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Review

STRAIN in vertebral artery during passive cervical range of motion and spinal manipulation therapy: A systematic review and meta-analysis

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ABSTRACT

Objective: To identify and synthesize studies examining the strain on the vertebral artery (VA) during cervical spinal manipulation therapy (cSMT). Additionally, we compared VA strains induced by cSMT with passive range of motion (ROM) across different cervical spine levels and VA segments.
Design: A systematic review and meta-analysis were conducted following PRISMA guidelines and registered with PROSPERO (CRD42024591457).
Literature search: The search was performed in May 2025 across SCOPUS, PubMed, MEDLINE, Web of Science, LILACS, SciELO, and the Index to Chiropractic Literature.
Study selection criteria: Studies that focused on VA strain during cSMT and passive ROM. Risk of bias was assessed using the Anatomical Quality Assessment (AQUA) Tool.
Data synthesis: Data extraction included descriptive, methodological, VA strain, and interventional details. Meta-analysis was performed for studies comparing VA strain between cSMT and ROM.
Results: ix studies met the inclusion criteria, with four providing data for meta-analysis. cSMT consistently produced lower VA strain (up to 3.8 %) compared to passive ROM (up to 12.5 %) in the V3 segment (C0–C2). Meta-analysis revealed greater strain during ROM compared to cSMT, particularly during rotation (standardized mean difference [SMD] = 1.05).
Conclusion: This systematic review and meta-analysis provide consistent evidence that cSMT induces less strain on the VA, particularly within the V3 segment, compared to passive cervical ROM. Although the evidence comes from studies conducted in human cadaveric specimens, the robustness of the methodologies and the consistency of findings across studies contribute to the growing body of biomechanical evidence supporting the relative safety of cSMT with respect to VA strain.

1. Introduction

Neck pain constitutes a highly prevalent musculoskeletal condition, currently affecting over 200 million individuals worldwide, and ranks among the foremost contributors to global disability (GBD 2021 Neck Pain Collaborators, 2024; Kazeminasab et al., 2022; Safiri et al., 2020). Its etiology is inherently multifactorial, arising from the complex interplay of biological, psychological, and environmental determinants. Beyond the immediate impact on individual well-being, neck pain imposes a significant societal and economic burden (Kazeminasab et al., 2022; Mazaheri-Tehrani et al., 2023; Meng et al., 2025). In light of this complexity, contemporary clinical guidelines advocate for multimodal, non-invasive management strategies, encompassing manual therapies, targeted exercise programs, ergonomic modifications, and patient education as core components of first-line care (Côté et al., 2016).

Within this paradigm, cervical spinal manipulative therapy (cSMT) has garnered increasing attention due to its demonstrated clinical efficacy in the management of both acute and chronic neck pain. Recent systematic reviews and meta-analyses have reported moderate to large therapeutic effect sizes, reinforcing the role of cSMT as a valuable adjunct within multidisciplinary pain management frameworks (Chaibi et al., 2021; Liu et al., 2023). However, despite its therapeutic benefits, cSMT has been associated with vertebral artery dissection (VAD), which may culminate in vertebrobasilar stroke (Whedon et al., 2015; Whedon

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et al., 2022).

VAD constitutes a leading cause of ischemic stroke in young and middle-aged adults, accounting for approximately 20 % of ischemic strokes in individuals under 45 years of age. Epidemiological data estimate the annual incidence of VAD to be between 1 and 1.5 cases per 100,000 population, with a higher prevalence in males and a substantial proportion occurring spontaneously, while roughly a quarter of cases are associated with trauma or mechanical stress (Amran et al., 2024).

To contextualize it, a precise anatomical overview of the vertebral artery and its relationship to the cervical spine is warranted. The vertebral artery (VA), a bilateral vessel typically originating from the subclavian arteries, plays a central role in the posterior cerebral circulation, supplying critical regions including the brainstem, cerebellum, and upper spinal cord. Its anatomical course is classically delineated into four segments: the V1 (preforaminal) segment, extending from its subclavian origin to the transverse foramen of the C6 vertebra; the V2 (foraminal) segment, ascending vertically through the transverse foramina of C6 to C2; the V3 (atlantoaxial or suboccipital) segment, which arcs laterally and dorsally around the atlas (C1) before perforating the atlanto-occipital membrane and dura mater; and the V4 (intracranial) segment, which traverses the subarachnoid space and converges with its contralateral counterpart to form the basilar artery (Peeters et al., 2024) (Fig. 1).

Owing to its intimate anatomical course along the cervical vertebrae, the VA is uniquely susceptible to biomechanical stresses induced by cervical motion (Symons et al., 2002). In this sense, it has been hypothesized that cSMT may impose excessive elongation or tensile strain upon the vertebral arteries, especially when cervical movements extend beyond physiological limits, thereby predisposing the vessel to intimal disruption or mural injury that may culminate in arterial dissection (Haynes et al., 2012). However, it is widely acknowledged that the cervical arteries possess the capacity to withstand substantial head and neck movements without sustaining injurious strain. Nonetheless, elongations of the cervical arteries exceeding those encountered within the physiological range of motion may precipitate vascular injury

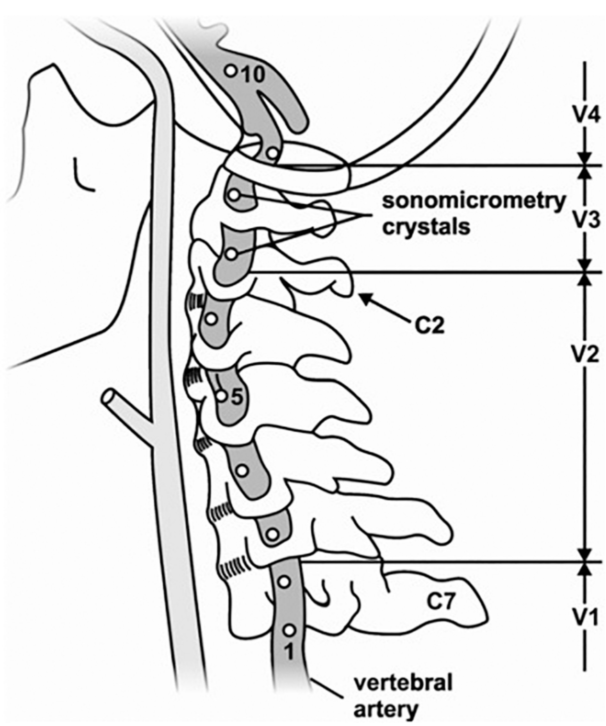

Fig. 1. Anatomical definition of the VA segments V1 through V4 and approximate placement of piezoelectric crystal markers used for strain measurements. Adapted from Piper et al. (*2014*).

(Paulus and Thaler, 2016). Despite this, existing evidence suggests a considerable margin of safety before such deleterious effects manifest (Symons et al., 2002).

From this perspective, the primary objective of this review was to identify, and provide a synthesis of existing studies and their methodologies exploring the strain caused on the VA during cSMT. In addition, this study sought to compare and report the strain impose on the VA between cSMT and passive range of motion (ROM) across different cervical spine levels and VA segments.

2. Methods

This systematic review was registered with PROSPERO (International Prospective Register of Systematic Reviews) under registration number CRD42024591457 and was conducted in accordance with the PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses (REF: doi: https://doi.org/10.1136/bmj.n71).

To ensure methodological robustness two-independent reviewers (CF and FCKD) conducted a three-stage strategy to systematically identify eligible studies, apply the pre-defined inclusion and exclusion criteria, risk of bias scale, extract the data, synthesize and conduct a meta-analysis of the eligible studies. Initially, a systematic search strategy was developed, tried on PubMed and adapted to the other databases (SCOPUS, PubMed, MEDLINE, Web of Science, LILACS, SciELO, and the Index to Chiropractic Literature) utilizing combinations of MeSH terms — "mechanical stress," "vertebral artery," "spinal manipulation," and "strain" — both individually and collectively, to maximize the sensitivity and breadth of the results retrieved. Each database was searched from date of inception to May 2025, with results limited to the English language.

In addition to database searches, we conducted backward and forward citation tracking to improve the comprehensiveness of the literature search. The reference lists of all included studies were manually reviewed to identify additional relevant articles. We also used Google Scholar to identify studies that cited the included articles ("Cited by" function), and screened those results for potentially eligible studies.

2.1. *Inclusion criteria*

Studies eligible for inclusion in this study were original studies written in English that reported direct measurement of VA strain during ROM and cSMT in humans. Exclusion criteria were applied and included literature reviews, letters to the editor, single-case studies, studies with incomplete data or a lack of full-text access, duplicate publications, animal studies, imaging studies, and those that failed to report direct measurement of mechanical stress or strain in the human VA during ROM and cSMT.

2.2. *Screening of titles and abstracts*

The initial screening of titles and abstracts was conducted independently by two reviewers using a standardized pre-piloted Excel spreadsheet, sorting for possibly relevant, irrelevant, and duplicate citations. Full texts of potentially eligible studies were then retrieved and assessed against the predefined inclusion criteria. In cases of disagreement regarding study selection, consensus was reached through discussion; if necessary, a third reviewer (WH) was consulted.

2.3. *Risk of bias*

To enhance the methodological quality of the present review, the Anatomical Quality Assessment (AQUA) Tool for the Quality Assessment of Anatomical Studies Included in Meta-Analyses and Systematic Reviews was applied to the included studies (Henry et al., 2017). Developed specifically for assessing the quality of anatomical studies, AQUA comprises five appraising questions in each of its five domains, totalling twenty questions, with classifications as low, high, and unclear risk of bias. An example of the five domains is: 1) study objective and subjective characteristics; 2) study design; 3) methodology, experimental assay characterization; 4) descriptive anatomical characterization; 5) reporting of results (Henry et al., 2017). Its application was particularly appropriate given the focus of the present review in summarizing the evidence of vertebral artery strain in human cadavers during cSMT.

2.4. Certainty of evidence

A formal assessment of the certainty of evidence, such as using the GRADE approach, was not conducted in this review. The GRADE system and similar frameworks are primarily designed for systematic reviews of clinical studies, particularly randomized controlled trials, and are not validated for use in experimental cadaveric studies. Currently, there is no widely accepted or standardized method for grading the certainty of evidence in this type of research. Therefore, while considerations such as risk of bias and consistency across studies were qualitatively addressed in the interpretation of the findings, no formal certainty rating was applied.

2.5. Data extraction

Data extraction was likewise conducted independently by two

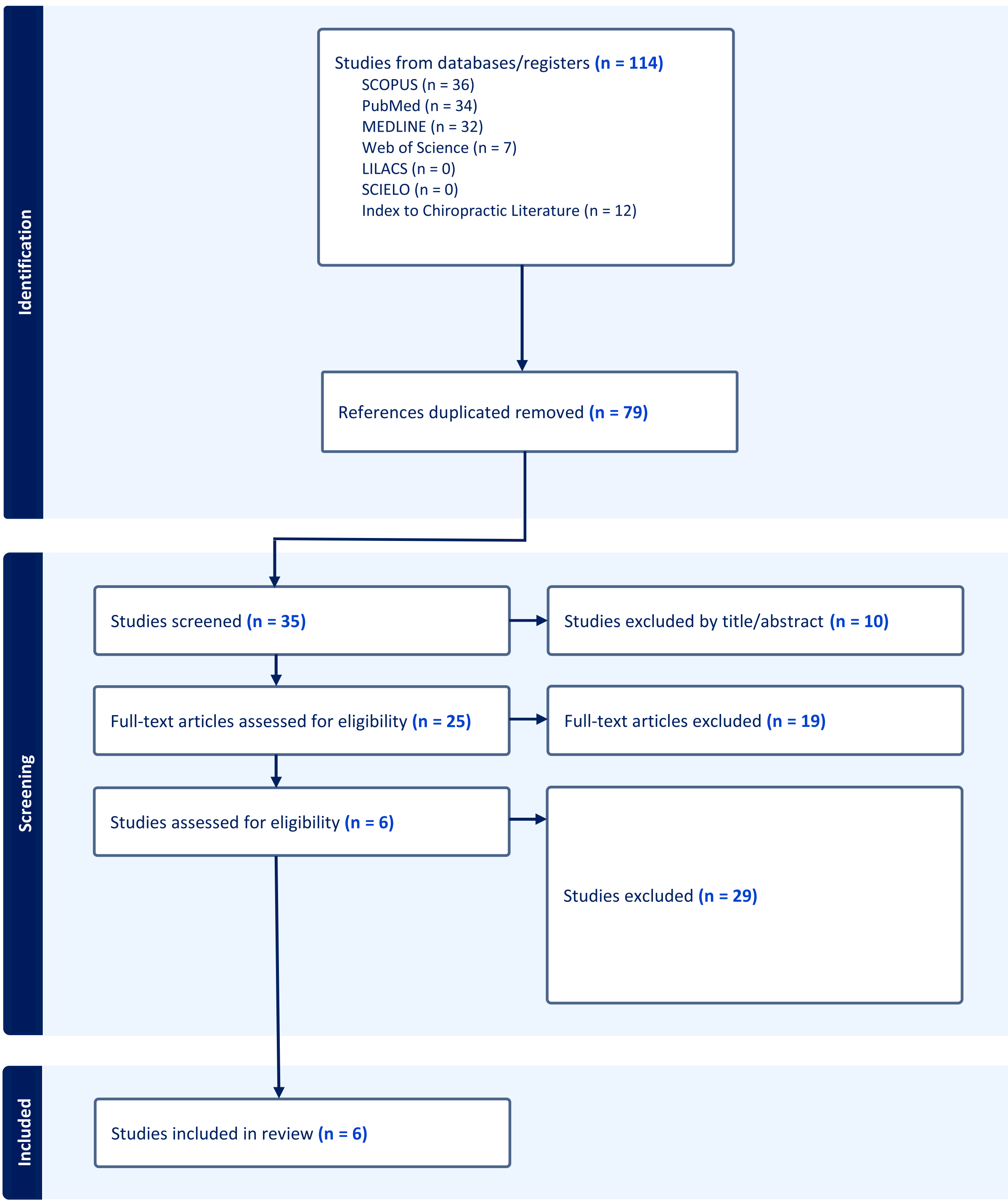

Fig. 2. PRISMA flow diagram illustrating the selection process for studies included in this research.

reviewers. Extracted variables included authorship, year of publication, sample characteristics, study methods, intervention details and mechanical strain on VA segments during ROM and cSMT. Where data were missing or ambiguities arose, an attempt was made to contact the study authors to obtain clarifications, thus ensuring the inclusion of the most complete and accurate datasets available.

2.6. Meta-analysis

The outcome of interest was the mechanical strain imposed in at least one VA segment (V1-V4) during cSMT compared to VA strain observed during at least one of the cervical ROM flexion, extension, lateral flexion, rotation and combined movements, flexion-rotation and extension-rotation, with the latter four performed in both ipsilateral and contralateral side.

Quantitative data, including mean values and standard deviations (SDs), were extracted from each study for meta-analytic synthesis. When SDs were not reported, they were estimated using the method proposed by Wan et al. (2014), based on available range values. A random-effects model was used to pool effect sizes, thereby accounting for between-study heterogeneity. Statistical significance was determined at a *p*-value <0.05, with heterogeneity between studies assessed using Tau^2, Chi-square, and I^2 statistics. Forest plots were generated to visually present the estimated pooled VA strain percentage change from neutral, between cSMT and ROM. The meta-analysis was performed using the Cochrane Collaboration's Review Manager (RevMan) software, version 5.4.

3. Results

The electronic search yielded a total of 114 citations. The number of articles found, screened, excluded, or included articles were reported in the Preferred Reporting Items for Systematic reviews and Meta-Analyses flow chart shown in Fig. 2. Six studies fulfilled the inclusion criteria and were included in the narrative synthesis: Symons et al. (2002), Wuest et al. (2010), Herzog et al. (2012), Piper et al. (2014), Gorrell et al. (2022) and Fagundes and Herzog (2024) (TABLE 1). Four of these studies, provided sufficient comparative data to estimate the overall effect size of the VA strain during cSMT and cervical spine ROM in at least one VA segment.

Risk of Bias Within the Included Studies:

Three studies published between 2014 and 2024 – Piper et al. (2014) Gorrell et al. (2022) and Fagundes and Herzog (2024) – were found to have a low risk of bias. In contrast, two studies were classified as unclear, and one study as high risk of bias (supplemental table 2). The potential bias in the anatomical description determined the unclear risk of bias classification in both Wuest et al. (2010) and Herzog et al. (2012) while anatomical description and methodology characterization domains determined the high risk "±" (standard deviation) of bias classification in the Symons et al. (2002).

3.1. Descriptive results

3.1.1. Methodological similarities between studies

Since all six included studies had a consistent methodological foundation, the analysis begins with a detailed description of these shared experimental procedures to establish a common analytical framework. Following this methodological overview, each study was examined individually to highlight its distinct principal findings.

In all included studies, an anatomist carefully exposed the anterolateral aspect of the VA along the cervical spine. A small incision was made to implant piezoelectric ultrasonographic crystals on the VA (Sonometrics Corporation, London, ON, Canada). These crystals, functioning as transmitters and receivers, allowed for accurate strain measurement. Strain was calculated based on the difference in time required for an ultrasound signal to travel from a transmitter to a receiver crystal in ROM and cSMT, using the formula: Strain = $(L_n - L_i) / L_n$, where L_n represents the length of the VA segments with the head and neck in the neutral anatomical position and L_i the instantaneous length of the VA cSMT or range of motion testing (Symons et al., 2002).

3.2. Study-specific summaries

3.2.1. Symons et al., 2002

Two pairs of ultrasonic crystals were sutured to the VA at the C0–C1 and C6–subclavian artery (SA) levels (four crystals per artery) in five unembalmed human cadaveric specimens. The VA was subjected to ROM (extension, flexion, rotation, lateral bending, and extension with rotation) and cSMT, followed by mechanical failure testing. The greatest strain during movement was observed at the C0–C1 level in the contralateral VA, occurring during passive ROM rotation (12.5 %) and passive ROM extension with rotation testing (11.8 %). During cSMT, peak strain was 10.7 % in the ipsilateral VA. Failure strain thresholds were determined ex-vivo as 153 % at the C0–C1 and 162 % at the C6–SA levels.

3.2.2. Wuest et al., 2010

Eight pairs of crystals were implanted from above C1 to below C6, covering each intervertebral level, in a single unembalmed human cadaveric specimen. ROM and two variants of cSMT — with and without rotational components —were evaluated. The highest strain during passive ROM was observed at the C4–C5 level (13 %) during passive ROM left rotation, followed by 8.5 % at the C2–C3 level. cSMT incorporating lateral flexion and rotation induced a peak strain of 3.1 % at C4–C5. The average force applied during cSMT was 121 N, with a peak mean force of 236.5 N.

3.2.3. Herzog et al., 2012

Nine cadavers were used in this study and the sonomicrometry crystals were sutured from the foramen magnum to the subclavian artery in cadavers 6–9 and to the upper and lower VA loops in cadavers 1–5. The cervical spine was divided into V1–V4 anatomical segments and the greatest strain occurred in the V3 segment during ROM (12.2 %) and in V1 during cSMT (6.2 %), followed by V3 (3.8 %).

3.2.4. Piper et al., 2014

In the study conducted by Piper et al. (2014), three fresh, unembalmed female cadaveric specimens were used, in which a total of 24 piezoelectric ultrasonic crystals were surgically implanted—eight per specimen, with four positioned along each VA. These crystals were

Table 1
Summary of the key characteristics of the studies included in the analysis.

Author and year	Country	Study design	Sample (n)	Type of intervention	Clinician	Main outcome
Symons et al. (2002)	Canada	Cadaveric experimental	5	ROM and cSMT	1 Chiropractor	Strain on the VA
Wuest et al. (2010)	Canada	Cadaveric experimental	1	ROM and cSMT	2 Chiropractors	Strain on the VA
Herzog et al. (2012)	Canada	Cadaveric experimental	9	ROM and cSMT	4 Chiropractors	Strain on the VA
Piper et al. (2014)	Canada	Cadaveric experimental	3	ROM and cSMT	4 Chiropractors	Strain on the VA
Gorrell et al. (2022)	Canada	Cadaveric experimental	3	cSMT	3 Chiropractors	Strain on the VA
Fagundes and Herzog (2024)	Canada	Cadaveric experimental	3	ROM and cSMT	4 Chiropractors	Strain on the VA

strategically positioned from C0 to C4. During ROM testing, the greatest strains were observed during contralateral rotation, reaching up to 6 % at the C0–C1 level, 4 % at C1–C2, and 3 % at C2–C3. In contrast, cSMT elicited lower strain magnitudes, with maximum values of 5 % at C0–C1, 4 % at C1–C2, and 2 % at C2–C3.

3.2.5. *Gorrell et al., 2022*

Eight crystals were placed from C0 to the SA in three unembalmed human cadaveric specimens. Two cSMT techniques, rotation and lateral flexion, were performed at each cervical level. For ipsilateral thrusts, the highest V3 strain occurred at C3 (4.5 %) with cSMT rotation and at C1 (2.6 %) with cSMT lateral flexion. For contralateral thrusts, the maximum V3 strain was 2.2 % at C3 with cSMT rotation and 2.0 % at C1 with cSMT lateral flexion.

3.2.6. *Fagundes and Herzog, 2024*

Four crystals were implanted from C0 to C4 in three unembalmed human cadaveric specimen. Strain was measured during ROM and three cSMT phases (neutral to pre-manipulative, thrust phase, and post-manipulative). ROM testing yielded the highest strains at C0–C1 (6.9 %) during ipsilateral flexion-rotation, followed by 4.3 % at C1–C2 during contralateral rotation. During cSMT, maximum strain was 1.3 % (C0–C1), 0.1 % (C1–C2), and 1.0 % (C2–C3). The highest mean strain during the thrust phase was 1.1 % at C0–C1 on the contralateral VA.

3.3. *Vertebral artery strain across cervical segments during passive ROM and cSMT*

With regard to the strain on the VA, it can be stated that there was variation according to the cervical level investigated, type of movement and laterality (ipsilateral vs. contralateral). Among all segments, C0–C1 consistently had the greatest strains during passive rotational movements, particularly on the contralateral side. Symons et al. (2002) reported a peak strain of 12.5 % ± 10.1, while Piper et al. (2014) and Fagundes and Herzog (2024) observed values of 6 % and 5.3 % ± 1.6, during ROM testing respectively. Similarly, during combined ROM extension-rotation testing, strain values reached 11.8 % ± 8.6 (Symons et al., 2002) and 6.0 % ± 3.5 (Fagundes and Herzog, 2024), resulting in the greatest elongations of the upper cervical VA during multiplanar ROM testing.

In the context of cSMT, the ipsilateral VA at the C0–C1 level exhibited the greatest strain, with Symons et al. (2002) reporting 10.7 % ± 5.5. However, more recent findings indicate a significant reduction in VA elongations during cSMT. Fagundes and Herzog (2024) recorded a peak strain of 1.3 % during the thrust phase of any cSMT.

At the C1–C2 segment, the highest strains during ROM testing were again observed during contralateral rotation, with Piper et al. (2014) and Fagundes and Herzog (2024) reporting values of 4 % and 4.3 % ± 0.5, respectively. When cSMT was applied at the C1-C2 level, strain was also observed, with contralateral VA values ranging from 2.5 % (Piper et al., 2014) to −1.0 % ± 0.6 (Fagundes and Herzog, 2024).

In the C2–C3 region, maximal strain during ROM was recorded during contralateral flexion-rotation (3.7 % ± 1.8) and extension-rotation (1.7 % ± 5.8) (Fagundes and Herzog, 2024). Strain during cSMT at this level remained minimal, with values not exceeding 1.0 %.

Specific attention was given to the V3 segment (C0–C2), which represents a highly mobile portion of the VA. Herzog et al. (2012) reported the highest strain values during passive ROM testing, peaking at 12.2 %. However, more recent studies revealed substantially lower values: 2.6 % (Fagundes and Herzog, 2024) and 1.8 % (Piper et al., 2014). During cSMT involving cervical rotation, Gorrell et al. (2022) and Fagundes and Herzog (2024) reported contralateral VA strain values of 1.4 % and − 1.1 %, respectively.

3.4. *Meta-analysis*

Only four of the six studies included in this systematic review provided comparative data on strain in the V3 segment of the VA during ROM and cSMT. These studies were conducted by Symons et al. (2002), Herzog et al. (2012), Piper et al. (2014), and Fagundes and Herzog (2024).

Our meta-analysis compares strain in the contralateral V3 segment of the vertebral artery (VA) during range-of-motion (ROM) rotation testing versus cervical spinal manipulative therapy (cSMT).

In the forest plot (Fig. 3), positive standardized mean difference (SMD) values, shown to the right of the vertical line, indicate that ROM testing produces higher strain than cSMT. Negative values, shown to the left, would indicate greater strain during cSMT.

The pooled analysis revealed that ROM rotation testing results in significantly greater strain than cSMT (SMD = 1.05; 95 % CI: 0.22 to 1.88; $P = 0.01$), suggesting that cSMT imposes less mechanical stress on the V3 segment of the VA than movements occurring during normal head and neck rotation.

Individual study results varied:

- Piper et al. (2014) found a small, non-significant difference (SMD = 0.27; 95 % CI: −1.35 to 1.89), indicating minimal difference in strain between interventions.
- Symons et al. (2002) and Herzog et al. (2012) reported significantly higher strain during ROM rotation testing, with SMDs of 0.73 and 1.44, respectively.
- Fagundes and Herzog (2024) observed the largest effect (SMD = 4.15; 95 % CI: 0.17 to 8.46), although the wide confidence interval suggests substantial within-sample variability.

Heterogeneity across studies was low ($I^2 = 17$ %), reflecting methodological consistency and strengthening the reliability of the pooled estimates. Collectively, these findings support the conclusion that cSMT produces significantly smaller elongations of the V3 segment of the VA compared to ROM rotation testing.

In a second meta-analysis, strains in the V3 segment during combined extension–rotation movements were compared to those during cSMT.

The pooled results again demonstrated significantly greater mechanical strain during passive ROM testing than during cSMT (SMD = 0.87; 95 % CI: 0.19 to 1.54; P = 0.01) (Fig. 4).

In the forest plot (Fig. 4), the direction of the SMD interpretation remains the same: positive values (to the right of the vertical line) favor cSMT, indicating that ROM produced greater strain; negative values (to the left) would favor ROM, indicating greater strain during cSMT.

Most studies, including Symons et al. (2002), Herzog et al. (2012), and Fagundes and Herzog (2024), reported moderate to large effect sizes in favor of cSMT (i.e., less strain during cSMT).

- Piper et al. (2014) reported a small, non-significant negative effect (SMD = −0.05; 95 % CI: −1.65 to 0.55), suggesting no meaningful difference.
- Symons et al. (2002) and Fagundes and Herzog (2024) showed moderate positive effects (SMDs of 0.74 and 0.67, respectively).
- Herzog et al. (2012) reported a large and significant effect (SMD = 1.44; 95 % CI: 0.37 to 2.50) in favor of cSMT.

No heterogeneity was detected ($I^2 = 0$ %), indicating strong consistency across the included studies.

The meta-analyses were limited to strain data on the V3 segment during contralateral rotation and/or extension, as these were the only outcomes consistently reported across studies. All included studies analyzed the same anatomical segment (V3), used comparable movement types, and provided numerical data in a compatible format (e.g., means and standard deviations).

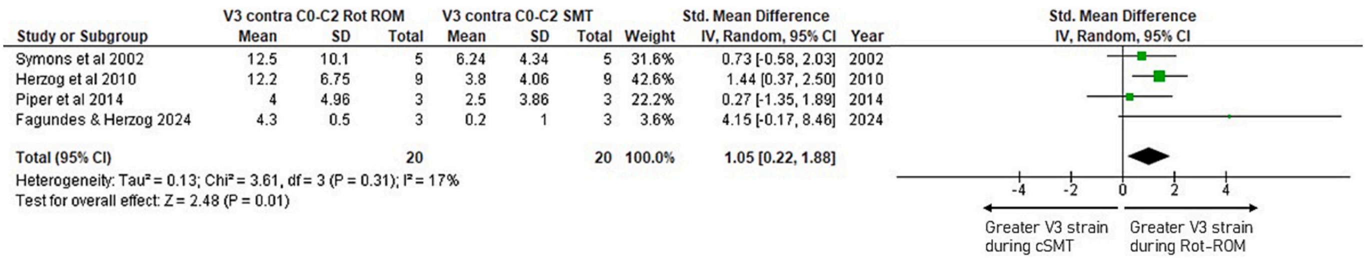

Fig. 3. Forest plot comparing vertebral artery (VA) strain in the V3 segment during cervical range-of-motion (ROM) rotation testing versus cervical spinal manipulative therapy (cSMT). Each black square represents the point estimate of the standardized mean difference (SMD) for an individual study, reflecting the magnitude and direction of the difference in VA strain between ROM and cSMT. The size of each square is proportional to the study's weight in the meta-analysis. The horizontal lines represent the 95 % confidence intervals (error bars) for each estimate, indicating the precision of the data. The diamond at the bottom represents the summary effect size (pooled SMD) across studies, with its width corresponding to the 95 % CI of the combined result. SMD values to the right of the vertical line (positive) indicate greater strain during ROM rotation testing compared to cSMT, while values to the left (negative) would indicate greater strain during cSMT. The vertical line at 0.00 represents no difference between interventions.

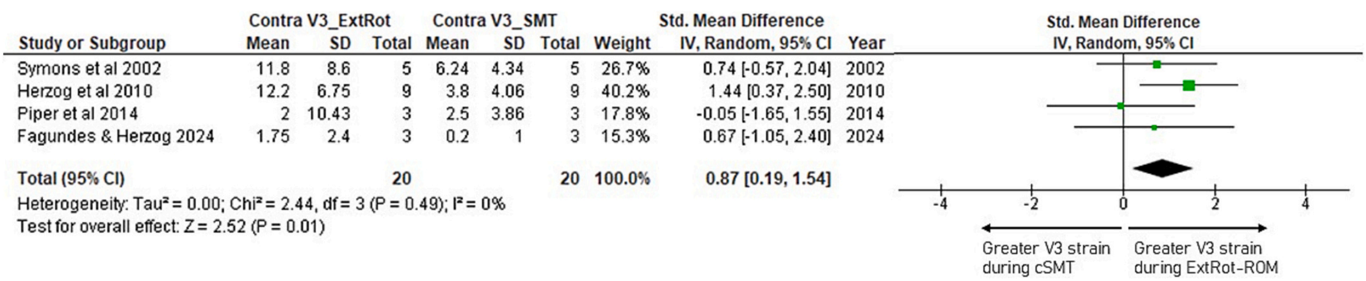

Fig. 4. Forest plot comparing vertebral artery (VA) strain in the V3 segment during combined extension–rotation range-of-motion (ROM) testing versus cervical spinal manipulative therapy (cSMT). Each black square shows the point estimate of the standardized mean difference (SMD) for each study, with horizontal lines indicating the 95 % confidence intervals. The size of each square reflects the relative weight of the study in the meta-analysis. The diamond at the bottom shows the summary (pooled) SMD, with the width indicating the 95 % CI. Positive SMD values (right side of the plot) indicate greater VA strain during ROM testing than during cSMT, favoring cSMT as the less stressful intervention. Negative values (left side) would indicate greater strain during cSMT. The vertical line at 0.00 denotes no difference between the two conditions.

Taken together, these findings reinforce that cervical spinal manipulative therapy, when performed under controlled conditions, results in lower strain on the V3 segment of the vertebral artery than passive range-of-motion testing involving rotation or combined extension–rotation movements.

3.5. Reporting and publication bias

Due to the limited number of studies included in the meta-analysis, formal statistical tests to assess publication bias (e.g., funnel plots or Egger's regression) were not conducted, in line with PRISMA 2020 guidelines. Instead, we reviewed potential sources of bias by examining study funding and searching trial registries for unpublished studies.

Several of the included studies received funding from chiropractic organizations, such as the Canadian Chiropractic Research Foundation and the Alberta College and Association of Chiropractors. While these sources reflect a professional interest in the topic, no study reported funding from commercial or industry sponsors. The included studies employed consistent and methodologically sound approaches. Additionally, no relevant unpublished studies were identified in the registries searched (Open Science Framework (OSF) and International Prospective Register of Systematic Reviews (PROSPERO)). Taken together, these findings suggest a low risk of reporting or publication bias.

4. Discussion

The findings of this systematic review and meta-analysis reinforce existing evidence that the magnitude of strain imposed on the VA during passive cervical ROM testing is substantially greater than that observed during the application of cSMT. These results are consistent with prior biomechanical investigations using fresh, unembalmed human cadavers in conjunction with high-precision methodologies—most notably, real-time strain measurements via piezoelectric ultrasonographic crystals (Fagundes and Herzog, 2024; Piper et al., 2014). The study of Fagundes and Herzog (2024) demonstrated that cSMT produces peak strain values of less than 1.3 % within the V3 segment of the VA, whereas passive movements such as contralateral cervical rotation and combined extension-rotation elicited strains exceeding 12 % (Symons et al., 2002).

Notably, the V3 segment of the VA — extending from C0 to C2—consistently demonstrated the highest levels of strain during passive contralateral cervical rotation and combined extension-rotation. Owing to its anatomical course through the transverse foramina of the upper cervical spine and its substantial mobility, this segment has been postulated as particularly vulnerable to vascular stress. For instance, Symons et al. (2002) reported peak strain values of 12.5 % ± 10.1 during contralateral rotation and 11.8 % ± 8.6 during extension with rotation at the C0–C1 level. Similarly, Piper et al. (2014) reported strain values of up to 6 % at the C0–C1 level during contralateral rotation, with corresponding values of 4 % at C1–C2 and 3 % at C2–C3. In contrast, the application of cSMT consistently resulted in markedly lower strain values. Fagundes and Herzog (2024) found peak strain during the thrust phase of cSMT was only 1.3 % at C0–C1 and 0.1 % at C1–C2. Likewise, Herzog et al. (2012) reported maximum cSMT-induced strain in the V3 segment at 3.8 %, which is still significantly smaller than values observed during passive ROM testing. These comparative findings suggest that psysiological head movements impose considerably more strain on the VA than cSMT performed using typical clinical procedures by trained clinicians. However, these findings derive from cadaveric models that lack physiological factors such as blood pressure, vascular tone, and hypertension, which may influence strain responses and susceptibility to injury in living humans.

It is essential to acknowledge the high methodological rigor of the biomechanical studies included in this analysis, which lends substantial robustness and credibility to the findings presented. The use of fresh, unembalmed human cadaveric specimens—an approach that preserves the native mechanical and structural properties of biological tissues, in contrast to embalmed bodies—represents a gold standard for anatomical and biomechanical research (Freedman et al., 2022). When combined with the application of piezoelectric ultrasonic crystals, this methodology enabled the acquisition of real-time, high-precision data on VA strain, accurately replicating physiological cervical motion conditions. Nonetheless, the potential interaction between vascular risk factors, such as hypertension, and mechanical strain cannot be captured in these models, and thus the findings should be generalized to clinical populations with caution.

4.1. Limitations

Although our literature search included multiple databases and incorporated backward and forward citation tracking to enhance comprehensiveness, we did not collaborate with a professional librarian or information specialist during the search strategy development. This may have limited the search sensitivity and completeness. Future reviews could benefit from involving a librarian to optimize search strategies and ensure the most exhaustive retrieval of relevant studies.

It is important to recognize that all cadavers used in this study were structurally intact and did not present pathology in the vertebral arteries. This imposes a limitation on the generalizability of these results to clinical populations with underlying VA compromise. Furthermore, there were only six studies that satisfied the inclusion criteria, and only four studies that were appropriate for the meta-analysis. Additionally, due to the technical and methodological complexity of these studies, all studies included in this review were performed by one research group, although the primary investigators were different for the different studies. However, this limitation highlights the need for more studies in this area to further elucidate the underlying mechanisms and safety concerns.

4.2. Clinical implications

The findings of this systematic review and meta-analysis demonstrate that cSMT induces significantly less strain on the VA compared to passive cervical ROM, particularly within the vulnerable V3 segment (C0–C2). This suggests that, as cSMT imposes less mechanical load on the VA than passive cervical ROM, the biomechanical risk of VAD may be correspondingly lower, given that, biomechanically, VAD is believed to result from strain exceeding the vessel's physiological tolerance. Nonetheless, rigorous clinical evaluation remains essential prior to administering cSMT, as additional risk factors, most notably the presence of vascular comorbidities, must be carefully considered to ensure patient safety.

5. Conclusion

These findings provide robust biomechanical evidence that cSMT, when performed under controlled conditions, induces markedly lower vertebral artery (VA) strain—particularly within the V3 segment—than physiological cervical movements such as contralateral rotation and combined extension-rotation. The methodological rigor of the included studies, notably the use of fresh, unembalmed human cadaveric specimens and high-precision, real-time strain measurement via piezoelectric ultrasonic crystals, lends considerable internal validity to these results. However, as these studies were conducted in cadavers without physiological factors such as blood pressure or vascular pathology, caution is warranted when generalizing to living populations, especially those with vascular risk factors. Other mechanisms of vertebral artery injury, including embolic causes unrelated to mechanical strain, are beyond the scope of this review. Therefore, while the data support the biomechanical safety of cSMT, clinical application should proceed with appropriate screening and judgment. Within an evidence-informed framework, cSMT can be considered biomechanically safe for managing neck pain when used judiciously.

CRediT authorship contribution statement

Caroline Fagundes: Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Felipe Coutinho Kullmann Duarte:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Walter Herzog:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinbiomech.2025.106685.

References

Amran, M.Y., Hawari, I., La'biran, F.J., Gunadi, S.G.A., Muslich, L.T., 2024. Vertebral artery dissection from etiopathogenesis to management therapy: a narrative review with neuroimaging's case illustration. Egypt J. Neurol. Psychiatry Neurosurg. 60, 118. https://doi.org/10.1186/s41983-024-00893-x.

Chaibi, A., Stavem, K., Russell, M.B., 2021. Spinal manipulative therapy for acute neck pain: a systematic review and meta-analysis of randomised controlled trials. J. Clin. Med. 10 (21), 5011. https://doi.org/10.3390/jcm10215011.

Côté, P., Wong, J.J., Sutton, D., Shearer, H.M., Mior, S., Randhawa, K., Ameis, A., Carroll, L.J., Nordin, M., Yu, H., Lindsay, G.M., Southerst, D., Varatharajan, S., Jacobs, C., Stupar, M., Taylor-Vaisey, A., van der Velde, G., Gross, D.P., Brison, R.J., Paulden, M., Salhany, R., 2016. Management of neck pain and associated disorders: a clinical practice guideline from the Ontario protocol for traffic injury management (OPTIMa) collaboration. Eur. Spine J. 25 (7), 2000–2022. https://doi.org/10.1007/s00586-016-4467-7.

Fagundes, C., Herzog, W., 2024. Strain of the vertebral artery during passive neck movements and spinal manipulation of the cervical spine: an observational study. J. Bodyw. Mov. Ther. 40, 569–574. https://doi.org/10.1016/j.jbmt.2024.05.011.

Freedman, B.R., Knecht, R.S., Tinguely, Y., Eskibozkurt, G.E., Wang, C.S., Mooney, D.J., 2022. Aging and matrix viscoelasticity affect multiscale tendon properties and tendon derived cell behavior. Acta Biomater. 143, 63–71. https://doi.org/10.1016/j.actbio.2022.03.006.

GBD 2021 Neck Pain Collaborators, 2024. Global, regional, and national burden of neck pain, 1990–2020, and projections to 2050: a systematic analysis of the global burden of disease study 2021. Lancet Rheumatol. 6 (3), e142–e155. https://doi.org/10.1016/S2665-9913(23)00321-1.

Gorrell, L.M., Kuntze, G., Ronsky, J.L., Carter, R., Symons, B., Triano, J.J., Herzog, W., 2022. Kinematics of the head and associated vertebral artery length changes during high-velocity, low-amplitude cervical spine manipulation. Chiropr. Man. Ther. 30 (1), 28. https://doi.org/10.1186/s12998-022-00438-0.

Haynes, M.J., Vincent, K., Fischhoff, C., Bremner, A.P., Lanlo, O., e Hankey, G.J., 2012. Assessing the risk of stroke from neck manipulation: a systematic review. Int. J. Clin. Pract. 66, 940–947.

Henry, B.M., Tomaszewski, K.A., Ramakrishnan, P.K., Roy, J., Vikse, J., Loukas, M., Tubbs, R.S., Walocha, J.A., 2017. Development of the anatomical quality assessment (AQUA) tool for the quality assessment of anatomical studies included in meta-analyses and systematic reviews. Clin. Anat. 30 (1), 6–13. https://doi.org/10.1002/ca.22799.

Herzog, W., Leonard, T.R., Symons, B., Tang, C., Wuest, S., 2012. Vertebral artery strains during high-speed, low amplitude cervical spinal manipulation. J. Electromyogr. Kinesiol. 22 (5), 740–746. https://doi.org/10.1016/j.jelekin.2012.03.005.

Kazeminasab, S., Nejadghaderi, S.A., Amiri, P., Pourfathi, H., Araj-Khodaei, M., Sullman, M.J.M., Kolahi, A.A., Safiri, S., 2022. Neck pain: global epidemiology, trends and risk factors. BMC Musculoskelet. Disord. 23 (1), 26. https://doi.org/10.1186/s12891-021-04957-4.

Liu, Z., Shi, J., Huang, Y., Zhou, X., Huang, H., Wu, H., Lv, L., Lv, Z., 2023. A systematic review and meta-analysis of randomized controlled trials of manipulative therapy for patients with chronic neck pain. Comp. Ther. Clin. Pract. 52, 101751. https://doi.org/10.1016/j.ctcp.2023.101751.

Mazaheri-Tehrani, S., Arefian, M., Abhari, A.P., Riahi, R., Vahdatpour, B., Baradaran Mahdavi, S., Kelishadi, R., 2023. Sedentary behavior and neck pain in adults: a systematic review and meta-analysis. Prev. Med. 175, 107711. https://doi.org/10.1016/j.ypmed.2023.107711.

Meng, Y., Xue, Y., Yang, S., Wu, F., Dong, Y., 2025. The associations between sedentary behavior and neck pain: a systematic review and meta-analysis. BMC Public Health 25 (1), 453. https://doi.org/10.1186/s12889-025-21685-9.

Paulus, J.K., Thaler, D.E., 2016. Does case misclassification threaten the validity of studies investigating the relationship between neck manipulation and vertebral artery dissection stroke? Yes. Chiropr. Man. Ther. 42, 1–6.

Peeters, J.B., Idriceanu, T., El Hage, G., Martin, T., Salaud, C., Champagne, P.O., Bojanowski, M.W., 2024. A comprehensive review of the vertebral artery anatomy. Neuro-Chirurgie 70 (3), 101518.

Piper, S.L., Howarth, S.J., Triano, J., Herzog, W., 2014. Quantifying strain in the vertebral artery with simultaneous motion analysis of the head and neck: a preliminary investigation. Clin. Biomech. 29 (10), 1099–1107. https://doi.org/10.1016/j.clinbiomech.2014.10.004.

Safiri, S., Kolahi, A.A., Hoy, D., Buchbinder, R., Mansournia, M.A., Bettampadi, D., Ashrafi-Asgarabad, A., Almasi-Hashiani, A., Smith, E., Sepidarkish, M., Cross, M., Qorbani, M., Moradi-Lakeh, M., Woolf, A.D., March, L., Collins, G., Ferreira, M.L., 2020. Global, regional, and national burden of neck pain in the general population, 1990–2017: systematic analysis of the global burden of disease study 2017. BMJ 368, m791. https://doi.org/10.1136/bmj.m791.

Symons, B.P., Leonard, T., Herzog, W., 2002. Internal forces sustained by the vertebral artery during spinal manipulative therapy. J. Manipulative Physiol. Ther. 25 (8), 504–510. https://doi.org/10.1067/mmt.2002.127076.

Wan, X., Wang, W., Liu, J., Tong, T., 2014. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med. Res. Methodol. 14, 135. https://doi.org/10.1186/1471-2288-14-135.

Whedon, J.M., Song, Y., Mackenzie, T.A., Phillips, R.B., Lukovits, T.G., Lurie, J.D., 2015. Risk of stroke after chiropractic spinal manipulation in Medicare B beneficiaries aged 66 to 99 years with neck pain. J. Manipulative Physiol. Ther. 38 (2), 93–101. https://doi.org/10.1016/j.jmpt.2014.12.001.

Whedon, J.M., Petersen, C.L., Li, Z., Schoelkopf, W.J., Haldeman, S., MacKenzie, T.A., Lurie, J.D., 2022. Association between cervical artery dissection and spinal manipulative therapy: a Medicare claims analysis. BMC Geriatr. 22 (1), 917. https://doi.org/10.1186/s12877-022-03495-5.

Wuest, S., Symons, B., Leonard, T., Herzog, W., 2010. Preliminary report: biomechanics of vertebral artery segments C1-C6 during cervical spinal manipulation. J. Manipulative Physiol. Ther. 33 (4), 273–278. https://doi.org/10.1016/j.jmpt.2010.03.007.