- Young age
- Current use of oral contraceptives
- Migraine
- Fibromuscular dysplasia
- Ultrastructural connective tissue abnormalities
- Vascular subtype of Ehlers-Danlos syndrome
- Marfan syndrome
- Turner syndrome
- Williams syndrome
- Familial cases
- Hereditary hemochromatosis
- Osteogenesis imperfecta type I
- α1-Antitrypsin deficiency
- 677T genotype MTHFR
- Hyperhomocysteinemia
- Cystic medial necrosis of intracranial vessels
- Styloid process length
- ICAM-1 E4690 K gene polymorphism
- Autosomal-dominant polycystic kidney disease
- Infections [INFECTION OR FQs???]
- Moyamoya disease
- Lentiginosis [FRECKLES…REALLY???]
- Vessel redundancies (coils, kinks, loops), especially if bilateral
- **Fluoroquinolones NOT Identified**

Stroke. 2014;45:3155-3174.

84

CAD Risk Factors?

- **Open Neurol J. 2010; 4: 50–55. Cervical Artery Dissection: Emerging Risk Factors**
  - Primary disease of arterial wall (fibrodysplasia), Ehlers Danlos-syndrome IV, Marfan's syndrome, vessel tortuosity, recent respiratory tract infection, migraine, hyperhomocysteinemia, major head/neck trauma like chiropractic maneuver, coughing or hyperextension injury associated to car.
- **Lancet Neurol. 2009 Jul;8(7):668-78. Cervical-artery dissections: predisposing factors, diagnosis, and outcome.**
  - Trauma to the neck, infection, migraine, hyperhomocysteinaemia, underlying arteriopathy
- **Stroke. 2005 Jul;36(7):1575-80. A systematic review of the risk factors for cervical artery dissection.**
  - Aortic root diameter >34 mm, trauma, homocysteine, and recent infection.

85

Arq Neuropsiquiatr 2005;63(2-B):523-526

INTERNAL CAROTID ARTERY DISSECTION IN A PATIENT WITH RECENT RESPIRATORY INFECTION

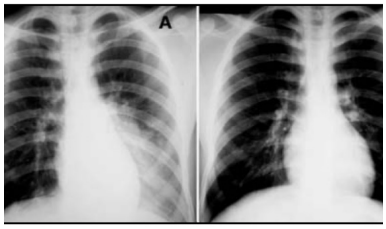
Case report of a possible link

Cynthia Resende Campos[1], Thiago Gasperini Bassi[2], Fabiano Pinto[2], Demétrius Kasak P. Abrahão[3]

ABSTRACT - The pathogenesis of spontaneous cervical artery dissection remains unknown. Infection-mediated damage of the arterial wall may be an important triggering mechanism. We describe a 21 year-old man with respiratory infection (bronchial pneumonia) which was diagnosed and treated with antibiotic few days prior to the right internal carotid artery dissection. The patient presented ischemic retinal and cerebral strokes. Based on literature review, we discuss the possibility of a causal link between infection and arterial dissection.

KEY WORDS: carotid dissection, infection, stroke.

- A 21- year-old man with fever, cough and purulent sputum was diagnosed as lobar pneumonia (leukocytosis: 16.9/nL and positive chest X-ray) and treated with levofloxacin for 3 days.



Chest X-ray. A: At first admission, prior to antibiotic t
. B. After the treatment, at the second admission.

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Arq Neuropsiquiatr 2005;63(2-B):523-526

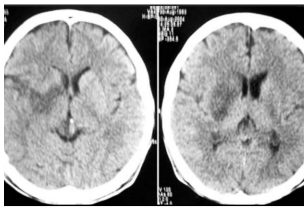
INTERNAL CAROTID ARTERY DISSECTION IN A PATIENT WITH RECENT RESPIRATORY INFECTION

Case report of a possible link

Cynthia Resende Campos[1], Thiago Gasperini Bassi[2], Fabiano Pinto[2], Demétrius Kasak P. Abrahão[3]

ABSTRACT - The pathogenesis of spontaneous cervical artery dissection remains unknown. Infection-mediated damage of the arterial wall may be an important triggering mechanism. We describe a 21 year-old man with respiratory infection (bronchial pneumonia) which was diagnosed and treated with antibiotic few days prior to the right internal carotid artery dissection. The patient presented ischemic retinal and cerebral strokes. Based on literature review, we discuss the possibility of a causal link between infection and arterial dissection.

KEY WORDS: carotid dissection, infection, stroke.



ı 2. Brain CT: right striatocapsular ischemic stroke.

- On the fourth day, pneumonia symptoms had improved, including coughing, and he was discharged.
- In the same night, he woke up with a sudden onset of intense right hemi-cranial and retroorbital pain followed by visual disturbance and left hemiplegia.
- Brain CT revealed a right striatocapsular ischemic stroke (Fig 2).
- Four-vessel digital angiography showed an irregular high-grade stenosis at the right internal carotid artery (ICA) starting about 2 cm distal to the carotid bulb extending until an occlusion into the petrous bone.
- The proximal segment of the right ICA had a tapered flame-like appearance. There was an accentuation of the filling of the external carotid artery branches (Fig 3).
- These findings supported the diagnosis of arterial dissection.

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Arq Neuropsiquiatr 2005;63(2-B):523-526

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KEY WORDS: carotid dissection, infection, stroke.

- In conclusion, we call attention to the diagnosis of CAD as an important cause of ischemic stroke in young patients and reinforce the possibility of recent infection as an environmental trigger factor for spontaneous CAD.

Infection??? How about iatrogenic Fluoroquinolone caused CAD?

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Published in final edited form as:
Neurologist. 2012 September ; 18(5): 245–254. doi:10.1097/NRL.0b013e31826754e1.

Clinical Characteristics of Symptomatic Vertebral Artery Dissection. A Systematic Review

Rebecca F. Gottesman, MD PhD[1], Priti Sharma, MBBS[1], Karen A. Robinson, PhD[2], Martinson Arnan, MD[1], Megan Tsui[1], Karim Ladha, BA[1], and David E. Newman-Toker, MD PhD[1,3]

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Neurologist. 2012 September ; 18(5): 245–254.

Table 2

Symptoms and signs associated with VAD.

	# Studies	Total sample size (N)	Number of subjects with symptom	Pooled proportion (pooled SE)	Range of proportions
Dizziness/ Vertigo	18 [8, 16, 19, 28, 30, 32, 44, 47, 52, 55-57, 60-62, 65, 73, 74]	467	273	0.58 (0.53)	5-100%
Headache	32 [2, 9, 11, 12, 15, 19, 21, 22, 24, 25, 27, 28, 30, 32, 33, 35, 38, 41-46, 52, 53, 57, 60, 64-66, 69, 73]	689	348	0.51 (0.7)	6-93%
Neck Pain	27 [11, 12, 14, 15, 21, 22, 24, 25, 30, 35, 37, 38, 41, 43-45, 52, 53, 56, 57, 60, 61, 64-66, 69, 73]	526	244	0.46 (0.69)	10-80%
Gait problems/ Ataxia	10 [1, 6, 8, 16, 52, 53, 56, 57, 61, 65]	150	57	0.38 (0.43)	7-71%
Visual symptoms	17 [1, 6, 8, 12, 16, 30, 32, 37, 47, 52, 53, 56, 57, 61, 65, 72, 73]	314	114	0.36 (0.53)	4-88%
Nausea/ Vomiting	13 [1, 8, 12, 30, 32, 44, 52, 56, 57, 60, 65, 73, 74]	306	108	0.35 (0.42)	5-79%
Nystagmus	7 [6, 8, 30, 37, 56, 61, 65]	150	44	0.29 (0.30)	4-55%
Horner's syndrome	11 [30, 41, 44, 47, 52, 55, 60, 61, 65, 72, 73]	265	58	0.22 (0.03)	6-36%
Sensory deficits	17 [1, 8, 16, 30, 32, 37, 47, 52, 53, 55-57, 60, 61, 65, 72, 73]	335	70	0.21 (0.43)	4-58%
Cranial nerve palsies	11 [8, 30, 37, 47, 52, 53, 55, 56, 65, 72, 73]	241	51	0.21 (0.32)	4-43%
Dysphagia	6 [16, 53, 57, 60, 65, 74]	102	13	0.13 (0.20)	5-29%
Tinnitus	4 [5, 32, 44, 65]	238	17	0.07 (0.09)	5-13%

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Table 3

Cerebrovascular complications of VAD by location of the dissection.

Cerebrovascular complication	Dissection Location	# Studies	Total sample size (N)	Number of subjects with complication	Pooled proportion (pooled SE)	Range of proportions
Stroke	Any	36 [1, 2, 5, 8, 9, 13-15, 19, 20, 23, 24, 27, 28, 32, 35, 36, 38, 40-43, 45, 46, 49, 51, 52, 55-57, 60, 62-65, 72]	944	571	0.60 (0.71)	10-89%
	Intracranial	7 [2, 19, 32, 40, 46, 60, 72]	176	57	0.32 (0.26)	13-48%
	Extracranial	6 [8, 14, 19, 35, 43, 65]	74	50	0.68 (0.38)	10-89%
TIA	Any	20 [2, 5, 6, 8, 9, 13, 15, 19, 20, 23, 24, 27, 35, 38, 41, 43, 45, 52, 63, 65]	571	80	0.14 (0.37)	7-26%
	Intracranial	2 [2, 19]	28	3	0.11 (0.12)	7-14%
	Extracranial	5 [6, 8, 19, 35, 65]	70	15	0.21 (0.30)	7-75%
SAH	Any	17 [5, 9, 19, 21, 32, 37, 40, 42, 45, 50-52, 57, 60, 62, 64]	865	304	0.35 (0.42)	0-93%
	Intracranial	8 [19, 21, 32, 37, 40, 50, 60, 71]	481	274	0.57 (0.31)	5-93%
	Extracranial	1 [21]	7	0	0.00	0%

Neurologist. 2012 September ; 18(5): 245–254.

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Table 4

History of trauma associated with VAD

	# Studies	Total sample size (N)	Number of subjects with symptom	Pooled proportion (pooled SE)	Range of proportions
Major trauma (primarily MVA)	6 [1, 8, 27, 31, 53, 69]	103	15	0.15 (0.22)	10-25%
Minor trauma*	16 [1, 6, 9, 16, 21, 28, 30-32, 35, 43, 57, 62, 65, 66, 69]	371	150	0.40 (0.47)	15-70%
Sporting injuries	13 [1, 6, 8, 16, 25, 30-32, 35, 57, 62, 65, 66]	261	40	0.15 (0.33)	3-42%
Chiropractic injury	14 [1, 8, 14, 21, 24, 30, 35, 42, 43, 53, 57, 65, 66, 69]	283	46	0.16 (0.36)	7-30%

*Some manuscripts included sports-related injuries or chiropractic manipulation as "minor trauma," so this category likely includes some VAD patients with these exposures.

Neurologist. 2012 September ; 18(5): 245–254.

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Table 5

Outcomes following routine clinical care for VAD in 570 individuals with reported outcome*

	N with outcome	Pooled proportion	SE	Range of proportions
Good outcome (mRS 0-1)	394	0.67	0.60	33-100%
Fair outcome (mRS 2-4)	105	0.18	0.49	0-53%
Poor outcome (mRS 5-6)	59	0.10	0.38	0-35%

*Studies including outcome information: 5, 6, 13, 14, 16, 19, 21, 24, 28, 31, 36-38, 41, 43, 45, 47, 50, 51, 55, 62, 69, 70, 72, 73

Neurologist. 2012 September ; 18(5): 245–254.

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JoS JOURNAL OF STROKE

Journal of Stroke 2019;21(1):112-115
https://doi.org/10.5853/jos.2018.03055

Letter to the Editor

Local Signs and Symptoms in Spontaneous Cervical Artery Dissection: A Single Centre Cohort Study

- Spontaneous cervical artery dissection (sCAD) is one of the main causes of ischemic stroke in young adults.1
- Local symptoms (LSs) are common in sCAD and often predate ischemic events, yet little is known about their frequency and prognosis.2-9

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Journal of Stroke 2019;21(1):112-115
https://doi.org/10.5853/jos.2018.03055

- Local Symptoms (LSs) were evident in 212 of the 259 sCAD patients (81.9%) with:
  - Head/neck pain being the most frequent (n=205, 79.2%),
  - followed by Horner's syndrome (n=42, 16.2%),
  - tinnitus (n=19, 7.3%), and
  - lower cranial nerve palsy (n=13, 5.0%).
- Multiple LSs were seen in 61 of 259 patients (23.6%).
- Headache was the only LS that was present in all patients with multiple LSs and head/ neck pain combined with Horner's syndrome was the most common combination of symptoms (34 of 61, 55.7%).

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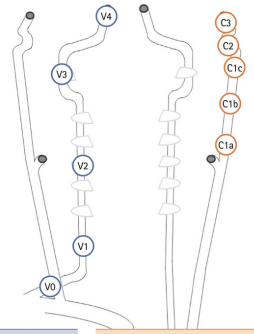

Vertebral artery	% V0-V4 (n=141)
Headache	84.4 (119)
Horner's	0.0
Cranial nerve palsy	0.0
Tinnitus	3.5 (5)

Internal carotid artery	% C1a-C3 (n=127)
Headache	74.8 (95)
Horner's	33.1 (42)
Cranial nerve palsy	10.2 (13)
Tinnitus	13.4 (17)

Vertebral artery	% V0-V2 (n=51)	% V3-V4 (n=119)
Headache	94.1 (48)	82.4 (98)
Horner's	0.0	0.0
Cranial nerve palsy	0.0	0.0
Tinnitus	3.9 (2)	2.5 (3)

Internal carotid artery	% C1a (n=23)	% C1b-C2 (n=118)	% C3 (n=5)
Headache	69.9 (16)	74.6 (88)	80.0 (4)
Horner's	30.4 (7)	33.9 (40)	20.0 (1)
Cranial nerve palsy	0.0	11.0 (13)	0.0
Tinnitus	21.7 (5)	11.9 (14)	40.0 (2)

Figure 2. Frequency of local symptoms according to vessel segment involvement in patients with spontaneous cervical artery dissection (sCAD). Patients with simultaneous anterior and posterior circulation sCAD (n=9) were excluded from this figure. In some patients, a singular dissection involved multiple vessel segments.

https://doi.org/10.5853/jos.2018.03055

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Stroke
Volume 52, Issue 3, March 2021; Pages 821-829
https://doi.org/10.1161/STROKEAHA.120.031579
American Heart Association.

CLINICAL AND POPULATION SCIENCES

Clinical Features of Patients With Cervical Artery Dissection and Fibromuscular Dysplasia

Table 2. Clinical Features, Triggering Factors, and Vascular Pathology of Index Cervical Artery Dissection by cFMD Status

Variable	cFMD+ (n=103)	cFMD− (n=1180)	*P* value
Clinical features			
Cervical pain	41 (39.8)	493 (41.8)	0.755
Headache	50 (48.5)	587 (49.7)	0.815
Tinnitus	6 (5.8)	57 (4.8)	0.633
Cranial nerve involvement	8 (7.8)	134 (11.4)	0.327
Horner syndrome	26 (25.2)	229 (19.4)	0.155
TIA	15 (14.6)	147 (12.5)	0.536
Cerebral infarct	73 (70.9)	864 (73.2)	0.607
Subarachnoid hemorrhage	0 (0.0)	18 (1.5)	0.390
Dissection site			0.547
Carotid	63 (61.2)	708 (60.0)	
Vertebral	19 (18.4)	277 (23.5)	
Intracranial arteries	2 (1.9)	25 (2.1)	
Multiple vessel	19 (18.4)	170 (14.4)	
Vascular pathology			≤0.001
Occlusion	33 (32.0)	520 (44.1)	
Stenosis	40 (38.8)	444 (37.6)	
Intimal flap	3 (2.9)	47 (4.0)	
Pseudoaneurysm	9 (8.7)	47 (4.0)	
Other	18 (17.5)	104 (9.0)	
Triggering factors			
Infections, past 30 d*	13 (12.6)	133 (11.3)	0.630
Antibiotics use	8 (61.5)	72 (54.1)	0.773
Trauma, minor	8 (7.8)	176 (14.9)	0.055
Strenuous physical activity	38 (36.9)	544 (46.1)	0.079
Acute-phase treatment			0.517
Antiplatelet therapy	51 (49.5)	538 (45.6)	
Anticoagulant treatment	40 (38.8)	457 (38.7)	
Any recanalization therapy	12 (11.7)	185 (15.7)	

cFMD indicates cerebrovascular fibromuscular dysplasia.

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Stroke
Volume 36, Issue 7, 1 July 2005; Pages 1575-1580
https://doi.org/10.1161/01.STR.0000169919.73219.30

COMMENTS, OPINIONS, AND REVIEWS

A Systematic Review of the Risk Factors for Cervical Artery Dissection

Sidney M. Rubinstein, MSc, Saskia M. Peerdeman, MD, PhD, Maurits W. van Tulder, PhD, Ingrid Riphagen, MSc, and Scott Haldeman, MD, PhD

- ***Conclusions***
  - CAD is a multi-factorial disease. Many of the reviewed studies contained 2 or more major sources of bias commonly found in case-control studies.
  - Only one study (of homocysteine) used healthy controls, a robust sample size, and had a low risk of biased results.

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Stroke
Volume 36, Issue 7, 1 July 2005; Pages 1575-1580
https://doi.org/10.1161/01.STR.0000169919.73219.30

COMMENTS, OPINIONS, AND REVIEWS

A Systematic Review of the Risk Factors for Cervical Artery Dissection

Sidney M. Rubinstein, MSc, Saskia M. Peerdeman, MD, PhD, Maurits W. van Tulder, PhD, Ingrid Riphagen, MSc, and Scott Haldeman, MD, PhD

- **Genetic or Inborn Predisposition/Disorders With a Familial Association**
  - Connective Tissue Disease
  - Gene-association Studies
  - Gene Mutation/Sequencing Studies
  - Homocysteine
  - Migraine
  - Vessel Abnormalities
- **Environmental Exposures**
  - Infection
  - Oral Contraceptive Use
  - Fluoroquinolones - Demetrious
- **Trauma**
  - Trivial Trauma

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e-Journal
Quarterly Journal of ACO – March 2008 – Volume 5; Issue 1

Original Articles

Iatrogenic Tendinopathy Associated with Levaquin (levofloxacin)

Ronald C Evans, DC, FACO, FICC
Senior Orthopedist, ICON Whole Health 1441 29th Street, Suite 100, West Des Moines, Iowa, 50266

Figure 1. Localized swelling at the 3-6 cm level (from the calcaneal insertion) in the left Achilles tendon.

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Fluoroquinolone adverse effects

Often prescribed for urinary, respiratory, dermatologic and other infections, severe adverse effects of fluoroquinolones have been reported in the U.S., causing the Food and Drug Administration to communicate advisories related to safety and utilization:

- October 2008- Warning on tendon injuries with fluoroquinolone antibiotics.
- August 2013- Warning on peripheral neuropathy injuries with fluoroquinolone antibiotics.
- May 12, 2016- FDA approves safety labeling changes for fluoroquinolones.
- July 26, 2016- FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects.

Demetrious *Chiropractic & Manual Therapies* (2018) 26:22
https://doi.org/10.1186/s12998-018-0193-z

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Journal of Athletic Training 2014;49(3):422–427
doi: 10.4085/1062-6050-49.2.09
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www.natajournals.org

systematic review

Fluoroquinolones and Tendinopathy: A Guide for Athletes and Sports Clinicians and a Systematic Review of the Literature

Trevor Lewis, MSc, MCSP*; Jill Cook, PhD†

*Physiotherapy Department, Aintree University Hospital National Health Service Foundation Trust, University Hospital Aintree, Liverpool, United Kingdom; †Department of Physiotherapy, Monash University–Peninsula Campus, Frankson, Victoria, Australia

Key Points

- Tendinopathy can be a complication of treatment with fluoroquinolone antibiotics and usually is linked with 1 or more synergistic factors.
- Symptoms of fluoroquinolone-related tendinopathy can present within hours of starting treatment or up to 6 months after ceasing treatment, and recovery can be slower and require a less aggressive approach early in rehabilitation than for other types of tendinopathy.
- Treatment with fluoroquinolones should be discontinued and treatment with a nonquinolone antibiotic should be considered in patients who present with tendinopathy.
- Clinicians, athletes, athletic trainers, and medical support teams should be aware of and alert to the potential adverse effects of fluoroquinolones.

Journal of Athletic Training 2014;49(3):422–427

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Unidentified Etiology of Cervical Artery Dissection?...Fluoroquinolones

Open Access Research

BMJ Open

Fluoroquinolones and collagen associated severe adverse events: a longitudinal cohort study

Nick Daneman,[1,2,3,4] Hong Lu,[1] Donald A Redelmeier[1,2,3,5]

To cite: Daneman N, Lu H, Redelmeier DA. Fluoroquinolones and collagen associated severe adverse events: a longitudinal cohort study. *BMJ Open* 2015;5:e010077. doi:10.1136/bmjopen-2015-010077

► Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2015-010077).

ABSTRACT

Objectives: Fluoroquinolone-associated tendon ruptures are a recognised complication, but other severe collagen-associated adverse events may also be possible. Our objectives were to confirm the association of fluoroquinolones and tendon rupture, to clarify the potential association of fluoroquinolones and retinal detachment, and to test for a potentially lethal association between fluoroquinolones and aortic aneurysms.

Setting: Population-based longitudinal cohort study in Ontario, Canada.

Participants: Older adults turning 65 years between April 1 1997 and March 31 2012 were followed until primary outcome, death, or end of follow-up (March 31

Strengths and limitations of this study

- This study reports a novel and important association of fluoroquinolone prescriptions with aortic aneurysms.
- The study design involves a population-based, longitudinal analysis of 1.7 million older adults.
- The findings are robust across multiple sensitivity, subgroup and tracer analyses.
- Misclassification of fluoroquinolone exposure is possible, if some patients did not use their dispensed prescriptions.
- Underdetection of mild or asymptomatic outcome events is possible.

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Research

Original Investigation

Risk of Aortic Dissection and Aortic Aneurysm in Patients Taking Oral Fluoroquinolone

Chien-Chang Lee, MD, ScD; Meng-tse Gabriel Lee, PhD; Yueh-Sheng Chen, MD; Shih-Hao Lee, MA; Yih-Sharng Chen, MD, PhD; Shyr-Chyr Chen, MD, MBA; Shan-Chwen Chang, MD, PhD

IMPORTANCE Fluoroquinolones have been associated with collagen degradation, raising safety concerns related to more serious collagen disorders with use of these antibiotics, including aortic aneurysm and dissection.

Editor's Note page 1847

Supplemental content at jamainternalmedicine.com

- Cipro (ciprofloxacin), Avelox (moxifloxacin), Levaquin (Levofloxacin),Floxin (ofloxacin), Factive (gemifloxacin), Noroxin (norfloxacin)

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RESEARCH

OPEN ACCESS

Fluoroquinolone use and risk of aortic aneurysm and dissection: nationwide cohort study

Björn Pasternak,[1,2] Malin Inghammar,[2,3] Henrik Svanström[2]

[1]Clinical Epidemiology Unit T2, Department of Medicine Solna, Karolinska Institutet, 17176 Stockholm, Sweden
[2]Department of Epidemiology Research, Statens Serum Institut, Copenhagen, Denmark
[3]Section for Infection Medicine, Department of Clinical Sciences Lund, Lund University, Lund, Sweden
Correspondence to: B Pasternak bjorn.pasternak@ki.se

Additional material is published online only. To view please visit the journal online.
Cite this as: BMJ 2018;360:k678
http://dx.doi.org/10.1136/bmj.k678
Accepted: 22 January 2018

ABSTRACT

OBJECTIVE
To investigate whether oral fluoroquinolone use is associated with an increased risk of aortic aneurysm or dissection.

DESIGN
Nationwide historical cohort study using linked register data on patient characteristics, filled prescriptions, and cases of aortic aneurysm or dissection.

SETTING
Sweden, July 2006 to December 2013.

PARTICIPANTS
360 088 treatment episodes of fluoroquinolone use (78%ciprofloxacin) and propensity score matched comparator episodes of amoxicillin use (n=360 088).

CONCLUSIONS
In a propensity score matched cohort, fluoroquinolone use was associated with an increased risk of aortic aneurysm or dissection. This association appeared to be largely driven by aortic aneurysm.

Introduction

Fluoroquinolones remain among the most commonly used antibiotics globally, and about 30 million outpatient prescriptions for fluoroquinolones are issued per year in the United States alone.[1,2] Fluoroquinolone use is associated with an increased risk of tendon disorders, including Achilles tendon rupture and tendinopathy.[3,4] The mechanisms behind these adverse events, which are recognised in a boxed warning, are thought to implicate non-antimicrobial properties of

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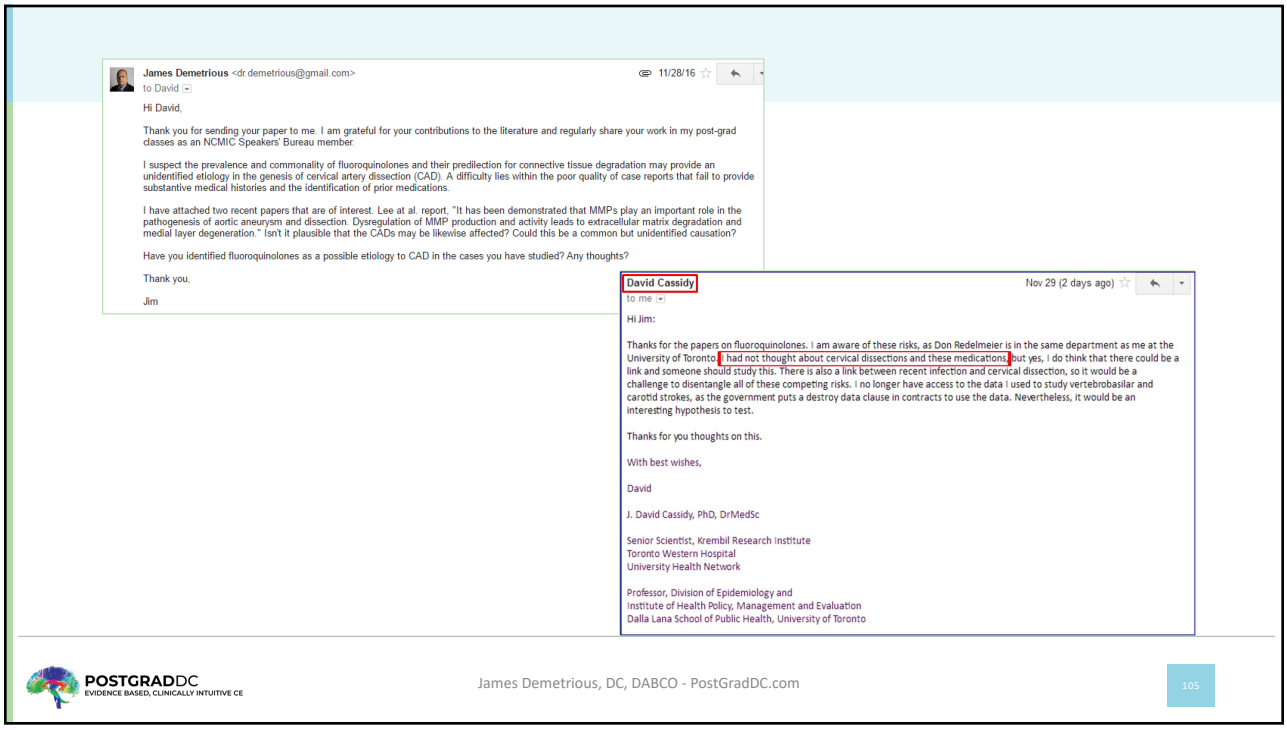

James Demetrious <dr.demetrious@gmail.com> 11/28/16
to David

Hi David,

Thank you for sending your paper to me. I am grateful for your contributions to the literature and regularly share your work in my post-grad classes as an NCMIC Speakers' Bureau member.

I suspect the prevalence and commonality of fluoroquinolones and their predilection for connective tissue degradation may provide an unidentified etiology in the genesis of cervical artery dissection (CAD). A difficulty lies within the poor quality of case reports that fail to provide substantive medical histories and the identification of prior medications.

I have attached two recent papers that are of interest. Lee at al. report, "It has been demonstrated that MMPs play an important role in the pathogenesis of aortic aneurysm and dissection. Dysregulation of MMP production and activity leads to extracellular matrix degradation and medial layer degeneration." Isn't it plausible that the CADs may be likewise affected? Could this be a common but unidentified causation?

Have you identified fluoroquinolones as a possible etiology to CAD in the cases you have studied? Any thoughts?

Thank you,

Jim

David Cassidy Nov 29 (2 days ago)
to me

Hi Jim:

Thanks for the papers on fluoroquinolones. I am aware of these risks, as Don Redelmeier is in the same department as me at the University of Toronto. I had not thought about cervical dissections and these medications but yes, I do think that there could be a link and someone should study this. There is also a link between recent infection and cervical dissection, so it would be a challenge to disentangle all of these competing risks. I no longer have access to the data I used to study vertebrobasilar and carotid strokes, as the government puts a destroy data clause in contracts to use the data. Nevertheless, it would be an interesting hypothesis to test.

Thanks for you thoughts on this.

With best wishes,

David

J. David Cassidy, PhD, DrMedSc

Senior Scientist, Krembil Research Institute
Toronto Western Hospital
University Health Network

Professor, Division of Epidemiology and
Institute of Health Policy, Management and Evaluation
Dalla Lana School of Public Health, University of Toronto

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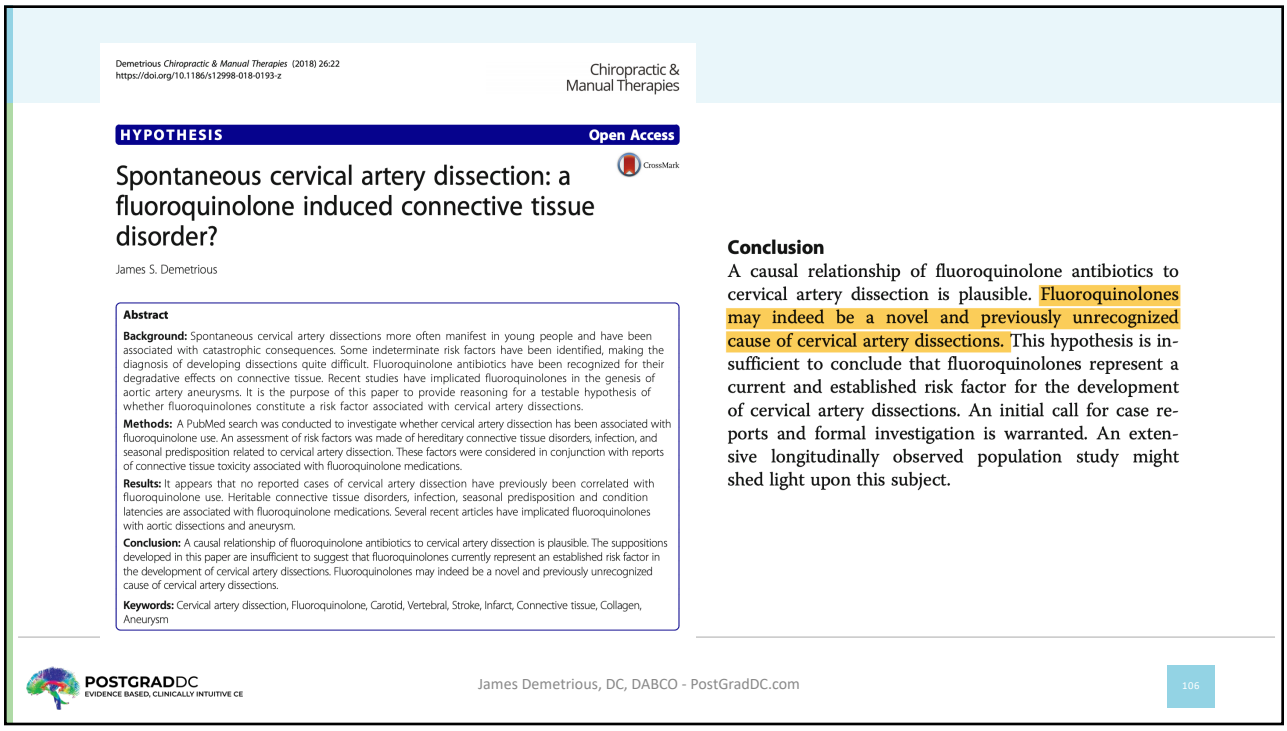

Demetrious *Chiropractic & Manual Therapies* (2018) 26:22
https://doi.org/10.1186/s12998-018-0193-z

Chiropractic & Manual Therapies

HYPOTHESIS Open Access

Spontaneous cervical artery dissection: a fluoroquinolone induced connective tissue disorder?

James S. Demetrious

Abstract

Background: Spontaneous cervical artery dissections more often manifest in young people and have been associated with catastrophic consequences. Some indeterminate risk factors have been identified, making the diagnosis of developing dissections quite difficult. Fluoroquinolone antibiotics have been recognized for their degradative effects on connective tissue. Recent studies have implicated fluoroquinolones in the genesis of aortic artery aneurysms. It is the purpose of this paper to provide reasoning for a testable hypothesis of whether fluoroquinolones constitute a risk factor associated with cervical artery dissections.

Methods: A PubMed search was conducted to investigate whether cervical artery dissection has been associated with fluoroquinolone use. An assessment of risk factors was made of hereditary connective tissue disorders, infection, and seasonal predisposition related to cervical artery dissection. These factors were considered in conjunction with reports of connective tissue toxicity associated with fluoroquinolone medications.

Results: It appears that no reported cases of cervical artery dissection have previously been correlated with fluoroquinolone use. Heritable connective tissue disorders, infection, seasonal predisposition and condition latencies are associated with fluoroquinolone medications. Several recent articles have implicated fluoroquinolones with aortic dissections and aneurysm.

Conclusion: A causal relationship of fluoroquinolone antibiotics to cervical artery dissection is plausible. The suppositions developed in this paper are insufficient to suggest that fluoroquinolones currently represent an established risk factor in the development of cervical artery dissections. Fluoroquinolones may indeed be a novel and previously unrecognized cause of cervical artery dissections.

Keywords: Cervical artery dissection, Fluoroquinolone, Carotid, Vertebral, Stroke, Infarct, Connective tissue, Collagen, Aneurysm

Conclusion

A causal relationship of fluoroquinolone antibiotics to cervical artery dissection is plausible. Fluoroquinolones may indeed be a novel and previously unrecognized cause of cervical artery dissections. This hypothesis is insufficient to conclude that fluoroquinolones represent a current and established risk factor for the development of cervical artery dissections. An initial call for case reports and formal investigation is warranted. An extensive longitudinally observed population study might shed light upon this subject.

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Use of fluoroquinolones and the risk of spontaneous cervical artery dissection

E. Del Zotto[a] and A. Pezzini[b]

[a]U.O. Neurologia, Istituto Ospedaliero Poliambulanza, Brescia; and [b]Dipartimento di Scienze Cliniche e Sperimentali Clinica Neurologica, Università degli Studi di Brescia, Brescia, Italy

Keywords: cervical artery dissection, fluoroquinolones, ischaemic, stroke

Received 16 October 2018
Accepted 23 January 2019

European Journal of Neurology 2019, **26:** 1028–1031

doi:10.1111/ene.13917

Background and purpose: Because of their potential to alter the integrity of collagen and other components of the extracellular matrix, fluoroquinolone antibiotics might be involved in the pathogenesis of spontaneous cervical artery dissection (sCeAD).

Methods: In the setting of a single-centre case–control study, whether fluoroquinolone use in the 30-day period before the index event is associated with sCeAD (cases) in comparison with a group of age- and sex-matched patients who suffered a first-ever acute cerebral infarction from a cause other than CeAD (non-CeAD IS, controls) was assessed.

Results: Overall, 284 cases (mean age 43.2 ± 10.4 years; 58.5% men) and 568 controls qualified for the analysis. Thirty (10.6%) patients in the sCeAD group and 16 (2.8%) in the non-CeAD IS group were fluoroquinolone users ($P \leq 0.001$). The use of these antibiotics was associated with a more than two-fold increased risk of sCeAD [odds ratio (OR) 2.31; 95% confidence interval (CI) 1.00–5.30] after adjusting for confounders. The risk was more substantial in the subgroup of patients with dissection involving the carotid artery (OR 2.78; 95% CI 1.14–6.78), in females (OR 4.58; 95% CI 1.04–20.1) and compared to that conferred by other antibiotics (OR 2.42; 95% CI 1.02–5.75).

Conclusions: Fluoroquinolones may represent a novel contributing factor involved in the pathogenesis of sCeAD.

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Internal Medicine
The Japanese Society of Internal Medicine

doi: 10.2169/internalmedicine.6736-20
Intern Med 60: 2863-2865, 2021
http://internmed.jp

【 CASE REPORT 】

Vertebral Artery Dissection after Exposure to Levofloxacin: A Report of Two Cases

Taku Harada[1,2], Yukinori Harada[2] and Taro Shimizu[2]

Abstract:

Exposure to quinolones is known to be an independent risk factor for aortic dissection; however, the association with vertebral artery dissection remains unclear. We report two cases of vertebral artery dissection that occurred 4 and 8 days after exposure to levofloxacin, respectively. Both patients had risk factors for vertebral artery dissection, and quinolone use could have been avoided. These two cases indicate that quinolone exposure can be a risk factor for vertebral artery dissection. Considering the possible mechanism, it is better to avoid the prescription of quinolones to patients who have insufficient connective tissues to avoid vertebral artery dissection.

Key words: vertebral artery dissection, quinolone, drug adverse effect

(Intern Med 60: 2863-2865, 2021)
(DOI: 10.2169/internalmedicine.6736-20)

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Journal of Clinical Neuroscience 87 (2021) 26–28

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journal homepage: www.elsevier.com/locate/jocn

Case report

Unilateral common carotid artery dissection in a patient with recent COVID-19: An association or a coincidence?

Onur Serdar Gencler [a,*], Meltem Refiker Ege [b], Aydın Aslan [c]

[a] Department of Neurology, Medical Park Ankara Hospital, Yuksek Ihtisas University, Kent Koop District, 1868 Street Batikent Avenue, No:15, Yenimahalle, Ankara 06680, Turkey
[b] Department of Cardiology, Medical Park Ankara Hospital, Yuksek Ihtisas University, Kent Koop District, 1868 Street, Batikent Avenue, No:15, Yenimahalle, Ankara 06680, Turkey
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ARTICLE INFO

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COVID-19
Carotid artery dissection
Ischemic stroke
Thromboinflammatory changes
Vascular complications

ABSTRACT

The "Corona Virus Disease 2019 (COVID-19)", caused by severe acute respiratory coronavirus 2 (SARS-CoV-2), progressed rapidly since its first outbreak, and quickly developed into a pandemic. Although COVID-19 mostly presents with respiratory symptoms, researchers have started reporting neurologic manifestations such as cerebrovascular diseases in patients, with COVID-19 as the pandemic has progressed. Herein, we report a case of 38-year-old female patient identified with a left common carotid artery dissection, with COVID-19. Clinicians must keep in mind that COVID-19 can cause vascular complications such as carotid artery dissections in the ensuing period, even after the acute phase, although there is currently a lack of sufficient evidence to identify any causal association between COVID-19 and arterial dissections.

"It was understood that the patient had presented to an external facility with complaints of fever and fatigue approximately 1 month earlier, and had received therapy after being diagnosed with COVID-19."

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CrossMark

What Fluoroquinolones Have the Highest Risk of Aortic Aneurysm? A Case/Non-case Study in VigiBase®

Agnès Sommet, MD, PhD[1], Justine Bénévent, PharmD, Msc[1], Vanessa Rousseau, PhD[1], Leila Chebane, VetD[1], Antonios Douros, MD, PhD[2,3,4], Jean-Louis Montastruc, MD, PhD[1], and François Montastruc, MD, PhD[1,2]

[1]Department of Medical and Clinical Pharmacology, Centre of PharmacoVigilance and Pharmacoepidemiology, INSERM UMR 1027, CIC 1426, Toulouse University Hospital, Faculty of Medicine, University of Toulouse, Toulouse, France; [2]Centre for Clinical Epidemiology, Lady Davis Institute, Jewish General Hospital, Montréal, Québec, Canada; [3]Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montréal, Québec, Canada; [4]Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institute of Clinical Pharmacology and Toxicology, Berlin, Germany.

- The study was conducted using Vigibase®, the World Health Organization Global Individual Case Safety Reports (ICSRs) database which includes more than 16 million reports forwarded to the WHO Uppsala Monitoring Center by national pharmacovigilance systems from over 130 countries around the world since 1967.
- Among the 6,383,318 ICSRs registered in Vigibase® between 1972 and 2017, 172,588 were reported with fluoroquinolones and 40,658 with amoxicillin.
- We found 113 aortic aneurysms or dissections with fluoroquinolones (including 12 with more than 1 fluoroquinolone) and 8 with amoxicillin.
- Fluoroquinolone exposure was associated with a higher risk of reporting aneurysms/dissections compared to amoxicillin exposure.

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What Fluoroquinolones Have the Highest Risk of Aortic Aneurysm? A Case/Non-case Study in VigiBase®

Agnès Sommet, MD, PhD[1], Justine Bénévent, PharmD, Msc[1], Vanessa Rousseau, PhD[1], Leila Chebane, VetD[1], Antonios Douros, MD, PhD[2,3,4], Jean-Louis Montastruc, MD, PhD[1], and François Montastruc, MD, PhD[1,2]

[1]Department of Medical and Clinical Pharmacology, Centre of PharmacoVigilance and Pharmacoepidemiology, INSERM UMR 1027, CIC 1426, Toulouse University Hospital, Faculty of Medicine, University of Toulouse, Toulouse, France; [2]Centre for Clinical Epidemiology, Lady Davis Institute, Jewish General Hospital, Montréal, Québec, Canada; [3]Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montréal, Québec, Canada; [4]Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institute of Clinical Pharmacology and Toxicology, Berlin, Germany.

Table 1 Crude and Adjusted Reporting Odds Ratios for the Association Between Aortic Aneurysms or Dissections and the Use of Individual Fluoroquinolones in Vigibase® (Comparisons Were Made Between Each Fluoroquinolone and All Other Ones Excluding Individual Case Safety Reports with More Than One Fluoroquinolone. No Case of Aneurysms or Dissections Was Reported with Enoxacin, Fleroxacin, Gemifloxacin, Grepafloxacin, Lomefloxacin, Norfloxacin, Pazufloxacin, Pefloxacin, Prulifloxacin, Rufloxacin, Sparfloxacin, Temafloxacin, Trovafloxacin)

	Cases[b]	Non-cases	Crude ROR	Adjusted ROR[c] (95% CI)
Levofloxacin	67	63,932	3.25	2.78 (1.83 4.23)
Ciprofloxacin	18	57,538	0.42	0.33 (0.20 0.55)
Moxifloxacin	10	16,687	1.01	0.86 (0.45 1.66)
Ofloxacin	3	12,330	0.39	1.29 (0.40 4.15)
Gatifloxacin	2	3008	[d]	[d]
Tosufloxacin	1	300	[d]	[d]

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Jun and Fang *BMC Cardiovasc Disord* (2021) 21:470
https://doi.org/10.1186/s12872-021-02258-1

REVIEW Open Access

Current progress of fluoroquinolones-increased risk of aortic aneurysm and dissection

Cui Jun[1] and Bian Fang[2*]

- Duration of FQ use and the incidence of AAD As depicted in Table 1, susceptible period analysis further revealed that current FQ use within 60 days was associated with the highest risk of AAD.
- Lee et al. observed that there was an increased risk of AAD with prolonged FQ use for 3- to 14-day exposure.
- More specifcally, FQ use within 60 days was associated with the highest risk of AAD.
- Howard et al. found a higher risk of AAD was associated with FQ exposure for longer than 14 days.
- What is more, Pasternak et al. observed that there was no increased risk of AAD with FQ exposure for more than 60 days .
- However, recent results indicated that FQ were associated with increased 90-day incidence of AAA, **iliac** artery aneurysm, and other AAA.

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Jun and Fang *BMC Cardiovasc Disord* (2021) 21:470
https://doi.org/10.1186/s12872-021-02258-1

BMC Cardiovascular Disorders

REVIEW Open Access

Current progress of fluoroquinolones-increased risk of aortic aneurysm and dissection

Cui Jun[1] and Bian Fang[2*]

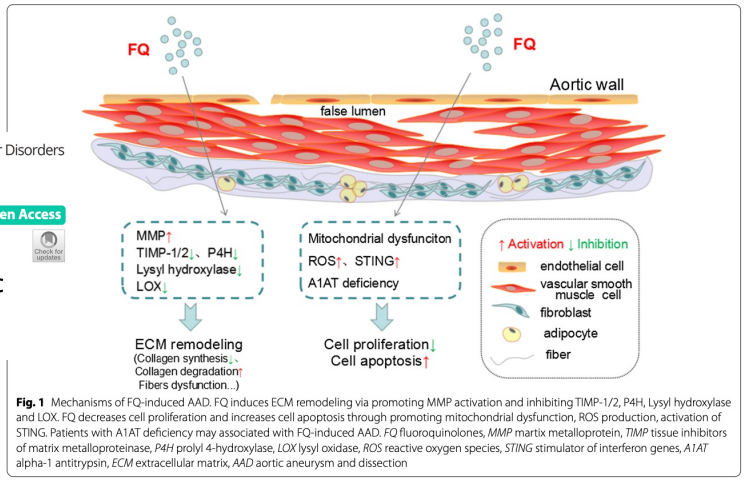

Fig. 1 Mechanisms of FQ-induced AAD. FQ induces ECM remodeling via promoting MMP activation and inhibiting TIMP-1/2, P4H, Lysyl hydroxylase and LOX. FQ decreases cell proliferation and increases cell apoptosis through promoting mitochondrial dysfunction, ROS production, activation of STING. Patients with A1AT deficiency may associated with FQ-induced AAD. *FQ* fluoroquinolones, *MMP* martix metalloprotein, *TIMP* tissue inhibitors of matrix metalloproteinase, *P4H* prolyl 4-hydroxylase, *LOX* lysyl oxidase, *ROS* reactive oxygen species, *STING* stimulator of interferon genes, *A1AT* alpha-1 antitrypsin, *ECM* extracellular matrix, *AAD* aortic aneurysm and dissection

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CAD...Protopathic Bias

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FQ and CAD… A Protopathic Event

- **History and Etymology for *protopathic***
  - International Scientific Vocabulary, from Middle Greek ***prōto****pathēs* affected **first**,
  - from Greek *prōt-* prot- + ***pathos*** experience, **suffering** — more at PATHOS

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Cerebrovascular Diseases

Letter to the Editor

Cerebrovasc Dis 2021;50:483–484
DOI: 10.1159/000515105

Received: January 1, 2021
Accepted: January 23, 2021
Published online: March 29, 2021

Response to Differential Risk Factors of Ischemic Stroke

Vivian Chun Kyle Lin Stephen M. Perle

University of Bridgeport, College of Health Sciences, School of Chiropractic, Bridgeport, CT, USA

"Given the fact that Garg et al. were aware of the potential for protopathic bias as the cause for the elevated risk for CeAD after cervical manipulation, why did they not test for this by including primary care physician visits and neck pain in their analysis."

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CAD is the Result of Pre-Existing Arteriopathy

Stroke
Volume 42, Issue 6, June 2011; Pages 1563-1568
https://doi.org/10.1161/STROKEAHA.110.599548

ORIGINAL CONTRIBUTIONS; CLINICAL SCIENCES

Vessel Wall Inflammation in Spontaneous Cervical Artery Dissection

A Prospective, Observational Positron Emission Tomography, Computed Tomography, and Magnetic Resonance Imaging Study

Thomas Pfefferkorn, MD, Tobias Saam, MD, Axel Rominger, MD, Maximilian Habs, MD, Lisa-Ann Gerdes, MD, Caroline Schmidt, MD, Clemens Cyran, MD, Andreas Straube, MD, Jennifer Linn, MD, Konstantin Nikolaou, MD, Peter Bartenstein, MD, Maximilian Reiser, MD, Marcus Hacker, MD, and Martin Dichgans, MD

- In conclusion, a subset of patients with spontaneous CAD showed signs of a generalized transient inflammatory arteriopathy in PET-CT and contrast enhanced hrMRI.
- This subset of patients may be more prone to multiple dissections.

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CAD is the Result of Pre-Existing Arteriopathy

ELSEVIER
Legal Medicine
Volume 14, Issue 5, September 2012, Pages 249-251

Case Report

Spontaneous bilateral carotid artery dissection following cervical manipulation

Marilyn Carprieaux [a], Alex Michotte [a, b], Dirk Van Varenbergh [a], Miriam Pipeleers Marichal [a]

[a] Department of Pathology, UZ Brussel, Vrije Universiteit Brussel, Brussels, Belgium
[b] Department of Neurology, UZ Brussel, Vrije Universiteit Brussel, Brussels, Belgium

Received 5 February 2012, Revised 29 March 2012, Accepted 8 April 2012, Available online 23 May 2012.

- To establish the etiology of a cervical artery dissection is important in view of possible legal implications and to exclude hereditary disorders, since cervical artery dissection has been linked to several arteriopathies.
- The underlying arteriopathy in the presented case was an idiopathic cystic medial degeneration.
- This report emphasizes the role of the pathologist in defining the underlying arteriopathy in carotid artery dissection.

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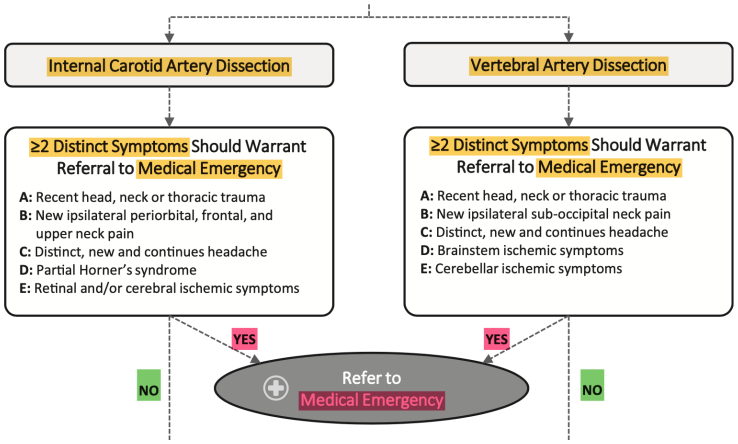
Chaibi and Russell's CAD Assessment Tool



- **Other Symptoms?:**
  - Severity/location
  - Cranial Nerves
  - CNS
  - Bladder/Bowel
  - Gait
  - ?

Chaibi A, Russell BR. Annals of Medicine. 2019; 51 (2)118-127.

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Annals of Medicine
ISSN: 0785-3890 (Print) 1365-2060 (Online) Journal homepage: https://www.tandfonline.com/loi/iann20

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

Aleksander Chaibi & Michael Bjørn Russell

To cite this article: Aleksander Chaibi & Michael Bjørn Russell (2019) A risk–benefit assessment strategy to exclude cervical artery dissection in spinal manual-therapy: a comprehensive review, Annals of Medicine, 51:2, 118-127, DOI: 10.1080/07853890.2019.1590627

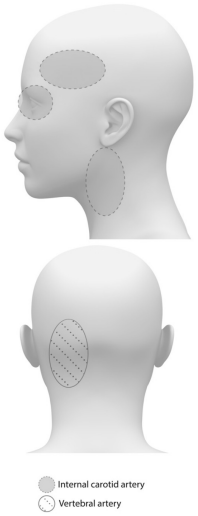

Figure 2. Typical pain distribution due to vertebral artery and internal carotid artery dissections.

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MAYO CLINIC

CONCISE REVIEW

Craniocervical Artery Dissections: A Concise Review for Clinicians

Zafer Keser, MD; James F. Meschia, MD; and Giuseppe Lanzino, MD

Mayo Clin Proc. ■ April 2022;97(4):777-783 ■ https://doi.org/10.1016/j.mayocp.2022.02.007
www.mayoclinicproceedings.org ■ © 2022 Mayo Foundation for Medical Education and Research

FIGURE 2. Dissection-related headache and neck pain (left). Miosis and ptosis of the left eye without anhidrosis, partial Horner syndrome. It is commonly seen in ipsilateral carotid dissections (right). (Used with permission of Mayo Foundation for Medical Education and Research, all rights reserved.)

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Asymptomatic CAD Presentations are Rare

Pain as the only symptom of cervical artery dissection

M Arnold, R Cumurciuc, C Stapf, P Favrole, K Berthet, M-G Bousser

1ST LINE

J Neurol Neurosurg Psychiatry 2006;**77**:1021–1024. doi: 10.1136/jnnp.2006.094359

See end of article for authors' affiliations

Correspondence to: M Arnold, Department of Neurology, University Hospital of Berne, Inselspital, Freiburgstrasse 18, 3010 Bern, Switzerland; marcel.arnold@insel.ch

Received 27 March 2006
Revised version received 22 June 2006
Accepted 23 June 2006
Published Online First 4 July 2006

Background: Headache or neck pain is a frequent symptom of spontaneous cervical artery dissection (sCAD).
Patients and methods: Patients were drawn from an ongoing hospital-based registry of consecutive cases diagnosed with sCAD. Only patients with isolated pain were included in this series. Pain topography, dynamics, severity and quality, imaging findings and outcome were analysed.
Results: 20 of 245 (8%) patients with sCAD presented with pain as the only symptom (mean (SD) age 39 (8) years; 14 (70%) women). Of them, 12 had vertebral artery dissection, 3 had internal carotid dissection and 5 had multiple dissections. The median delay from symptom onset to diagnosis was 7 days (range 4 h to 29 days). 6 patients presented with headache, 2 with neck pain and 12 with both. Onset of headache was progressive in 6, acute in 8 and thunderclap-type in 4 patients; neck pain was progressive in 7 and acute in 7. Headache was throbbing in 13 and constrictive in 5 patients; neck pain was throbbing in 4 and constrictive in 10. Pain was unilateral in 11 and bilateral in 9. Pain was different from earlier episodes in all but one case. All patients were pain free at 3 months.
Conclusion: Pain may be the only symptom in sCAD, even when multiple arteries are dissected. Pain topography, dynamics, quality and intensity were heterogeneous. Data from this study lend support to recommendations favouring imaging studies of the cervical arteries in patients with new-onset unexplained headache or neck pain.

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Sudden onset of Headache/Neck/Face Pain that's Different than the Patient has Experienced Before?

These are also known as the 5 D's and the 3 N's:

- **Diplopia** → Double vision or other vision problems
- **Dizziness** → Vertigo, light-headedness
- **Drop Attacks** → Sudden numbness/weakness of face/arm/leg
- **Disarthria** → Difficulty speaking
- **Dysphagia** → Difficulty swallowing
- **Ataxia of Gait** → Difficulty walking
- **Nausea** → Vomiting or queasiness
- **Numbness** → Loss of sensation on one side
- **Nystagmus** → Involuntary rapid eye movements

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Questions

- What percentage of CAD patients present to chiropractic without head/neck pain, signs or symptoms of neurologic deficits or connective tissue disorders?
- What risk factors or symptoms should we list on our intake forms that may provide insight into CAD?
- Are connective tissue disorder patients absolute contraindications to HVLA-SM of the cervical spine?

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Opinions Related to Asymptomatic CADs

On Mon, Jul 25, 2022 at 12:37 PM Schneider, Michael Jacob <mjs5@pitt.edu> wrote:

> Hi Jim,
>
> No, I don't know of any reports of CAD cases in asymptomatic patients or those without connective tissue disorders.
> As we have discussed, it appears that almost every reported case of CAD involves a symptomatic patient who presents to a DC with suboccipital pain and an unusual headache.
> The DC does not recognize these symptoms as related to a possible dissection in progress and the ensuing manipulation may aggravate the pre-existing dissection.
>
> Regarding connective tissue disorders, this seems to be the underlying factor in most cases of younger patients who develop dissections.
>
> Mike

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Opinions Related to Asymptomatic CADs

crisp4psp@gmail.com Mon, Jul 25, 7:30 AM (2 days ago)
to me

Jim,

Good question. I recall seeing one or more cases in the literature of patients who have had stroke post-manip without neck pain/ HA but I don't recall for sure. Certainly the overwhelming majority do have neck pain/HA. And most case reports are so poorly reported that it is always difficult to say. Certainly the majority of cases have no known connective tissue disorder or neurologic symptoms. But, again, the reports are usually poorly documented.

Take care!

Donald R. Murphy, DC, FRCC
Director of Primary Spine Care
Ortho Rhode Island

Clinical Assistant Professor, Dept of Family Medicine
Alpert Medical School of Brown University

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Asymptomatic CAD Presentations are Rare

Commentary | Open Access | Published: 03 August 2010

Current understanding of the relationship between cervical manipulation and stroke: what does it mean for the chiropractic profession?

Donald R Murphy

Chiropractic & Osteopathy **18**, Article number: 22 (2010) | Cite this article
22k Accesses | **25** Citations | **11** Altmetric | Metrics

- Also, in 20% of cases of VADS [Review of the Lee paper "Three patients were asymptomatic **(6%)**, and neuroimaging was performed for unrelated reasons."] of their cohort the individual does not have neck pain or headache and in a very small percentage of patients vertebral artery dissection can occur in a person who has no symptoms of any kind [48].
  - [48] Lee VH, Brown RD, Mandrekar JN, Mokri B: Incidence and outcome of cervical artery dissection: a population-based study. Neurology. 2006, 67 (10): 1809-12.

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Asymptomatic CAD Presentations are Rare

PMC | Alt | No PDF
A Rare Case of Isolated, Spontaneous, and Asymptomatic Common ...
J Emerg Trauma Shock. 2021 Oct-Dec; 14(4): 240–242.

Journal of Emergencies, Trauma, and Shock
Wolters Kluwer -- Medknow Publications

A Rare Case of Isolated, Spontaneous, and Asymptomatic Common Carotid Artery Dissection

Iyad Farouji, Hossam Abed, [...], and Addi Suleiman

- Herein, we report a very unique case of isolated, spontaneous, and asymptomatic common carotid artery dissection.

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Asymptomatic CAD Presentations are Rare

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November 28, 2006; 67 (10) ARTICLES

Incidence and outcome of cervical artery dissection

A population-based study

Vivien H. Lee, Robert D. Brown, Jayawant N. Mandrekar, Bahram Mokri

First published November 27, 2006, DOI: https://doi.org/10.1212/01.wnl.0000244486.30455.71

- Three patients were asymptomatic (6%), and neuroimaging was performed for unrelated reasons.
- Three patients (6%) had known disorders of connective tissue and an additional three patients had a family history of connective tissue disorder in first-degree relatives.

From the Departments of Neurology (V.H.L., R.D.B., B.M.), and Biostatistics (J.N.M.), Mayo Clinic College of Medicine, Rochester, MN. Dr. Lee is currently with the Department of Neurology, Rush University Medical Center, Chicago, IL.

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November 28, 2006; 67 (10) ARTICLES
Incidence and outcome of cervical artery dissection
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Vivien H. Lee, Robert D. Brown, Jayawant N. Mandrekar, Bahram Mokri
First published November 27, 2006, DOI: https://doi.org/10.1212/01.wnl.0000244486.30455.71

Table 2 *ICAD and VAD patients in Olmsted County, MN (1987–2003)*

	ICAD	VAD	CAD
Demographics			
Total patients	32 (67)	18 (38)	48
Mean age, y	47.0	43.4	45.8
Male	12 (38)	12 (67)	24 (50)
Female	20 (63)	6 (33)	24 (50)
Medical history			
Connective tissue disorder	3 (9)	0	3 (6)
Migraine	13 (41)	4 (22)	16 (33)
Hypertension	6 (19)	3 (17)	9 (19)
Smoker	11 (34)	4 (22)	14 (29)
Clinical symptoms			
Asymptomatic	1 (3)	2 (11)	3 (6)
Pain	25 (78)	15 (83)	38 (80)
Neck pain	6 (19)	7 (39)	13 (27)
HA	23 (72)	12 (67)	33 (69)
Horner syndrome	8 (25)	4 (22)	12 (25)
Cerebral ischemia (stroke or TIA)	19 (59)	14 (78)	32 (67)
TIA	9 (29)	2 (11)	11 (23)
Stroke	13 (41)	15 (83)	27 (56)

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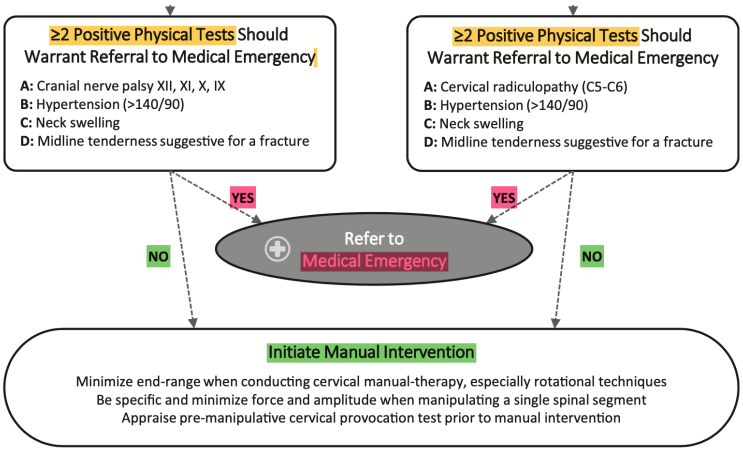
Chaibi and Russell's CAD Assessment Tool



- **Exams:**
  - Neuro exam
  - Connective tissue / Joint Hypermobility Syndrome exam
  - Other Tests?:
    - ~~Provocative tests~~
- **Evidence?**
  - Lacking

Chaibi A, Russell BR. Annals of Medicine. 2019; 51 (2)118-127.

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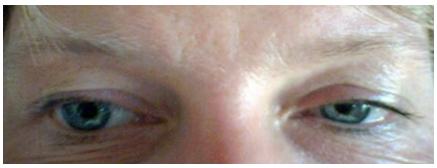
CAD Examination

Cervical Artery Dissection: The Elusive Diagnosis

APR 14TH, 2020 JOHN RIGGINS JR CATEGORIES: PRACTICE UPDATES

Authors: John Riggins Jr, MD (EM Resident Physician, SUNY Downstate/Kings County Hospital) and Richard Sinert, DO (Professor of Emergency Medicine, SUNY Downstate/Kings County Hospital) // Reviewed by: Alex Koyfman, MD (@EMHighAK) and Brit Long, MD (@long_brit)



- **Physical Exam:**
  - Look for signs of trauma to neck (ecchymosis, bruising, crepitus) and listen for carotid bruits indicating a disruption in the blood flow of a vessel.
  - Look for a partial's Horner syndrome, evaluate for constriction of the pupils (miosis) and ipsilateral drooping of the eyelid (ptosis).
  - Palpation of the neck, around the bilateral temporal regions or in the occiput region might elicit pain in some patients presenting with CAD.
  - Patients can also present with tongue weakness and dysgeusia resulting from ischemia of the hypoglossal nerve, which is the most common cranial nerve affected.
  - In some cases, patients will present with symptoms of brain ischemia that can include dysphagia, dysarthria, and hemiplegia
  - Patients can also experience signs of optic nerve ischemia which can lead to amaurosis fugax and other visual disturbances when a dissection occurs near the carotid siphon.
  - Weakness and paresthesias.
  - Head, facial and neck pain were seen in up 74% of patients with symptomatic cervical artery dissection.

http://www.emdocs.net/cervical-artery-dissection-the-elusive-diagnosis/

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VBI Tests?

Musculoskeletal Science and Practice
Volume 49, October 2020, 102181

Professional issue

Yes, we should abandon pre-treatment positional testing of the cervical spine

Nathan Hutting [a], Hendrikus Antonius "Rik" Kranenburg [b], Roger Kerry [c]

[a] Department of Occupation and Health, School of Organisation and Development, HAN University of Applied Sciences, Nijmegen, the Netherlands
[b] Research Group on Healthy Aging, Allied Health Care and Nursing, Hanze University of Applied Sciences, Groningen, the Netherlands
[c] Division of Physiotherapy and Rehabilitation Sciences, University of Nottingham, Nottingham, UK

- VBI tests are not able to predict major adverse events and seem not to have any added value to the patient interview with regard to detecting VBI or another vascular pathology.
- Furthermore, a negative VBI test can be wrongly interpreted as 'safe to manipulate'.
- Therefore, the use of VBI tests cannot be recommended and should be abandoned.

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MAYO CLINIC

CONCISE REVIEW

Craniocervical Artery Dissections: A Concise Review for Clinicians

Check for updates

Zafer Keser, MD; James F. Meschia, MD; and Giuseppe Lanzino, MD

- Interestingly, many patients with CAD have isolated mild connective tissue abnormalities, such as:
  - joint hypermobility,
  - easy bruising,
  - and poor wound healing,

  suggesting that CAD may be another expression of a yet undefined connective tissue disorder. 9

- Giossi A, Ritelli M, Costa P, et al. Connective tissue anomalies in patients with spontaneous cervical artery dissection. Neurology. 2014;83(22):2032-2037.

Mayo Clin Proc. ■ April 2022;97(4):777-783 ■ https://doi.org/10.1016/j.mayocp.2022.02.007
www.mayoclinicproceedings.org ■ © 2022 Mayo Foundation for Medical Education and Research

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Connective Tissue / Joint Hypermobility Syndrome Examination

frontiers in Neurology

PERSPECTIVE
published: 31 May 2021
doi: 10.3389/fneur.2021.663830

Cervical Artery Dissection and Sports

Stefan T. Engelter[1,2], Christopher Traenka[1,2], Caspar Grond-Ginsbach[2,3], Tobias Brandt[4], Maani Hakimi[5], Bradford B. Worrall[6], Stephanie Debette[7,8], Alessandro Pezzini[9], Didier Leys[10], Turgut Tatlisumak[11], Christian H. Nolte[12] and Philippe Lyrer[1]*

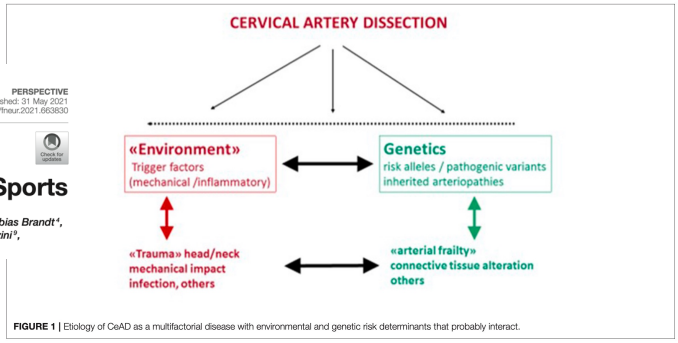

FIGURE 1 | Etiology of CeAD as a multifactorial disease with environmental and genetic risk determinants that probably interact.

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- However, mild clinical signs of a connective tissue weakness, including slight joint hypermobility, thin and translucent skin, or easy bruising, are common and associated with CeAD (25, 26).

- 25. Grond-Ginsbach C, Debette S. The association of connective tissue disorders with cervical artery dissections. *Curr Mol Med.* (2009) 9:210–4. doi: 10.2174/156652409787581547
- 26. Giossi A, Ritelli M, Costa P, Morotti A, Poli L, Del Zotto E, et al. Connective tissue anomalies in patients with spontaneous cervical artery dissection. *Neurology.* (2014) 83:2032–7. doi: 10.1212/WNL.0000000000001030

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- Approximately 40% of the CeAD patients reported any kind of recent head or neck trauma in the month prior to symptom onset (4), as compared to 10% of the patients with ischemic stroke attributable to a cause other than CeAD and 20% of the healthy controls (4).
- More than 90% of the trauma events recalled by the CeAD patients were trivial and so mild that the individuals did not seek for medical care or advice.
- As a causal relationship with the CeAD is either questionable or unclear, the term *mechanical trigger event* is preferred.

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Connective Tissue / Joint Hypermobility Syndrome Examination

American Journal of Medical Genetics Part C (Seminars in Medical Genetics) 169C:6–22 (2015)

ARTICLE

Differential Diagnosis and Diagnostic Flow Chart of Joint Hypermobility Syndrome/Ehlers–Danlos Syndrome Hypermobility Type Compared to Other Heritable Connective Tissue Disorders

MARINA COLOMBI, CHIARA DORDONI, NICOLA CHIARELLI, AND MARCO RITELLI

TABLE I. The Villefranche Criteria for the Historical EDS Types [Beighton et al., 1998] and the Underlying Molecular Defect

EDS type	Major criteria	Minor criteria	Gene(s)
Classic AD OMIM #130000, #130010	**Skin hyperextensibility**[a] **Widened atrophic scars** JHM	Smooth, velvety skin **Molluscoid pseudotumors** Subcutaneous spheroids Complications of JHM (e.g., sprains, dislocations/subluxations, *pes planus*) Muscle hypotonia, delayed gross motor development Easy bruising Manifestations of tissue fragility (e.g., hiatal hernia, anal prolapse in childhood, cervical insufficiency) Surgical complications (postoperative hernias) Positive family history	*COL5A1* *COL5A2*
Hypermobility AD OMIM #130020	Skin involvement (hyperextensibility and/or smooth, velvety skin) Generalized JHM	Recurring joint dislocations **Chronic joint/limb pain** Positive family history	?
Vascular AD OMIM #130050	Thin, translucent skin **Arterial/intestinal/uterine fragility or rupture** **Extensive bruising** Characteristic facial appearance	**Acrogeria** Hypermobility of small joints Tendon and muscle rupture *Talipes equinovarus* (clubfoot) Early-onset varicose veins Arteriovenous, carotid-cavernous *sinus fistula* **Pneumothorax/pneumohemothorax** Gingival recession Positive family history, **sudden death in (a) close relative(s)**	*COL3A1*
Kyphoscoliotic AR OMIM #225400	Generalized JHM Severe muscle hypotonia at birth **Scoliosis at birth, progressive** **Scleral fragility and rupture of the ocular globe**	Tissue fragility, including atrophic scars Easy bruising Arterial rupture *Marfanoid habitus* **Microcornea** Radiologically considerable osteopenia Family history, i.e., affected sibs	*PLOD1*
Arthrochalasia AD OMIM #130060	Severe generalized JHM, with recurrent subluxations **Congenital bilateral hip dislocation**	Skin hyperextensibility Tissue fragility, including atrophic scars Easy bruising Muscle hypotonia Kyphoscoliosis Radiologically mild osteopenia	*COL1A1* *COL1A2*

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The Beighton Score

Rheumatology International (2021) 41:1707–1716
https://doi.org/10.1007/s00296-021-04832-4

Rheumatology
INTERNATIONAL

REVIEW

The Beighton Score as a measure of generalised joint hypermobility

Sabeeha Malek[1] · Emma J. Reinhold[2] · Gemma S. Pearce[3]

Received: 4 February 2021 / Accepted: 2 March 2021 / Published online: 18 March 2021

- The evidence presented here brings into question the validity of the BS as a direct and indirect indicator of GJH and disputes its continued use as a diagnostic tool.
- The BS should be used as intended, i.e. as an initial screening method, after which other notable joints, for example, the shoulder, hips, ankles, and remaining digits, could be examined until the clinician is satisfied that no evidence of systemic JH conclusively exists, nor any associated syndromic features, before excluding Heritable Connective Tissue Disorders (HCTD) as a diagnosis.

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The Beighton Score

Review

Interrater and Intrarater Reliability of the Beighton Score

A Systematic Review

Lauren N. Bockhorn,* MD, Angelina M. Vera,* MD, David Dong,* BS, Domenica A. Delgado,* MBA, Kevin E. Varner,* MD, and Joshua D. Harris,*† MD
Investigation performed at Houston Methodist Orthopedics and Sports Medicine, Houston, Texas, USA

The Orthopaedic Journal of Sports Medicine, 9(1), 2325967120968099
DOI: 10.1177/2325967120968099

- The Beighton score is a highly reliable clinical tool that shows substantial to excellent inter- and intrarater reliability when used by raters of variable backgrounds and experience levels.

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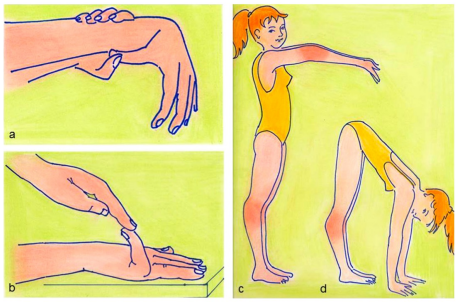

Figure 1. Assessment of joint hypermobility with the Beighton score: (a) passive dorsiflexion of the fifth metacarpophalangeal joint to ≥90°, (b) opposition of the thumb to the volar aspect of the ipsilateral forearm, (c) hyperextension of the elbow to ≥10°, and hyperextension of the knee to ≥10°, d) placement of hands flat on the floor without bending the knees (Figure drawn by L. Manenti). The Beighton score is incorporated into the diagnostic criteria for EDSs, MFS, LDS, ATS, and OI.

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Connective Tissue / Joint Hypermobility Syndrome Examination

Brighton criteria for JHS

Major criteria

Beighton score ≥4/9
Arthralgia for >3 months in >4 joints

Minor criteria

Beighton score 1–3
Arthralgia in 1–3 joints
History of joint dislocations
Soft tissue lesions >3
Marfan-like *habitus*
Skin *striae*, hyperextensibility, or scarring
Downslanting palpebral fissures, lid laxity, myopia
History of varicose veins, hernia, visceral prolapse

Agreement: both major, or 1 major and 2 minor, or 4 minor criteria. Criteria major 1 and minor 1 are mutually exclusive as/are major 2 and minor 2.

Source: Grahame et al., [2000] and subsequent modifications (see, for example, Tinkle et al., [2009]).

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5-point questionnaire for JHM

1. Could you ever place your hands flat on the floor without bending your knees?
2. Could you ever bend your thumb to touch your forearm?
3. As a child did you amuse your friends by contorting your body into strange shapes OR could you do the splits?
4. As a child or teenager did your shoulder or kneecap dislocate on more than one occasion?
5. As a child or teenager did you consider yourself double-jointed?

Agreement: affirmative answer for two or more questions.

Source: modified from Hakim and Grahame [2003].

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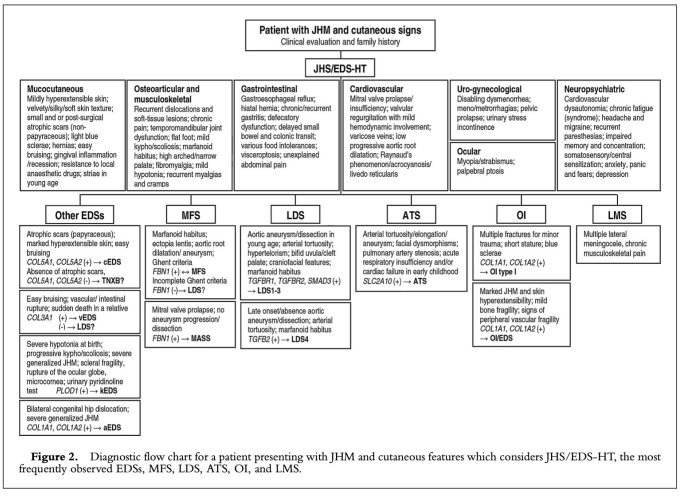

Figure 2. Diagnostic flow chart for a patient presenting with JHM and cutaneous features which considers JHS/EDS-HT, the most frequently observed EDSs, MFS, LDS, ATS, OI, and LMS.

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Instructive Cases

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Journal of Chiropractic Medicine (2011) 10, 283–287
ELSEVIER
JCM Journal of Chiropractic Medicine
www.journalchiromed.com

Vertebral artery dissection in a patient practicing self-manipulation of the neck

John S. Mosby DC, MD[a,*], Stephen M. Duray PhD[b]

[a] Associate Professor, Division of Clinics, Palmer College of Chiropractic, Davenport, IA 52803
[b] Professor, Division of Life Sciences, Palmer College of Chiropractic, Davenport, IA 52803

Received 15 October 2010; received in revised form 1 December 2010; accepted 6 January 2011

- A 42-year-old female patient complained of leftsided neck pain and shoulder pain at a chiropractic college community outreach clinic.
- The patient had not seen a chiropractor for 8 years according to records; however, she reported that she would regularly self manipulate or “crack” her neck to reduce neck pain.
- She reported that she had performed this self-manipulation of her neck several times a day for the past several years. She was not a chiropractor and had no training in manipulative therapy.
- When she arrived at the clinic, she appeared tired and distressed.
- She stated that she had burning, sharp pain and requested that her neck and shoulder be adjusted.

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- She reported a persistent headache that started 12 days prior while driving her vehicle.
- The pain was in her lower neck and shoulder and ascended to the temporal region on her left side.
- She described her headache as a stabbing pain, worse than she had ever experienced before, that moved throughout her head and occurred for approximately 5 to 10 minutes at a time.
- The pain was intense and burning, rating a 10/10 on a numerical rating scale.
- This pain was followed by episodes of nausea and vomiting. She stated that she would have these headaches for 3 hours per day and, for most of the time, she would be on her hands and knees in a dark corner of a room.
- She denied any tobacco or oral contraceptive use and noted drinking socially.
- Throughout the visit, she repeatedly requested that she wanted to have her neck manipulated. The supervising chiropractor stated that he would not perform a chiropractic manipulation due to the seriousness of her suspected condition.
- He quickly referred her out to an emergency department for consult and advised her not to self-manipulate her neck.

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Patient History

1. Ipsilateral facial dysesthesia (pain and numbness)- Most common symptom
2. Dysarthria or hoarseness (cranial nerves [CN] IX and X)
3. Contralateral loss of pain and temperature sensation in the trunk and limbs
4. Ipsilateral loss of taste (nucleus and tractus solitarius)
5. Hiccups
6. Vertigo
7. Nausea and vomiting
8. Diplopia or oscillopsia (image movement experienced with head motion)
9. Dysphagia (CN IX and X)
10. Disequilibrium
11. Unilateral hearing loss
12. Contralateral weakness or paralysis (pyramidal tract)
13. Contralateral numbness (medial lemniscus)

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Clinical findings

1. Limb or truncal ataxia
2. Nystagmus
3. Ipsilateral Horner syndrome in as many as one third of patients with VAD (ie, impairment of descending sympathetic tract)
4. Ipsilateral hypogeusia or ageusia (ie, diminished or absent sense of taste)
5. Lateral medullary syndrome
6. Medial medullary syndrome
7. Tongue deviation to the side of the lesion (impairment of CN XII)
8. Contralateral hemiparesis
9. Internuclear ophthalmoplegia (lesion of the medial longitudinal fasciculus)
10. Ipsilateral impairment of fine touch and proprioception
11. Contralateral impairment of pain and thermal sensation in the extremities (ie, spinothalamic tract)

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Vertebral artery dissection

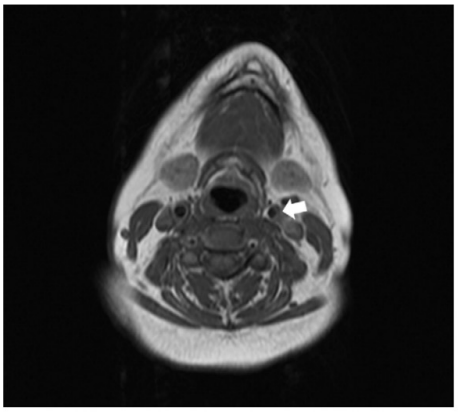

Fig. 1. Presurgical magnetic resonance angiogram showing arterial narrowing as indicated by arrow.

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Limitations

- There are several important limitations to this case report. Although the present report represents the first to describe a case of VAD for a patient who habitually practiced self-manipulation before the onset of symptoms, a sample of 1 cannot "prove" that a relationship exists between self-manipulation of the neck and VAD.
- It merely suggests a chronological association and need for future studies to determine causality. Second, as this is a retrospective study, it was not possible to determine the exact interval of time between the last cervical self-manipulation and the onset of symptoms.
- All that is known, as stated earlier, is that the patient reportedly self-manipulated her neck several times a day.
- This raises the question of whether or not the patient was undergoing a VAD and had resultant head and neck pain for which she tried to self manipulate, leading to further complication of the condition.
- This also raises another question of whether her crude attempts at replicating a chiropractic adjustment were the cause of the VAD in the first place.

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Conclusion

- It is critical for doctors of chiropractic to exercise proper clinical evaluation and treatment when addressing their patients, specifically when dealing with suspected VAD.
- This case report should serve as a reminder that recognizing "red flags" is critical to a proper diagnosis.
- By taking a proper history, realizing the warning signs, and performing the right action plan (ie, immediate referral to an emergency department), the chiropractic doctor and intern contributed to the preservation of this patient's life.

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Myth exploded

CASE REPORT

Vertebral artery dissection in evolution found during chiropractic examination

Dan Futch,[1] Michael J Schneider,[2] Donald Murphy,[3] Allison Grayev[4]

"Based on the history of sudden onset of **severe upper cervical pain and headache with visual disturbance and ocular numbness**, the DC was concerned about the possibility of early VAD. Urgent MR angiography (MRA) of the neck and head, along with MRI of the head, was ordered. No cervical spine examination or manipulation was performed…"

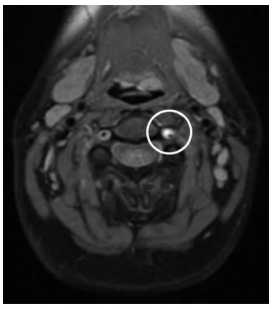
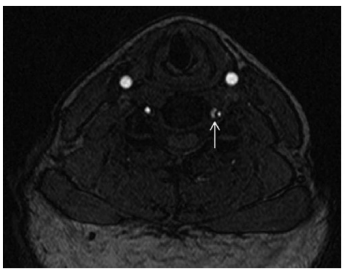


Figure 1 Axial proton density image demonstrates circumferential hyper-intensity surrounding the left cervical vertebral artery (representing the false lumen). Note decreased calibre of true lumen (black flow void) with respect to the right vertebral artery.



igure 2 Axial image from three-dimensional time-of-flight MRA emonstrates T1 hypointense dissection flap separating the true lumen ateral) from the false lumen (medial). MRA, MR angiography.

Futch D, et al. BMJ Case Rep 2015. doi:10.1136/bcr-2015-212568.

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Clinical Condition: Headache

Variant 4: Sudden onset of unilateral headache or suspected carotid or vertebral dissection or ipsilateral Horner syndrome.

Radiologic Procedure	Rating	Comments	RRL*
CTA head and neck with IV contrast	8		☢☢☢
MRA head without IV contrast	8		O
MRA neck without and with IV contrast	8	Include T1 fat-saturated axial images in this procedure.	O
MRI head without and with IV contrast	8	Perform this procedure with DWI sequences.	O
MRI head without IV contrast	8	Perform this procedure with DWI sequences.	O
MRA neck without IV contrast	7	Include T1 fat-saturated axial images in this procedure.	O
CT head without IV contrast	7		☢☢☢
MRA head without and with IV contrast	6		O
MRI neck without and with IV contrast	6	Include T1 fat-saturated axial images in this procedure.	O
Arteriography cervicocerebral	6		☢☢☢
CT head without and with IV contrast	6		☢☢☢
CT head with IV contrast	6		☢☢☢
MRI neck without IV contrast	5	Include T1 fat-saturated axial images in this procedure.	O
MRI cervical spine without and with IV contrast	5		O
MRI cervical spine without IV contrast	4		O
CT neck with IV contrast	4		☢☢☢
CT neck without and with IV contrast	4		☢☢☢
CT neck without IV contrast	3		☢☢☢
US duplex Doppler carotid	3		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

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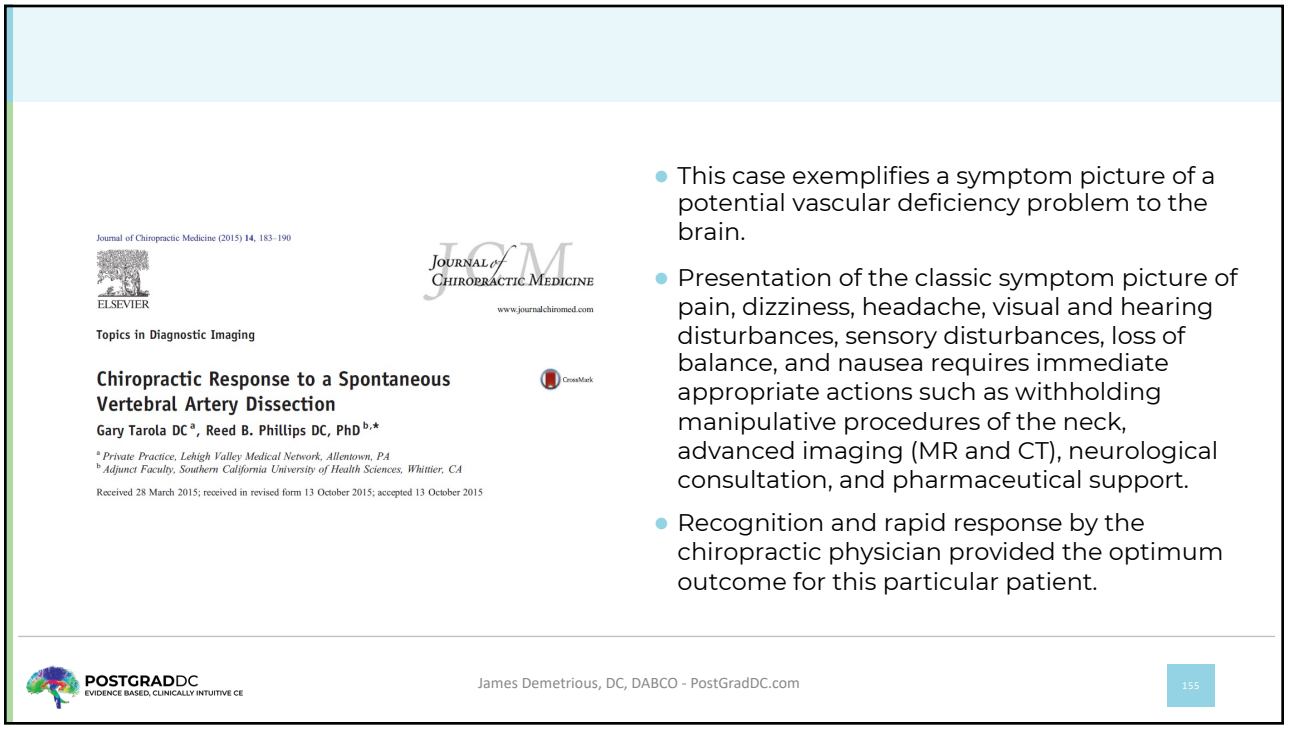
Journal of Chiropractic Medicine (2015) 14, 183–190
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Topics in Diagnostic Imaging
Chiropractic Response to a Spontaneous Vertebral Artery Dissection
Gary Tarola DC [a], Reed B. Phillips DC, PhD [b,*]
[a] Private Practice, Lehigh Valley Medical Network, Allentown, PA
[b] Adjunct Faculty, Southern California University of Health Sciences, Whittier, CA
Received 28 March 2015; received in revised form 13 October 2015; accepted 13 October 2015
This case exemplifies a symptom picture of a potential vascular deficiency problem to the brain.
Presentation of the classic symptom picture of pain, dizziness, headache, visual and hearing disturbances, sensory disturbances, loss of balance, and nausea requires immediate appropriate actions such as withholding manipulative procedures of the neck, advanced imaging (MR and CT), neurological consultation, and pharmaceutical support.
Recognition and rapid response by the chiropractic physician provided the optimum outcome for this particular patient.
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James Demetrious, DC, DABCO - PostGradDC.com
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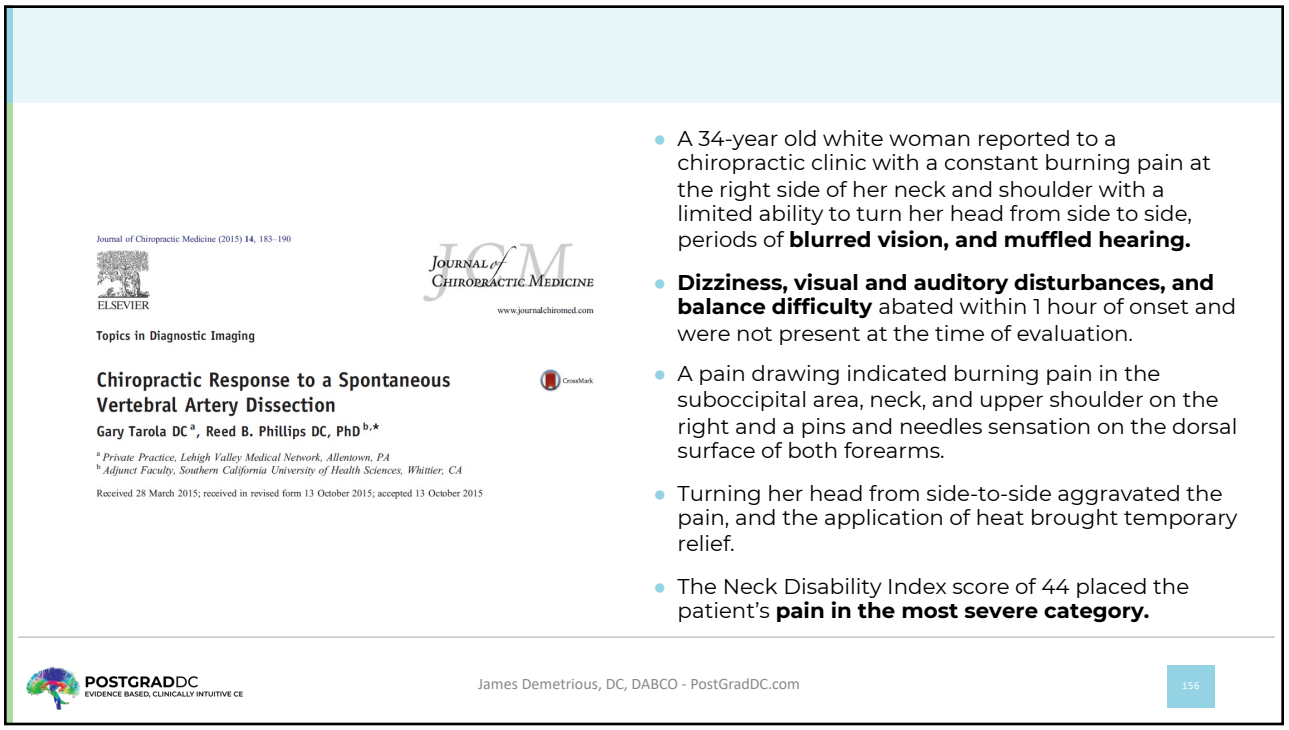
Journal of Chiropractic Medicine (2015) 14, 183–190
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Topics in Diagnostic Imaging
Chiropractic Response to a Spontaneous Vertebral Artery Dissection
Gary Tarola DC [a], Reed B. Phillips DC, PhD [b,*]
[a] Private Practice, Lehigh Valley Medical Network, Allentown, PA
[b] Adjunct Faculty, Southern California University of Health Sciences, Whittier, CA
Received 28 March 2015; received in revised form 13 October 2015; accepted 13 October 2015
A 34-year old white woman reported to a chiropractic clinic with a constant burning pain at the right side of her neck and shoulder with a limited ability to turn her head from side to side, periods of blurred vision, and muffled hearing.
Dizziness, visual and auditory disturbances, and balance difficulty abated within 1 hour of onset and were not present at the time of evaluation.
A pain drawing indicated burning pain in the suboccipital area, neck, and upper shoulder on the right and a pins and needles sensation on the dorsal surface of both forearms.
Turning her head from side-to-side aggravated the pain, and the application of heat brought temporary relief.
The Neck Disability Index score of 44 placed the patient's pain in the most severe category.
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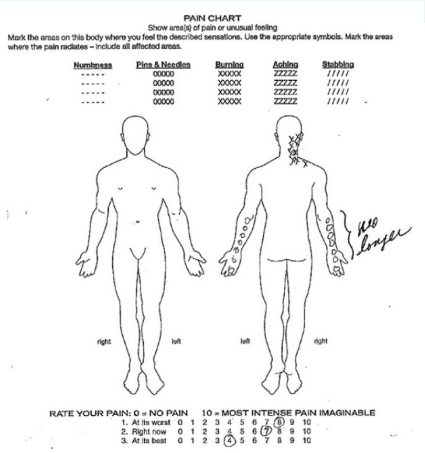

Fig. 1. Pain drawing indicating burning pain in the area of the right sub-occipital and cervical area and pins and needles sensation on the dorsal surface of both forearms.

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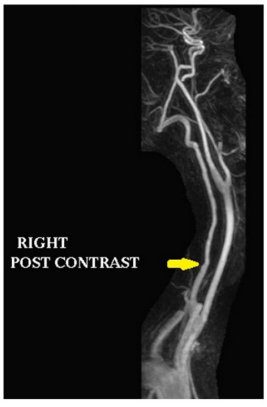

Fig. 2. MRA neck image. Three-dimensional dynamic time-resolved contrast-enhanced MRA of the neck reveals abrupt moderate long segment narrowing of the right vertebral artery involving the V2 and distal V1 segments. *(Color version of figure appears online.)*

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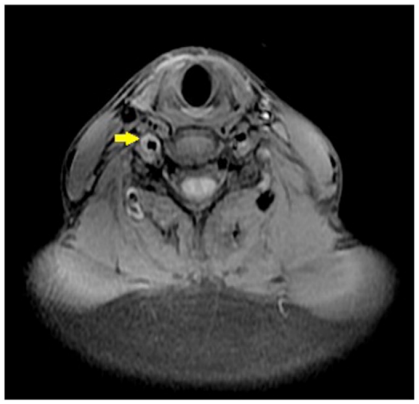

Fig. 3. MRA neck image. Fat suppressed axial T1 weighted imaging of the neck utilizing IDEAL technique (Iterative Decomposition of water and fat with Echo Asymmetry and Least squares estimation) reveals high signal within the wall of the V2 segment of the right vertebral artery compatible with intramural hematoma. *(Color version of figure appears online.)*

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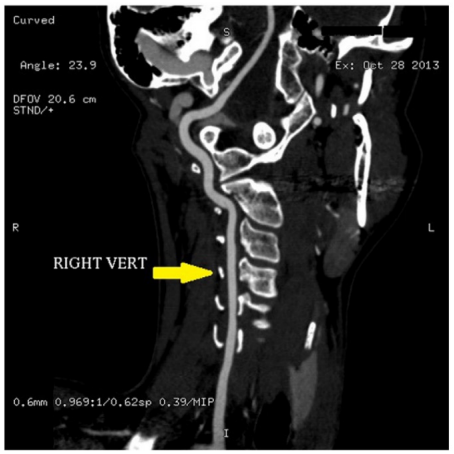
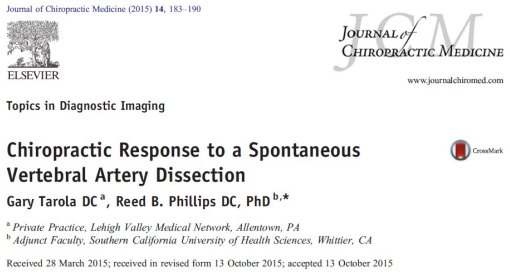


Fig. 6. CT angiography neck image. Curved planar reformatted imaging of the right vertebral artery from CT angiography of the neck performed 3 months after initial imaging reveal near complete resolution of the right vertebral artery narrowing related to arterial dissection.



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- While this particular patient had a spontaneous vertebral artery dissection, not all cases with a similar signs or symptoms will result in similar diagnoses, and some positive cases may exhibit asymptomatic presentations.
- Nevertheless, when patients present with symptoms that are suggestive of a possible cerebral vascular event, caution in providing manipulative care seems advisable until the vascular disruption has been ruled out through proper examination procedures.
- This procedure may be construed as an error on the side of excessive caution or defensive medicine that requires unnecessary costly additional procedures and patient anxiety, but in the opinions of the authors, the potential for significant adverse results justifies these actions.

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Recognition of Spontaneous Vertebral Artery Dissection Preempting Spinal Manipulative Therapy: A Patient Presenting With Neck Pain and Headache for Chiropractic Care

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- A 45-year-old otherwise healthy female presented for evaluation and treatment of neck pain and headache.
- Within minutes, non-specific musculoskeletal symptoms progressed to **neurological deficits, including limb ataxia and cognitive disturbances.**
- Suspicion was raised for cerebrovascular ischemia and emergent referral was initiated.

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- A 45-year-old white female, well-nourished and employed as a school administrator, presented to a chiropractic clinic complaining of upper back/neck pain and stiffness as well as headache and pain in the posterior portion of the right arm down to the elbow of 3 days duration.
- Her level of discomfort progressed in severity in the 24 hours prior to presentation, which is what prompted her appointment. Because this was a new complaint, an updated history and examination were performed.
- No history of trauma was disclosed.
- Physical examination revealed painful and limited active range of motion in the cervical region. Palpation was provocative for tenderness.

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- After the initial examination, a working diagnosis of myofascial pain syndrome was established.
- Therapeutic ultrasound (Chattanooga Medical Supply, TN) was applied (4 minutes, 1 W/cm2 at 1 MHz) in the seated position over the suboccipital and posterior cervical musculature.
- While still in the seated position, soft tissue treatment was performed by a licensed massage therapist on the suboccipital and posterior cervical musculature.
- The patient was shown to a treatment room and was supine when the clinician entered and asked how she felt.
- The patient responded that her neck pain was much better, but she was more aware of her headache.

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- The patient was assisted to the seated posture, became dizzy, reported visual and cognitive disturbances, and had difficulty speaking.
- She proceeded to lose control of her right leg, which spontaneously assumed a flexion contracture.
- The clinician suspected a vascular etiology at this time and SMT was not performed.
- Paramedics were immediately summoned and the patient was transported to a local hospital with a working diagnosis of acute cerebrovascular ischemia.

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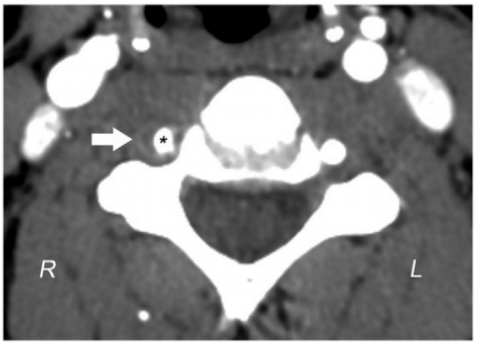

Fig 1. CTA with intravenous contrast at the level of C5 demonstrates a crescent-shaped mural thickening with annular enhancement (arrow) around a narrowed lumen of the right vertebral artery (asterisk).

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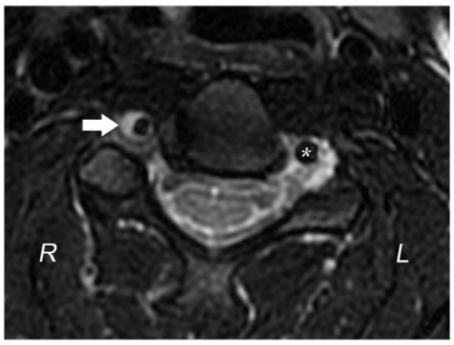

Fig 3. Axial gradient echo MRI demonstrates a narrowed lumen of the right vertebral artery compared to the left (asterisk) with a crescent-shaped mural thickening of high intensity (arrow) compared to the flow void within the lumen.

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Fig 2. TOF-MRA with intravenous contrast demonstrates a narrowed V_2 segment of the right vertebral artery (arrow), with normal caliber vessel both cranial and caudal to the short stenotic region.

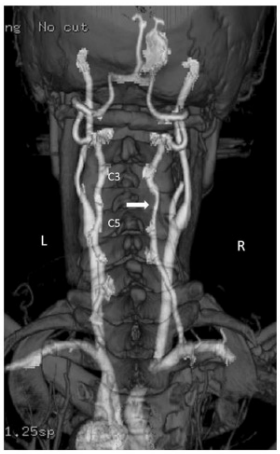

Fig 4. 3D reformat CTA viewed from posterior demonstrates narrowing of the V_2 segment of the right vertebral artery (arrow) extending from C5 to C3, with normal caliber vessel both cranially and caudally.

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Diligence to Identify a Developing CAD…

- Patients may present to physicians with developing CADs.
- While rare and difficult to diagnose the developing CAD, it is vitally important to exert clinical diligence.
- The result of an undiagnosed CAD and resultant stroke can be catastrophic:
  - Death
  - Infarcts
  - Paralysis
  - Locked-in Syndrome

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Locked In Syndrome

Locked-in syndrome (LiS) has three main types, or forms, including:

- **The classical form**: In this type of LiS, you have total immobility (lack of voluntary movement) but can move your eyes vertically (up and down), blink and maintain your usual cognitive abilities. You can also hear.
- **The incomplete form**: This type of LiS is just like the classical form except you can have some sensation and movement functions in certain areas of your body.
- **The total immobility form**: In this type of LiS, you have complete body paralysis and loss of eye movement, but you have your normal cognitive abilities. Healthcare providers can tell a person with this form still has cognitive (thinking and reasoning) function by examining cortical function with an electroencephalogram (EEG), a test that measures brain waves.

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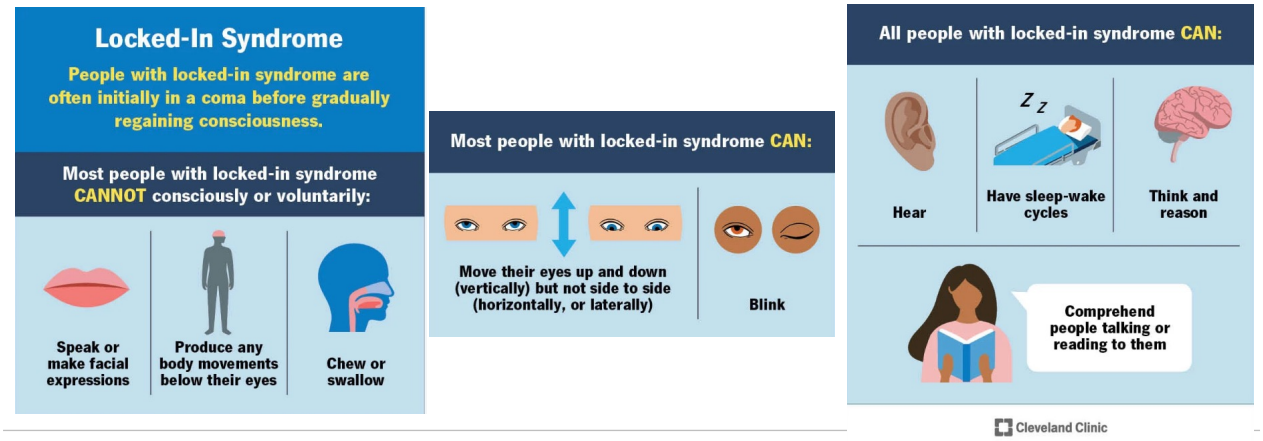
What causes locked-in syndrome?
Locked-in syndrome (LiS) is caused by damage to a specific part of your brainstem called the pons.



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- **Detecting the Burgeoning CAD:**
  - Detailed History
  - Due Diligence
  - Emphasis on Importance to Reporting S/S
  - Re-Evaluations

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Thank you!

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