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REVIEW ARTICLE

Heart rate changes after manual techniques on cervical spine: Systematic review

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Abstract

Background: The autonomic nervous system (ANS) can be modulated through various manual therapy techniques (MTT) on the cervical spine. However, it remains unclear whether these modulations have clinically relevant effects on the heart rate (HR) of individuals with craniocervical dysfunctions (CCD). **Objective:** This study aims to review existing research on MTT applied to the cervical spine and its effects on HR in patients with CCD. **Methods:** This study was registered with the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42019126739. No funding was received for this study. Articles were identified through searches in PubMed, Web of Science, CENTRAL and EMBASE. Eligible studies assessed HR before and after MTT. The risk of bias was evaluated using the Physiotherapy Evidence Database (PEDro) scale, and the certainty of the evidence was determined using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach. **Results:** Three articles met the eligibility criteria. One study reported a significant increase in HR following the application of the high-velocity low-amplitude (HVLA) technique, while another indicated clinically significant increase in HR after mobilization techniques. Both studies demonstrated high methodological quality but were classified as having a very low level of evidence. **Discussion:** The findings suggest that MTT can stimulate the ANS, whether through HVLA or mobilization techniques, regardless of the specific cervical level targeted. However, the inconsistency of the data across studies complicates more precise analyses.

Keywords: Musculoskeletal manipulation; heart rate; autonomic nervous system; systematic review.

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BACKGROUND

The autonomic nervous system (ANS) is responsible for controlling the contraction of the heart muscle, generating responses on heart rate (HR). The ANS works unconsciously, controlled by centers located in the spinal cord, brain stem and hypothalamus through synapses that are sent by peripheral nerves to the myocardium. The ANS is subdivided into the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). The SNS is responsible for stimulating HR increase, through the release of norepinephrine, while on the other hand, the PNS is responsible for reducing HR, through the release of acetylcholine[1,2]. A large part of the viscera receives innervation from these two systems, however, most part of blood vessels do not have parasympathetic innervation, and their diameter is regulated by sympathetic input[1,3,4].

The cervical spine is a region where these cardiac sympathetic neural structures emerge, especially postganglionic axons, structures responsible for sending neural control synapses to the heart[5–7]. It is known that stimuli in this cervical region can generate changes in cardiac neural conduction, among these stimuli are the application of electrotherapy[8,9] and manual therapy techniques (MTT)[10–12].

In this sense, it is known that patients who present craniocervical dysfunctions (CCD), that is, changes in mobility, muscle tension, especially in the cervical spine with the presence of pain, can alter heart rate variability (HRV)[13,14], this is because the SNS and PNS are involved in pain physiology[15], therefore, CCD may be present in migraines, headaches and torticollis may be related to ANS dysfunction, resulting in changes in HRV[16,17].

Traditionally MTT is composed, among others, of joint mobilization and manipulation techniques and are used to relieve musculoskeletal pain and increase range of motion[18], however, in recent years studies have demonstrated the effects of MTT applied to the cervical spine on the ANS[19,20], generating responses on some hemodynamic markers[10,11,21], however, these response pathways are still unclear[22].

ANS activity is usually assessed indirectly through some non-invasive markers such as HRV[23] and skin conductance[24], however, the analysis of these cardiovascular control indices appears to be poorly objective and not clinically relevant[25]. Therefore, the literature remains contradictory regarding the clinically relevant effects of applying MTT to the cervical spine on HR in patients with CCD. In this sense, the objective of this systematic review is to evaluate the effects of MTT in the cervical spine on the HR of patients with CCD.

METHODS

Protocol and Registration

The study protocol was designed a priori and prospectively registered in the PROSPERO with registration number: CRD42019126739, therefore, there was no change in the registered protocol. The review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[27].

The protocol can be accessed on the PROSPERO website through the address: www.crd.york.ac.uk/prospero/display_record.php?RecordID=126739.

PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pages 3-4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Chart 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Chart 2
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 3-4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 4-5
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 4

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 5
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 5
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 5
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 6 (figure 1)
Study characteristics	17	Cite each included study and present its characteristics.	Pages 7
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 9 and Table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 7-8
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 9
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 8
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 9
Certainty of	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 9

Section and Topic	Item #	Checklist item	Location where item is reported
evidence			
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 11
	23b	Discuss any limitations of the evidence included in the review.	Page 12
	23c	Discuss any limitations of the review processes used.	Page 12
	23d	Discuss implications of the results for practice, policy, and future research.	Pages 12
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 3
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 13
Competing interests	26	Declare any competing interests of review authors.	Page 13
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Journal page

Note: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Search Strategy and Study Selection

We developed a comprehensive search strategy informed by previously published methodologies. The search was conducted from July to August 2024. Relevant search terms were utilized and tailored to each database. Medical Subject Headings (MeSH) were employed alongside commonly used terms in literature. The databases accessed included PubMed, Web of Science, CENTRAL, EMBASE (see Chart 1), and various clinical trial registries.

After removing duplicates using EndNote's duplicate checker, two independent reviewers screened all studies according to pre-specified inclusion and exclusion criteria based on the title and abstract, followed by a full-text review. Any discrepancies identified during the screening process were resolved through a consensus meeting. To identify additional articles, we manually screened the references of relevant systematic reviews and included studies, as well as the references of articles that cited the included studies. Additionally, an expert in the field was consulted to identify any potentially missing studies for inclusion.

Chart 1. Database search strategy

PubMed	
Search	**Query**
#1	("Manipulation, Osteopathic"[MeSH Terms]) OR ("Manipulation, Spinal"[MeSH Terms])) OR ("musculoskeletal manipulations"[MeSH Terms])) OR ("Osteopathic Physicians"[MeSH Terms])) OR ("osteopathic medicine"[MeSH Terms])) OR ("Myofascial Release therapy"[MeSH Terms])) OR ("Therapy, Soft Tissue"[MeSH Terms])) OR ("osteopathic manipulative procedure"[Title/Abstract])) OR ("osteopathic manipulative technique"[Title/Abstract])) OR ("osteopathic manipulative treatment"[Title/Abstract])) OR ("osteopathic manipulative therapy"[Title/Abstract])) OR ("osteopathic manipulative medicine"[Title/Abstract])) OR ("osteopathic manipulation"[Title/Abstract])) OR ("Osteopathic Manipulation Treatment"[Title/Abstract])) OR ("osteopathic manual therapy"[Title/Abstract])) OR ("osteopathic manual treatment"[Title/Abstract])) OR ("spine manipulation"[Title/Abstract])) OR ("spinal manipulation procedure"[Title/Abstract])) OR ("spinal manipulation technique"[Title/Abstract])) OR ("spinal manipulation therapy"[Title/Abstract])) OR ("spinal manipulative technique"[Title/Abstract])) OR ("spine manipulation"[Title/Abstract])) OR ("spinal manipulation"[Title/Abstract])) OR ("spinal manipulative therapy"[Title/Abstract])) OR ("musculoskeletal manipulation"[Title/Abstract])) OR ("musculoskeletal manipulations"[Title/Abstract])) OR ("osteopath"[Title/Abstract])) OR ("osteopathic medicine"[Title/Abstract])) OR ("osteopathy"[Title/Abstract])) OR ("osteopathic research"[Title/Abstract])) OR ("osteopathic care"[Title/Abstract])) OR ("osteopathic intervention"[Title/Abstract])) OR ("atlanto-occipital joint manipulation"[Title/Abstract])) OR ("high velocity low amplitude spinal manipulation"[Title/Abstract])) OR ("high velocity low amplitude"[Title/Abstract])) OR ("high-velocity low-amplitude"[Title/Abstract])) OR ("HVLA"[Title/Abstract])) OR ("spinal mobilization*"[Title/Abstract])) OR ("spinal mobilisation*"[Title/Abstract])) OR ("joint mobilization"[Title/Abstract])) OR ("joint mobilisation*"[Title/Abstract])) OR ("joint manipulation*"[Title/Abstract])) OR ("somatic dysfunction"[Title/Abstract])) OR (“joint mobilization”[Title/Abstract])) OR (“joints mobilizations”[Title/Abstract])) OR (“spinal mobilization”[Title/Abstract])) OR (“spinal mobilizations”[Title/Abstract])) OR (“joint mobilisation”[Title/Abstract])) OR (“joins mobilisations”[Title/Abstract])) OR (“maitland mobilisation”[Title/Abstract])) OR (“maitland mobilisation”[Title/Abstract])) OR (“mulligan mobilisation”[Title/Abstract])) OR (“mulligan mobilization”[Title/Abstract])) OR (“oscillatory mobilization”[Title/Abstract])) OR (“oscillatory

	mobilisation"[Title/Abstract])) OR ("snags"[Title/Abstract])) OR ("nags"[Title/Abstract])) OR ("mwm"[Title/Abstract])) OR ("mobilization with movement"[Title/Abstract])) OR ("chiropractic"[Title])) OR ("chiropractic practice"[Title])) OR ("chiropractic manipulation"[Title])) OR ("Chiropractic Spinal Adjustment*"[Title]) OR ("chiropractic spinal manipulation"[Title])) OR ("Chiropractic Adjustment*"[Title])) OR ("cheirotherapy"[Title])) OR ("chiropraxia"[Title])) OR ("chiropraxis"[Title])) OR ("chirotherapy"[Title])) AND
#2	("Neck Pain"[Title/Abstract])) OR ("Neck Pains"[Title/Abstract])) OR ("Neck Ache"[Title/Abstract])) OR ("Neck Aches"[Title/Abstract])) OR ("Cervicalgia"[Title/Abstract])) OR ("Cervicalgias"[Title/Abstract])) OR ("Cervicodynia"[Title/Abstract])) OR ("Cervicodynias"[Title/Abstract])) OR ("Neckache"[Title/Abstract])) OR ("Neckaches"[Title/Abstract])) OR ("Cervical Pain"[Title/Abstract])) OR ("Posterior Cervical Pain"[Title/Abstract])) OR ("Posterior Neck Pain"[Title/Abstract])) OR ("Anterior Cervical Pain" [Title/Abstract])) OR ("Upper Spine Pain"[Title/Abstract])) OR ("Anterior Neck Pain"[Title/Abstract])) OR ("Back Pain"[Title/Abstract])) OR ("Backache"[Title/Abstract])) OR ("Back Ache"[Title/Abstract])) OR ("Back Pain without Radiation"[Title/Abstract])) OR ("Vertebrogenic Pain Syndrome"[Title/Abstract])) OR ("Syndrome, Vertebrogenic Pain"[Title/Abstract])) OR ("Vertebrogenic Pain Syndromes"[Title/Abstract])) OR ("Back Pain with Radiation"[Title/Abstract])) OR ("Torticollis"[Title/Abstract])) OR ("Wryneck"[Title/Abstract])) OR ("Cervical Dystonia"[Title/Abstract])) OR ("Spasmodic Torticollis"[Title/Abstract])) OR ("orticollis, Psychogenic"[Title/Abstract])) OR ("Intermittent Torticollis)) AND
#3	((((((((((("randomized controlled trial"[MeSH Terms] OR ("randomized controlled trial"[Title/Abstract])) OR ("controlled clinical trial"[Title/Abstract])) OR ("Randomized Clinical Trial"[Title/Abstract])) OR ("randomized trial"[Title/Abstract])) OR ("randomized"[Title/Abstract])) OR ("randomized crossover trial"[Title/Abstract])) OR ("crossover trial"[Title/Abstract]))) OR ("placebo"[Title/Abstract])) OR ("randomly"[Title/Abstract])) OR ("trial"[Title]))) OR ("Clinical Trials as Topic"[Mesh:NoExp])) OR (Random Allocation[Title/Abstract]) NOT
#4	(((((((("systematic review and meta-analysis"[Title]) OR ("Review"[Title]) OR ("systematic review"[Title])) OR ("meta-analysis"[Title])) OR ("systematic review meta-analysis"[Title])) OR ("systematic review with meta-analysis"[Title])) OR ("Synthesis"[Title])) OR ("Consensus"[Title])) OR ("Systematic Reviews as Topic"[Mesh:NoExp]))
	#1 AND #2 AND #3 NOT #4

Web of Science

Search	Query
#1	TS=("Manipulation, Osteopathic"[MeSH Terms] OR "Manipulation, Spinal"[MeSH Terms] OR "musculoskeletal manipulations"[MeSH Terms] OR "Osteopathic Physicians"[MeSH Terms] OR "osteopathic medicine"[MeSH Terms] OR "Myofascial Release therapy"[MeSH Terms] OR "Therapy, Soft Tissue"[MeSH Terms] OR "osteopathic manipulative procedure" OR "osteopathic manipulative technique" OR "osteopathic manipulative treatment" OR "osteopathic manipulative therapy" OR "osteopathic manipulative medicine" OR "osteopathic manipulation" OR "Osteopathic Manipulation Treatment" OR "osteopathic manual therapy" OR "osteopathic manual treatment" OR "osteopathic visceral treatment" OR "visceral osteopathic treatment" OR "OMT" OR "osteopathic treatment" OR "osteopathic therapy" OR "visceral manipulation" OR "visceral osteopathy" OR "osteopathic visceral manipulation" OR "spine manipulation" OR "spinal manipulation procedure" OR "spinal manipulation technique" OR "spinal manipulation therapy" OR "spinal manipulative technique" OR "spine manipulation" OR "spinal manipulation" OR "spinal manipulative therapy" OR "musculoskeletal manipulation" OR "musculoskeletal manipulations" OR "osteopath" OR "osteopathic medicine" OR "osteopathy" OR "osteopathic research" OR "osteopathic care" OR "osteopathic intervention" OR "atlanto-occipital joint manipulation" OR "high velocity low amplitude spinal manipulation" OR "high velocity low amplitude" OR "high-velocity low-amplitude" OR "HVLA" OR "spinal mobilization*" OR "spinal mobilisation*" OR "joint mobilization" OR "joint mobilisation*" OR "joint manipulation*" OR "somatic dysfunction" OR "spinal mobilization" OR "spinal mobilisation" OR "joint mobilization" OR "joint mobilisation" OR "joint manipulation" OR "maitland mobilisation" OR "mulligan mobilisation" OR "mulligan mobilization" OR "oscillatory mobilization" OR "oscillatory mobilisation" OR "snags" OR "nags" OR "mwm" OR

	"mobilization with movement) OR "chiropractic" OR "chiropractic practice" OR "chiropractic manipulation" OR "Chiropractic Spinal Adjustment*" OR "chiropractic spinal manipulation" OR "Chiropractic Adjustment*" OR "cheirotherapy" OR "chiropraxia" OR "chiropraxis" OR "chirotherapy" AND
#2	TS=("Neck Pain"OR "Neck Pains" OR "Neck Ache" OR "Neck Aches" OR "Cervicalgia" OR "Cervicalgias" OR "Cervicodynia" OR "Cervicodynias" OR "Neckache" OR "Neckaches" OR "Cervical Pain" OR "Posterior Cervical Pain" OR "Posterior Neck Pain" OR "Anterior Cervical Pain" OR "Upper Spine Pain" OR "Anterior Neck Pain" OR "Back Pain" OR "Backache" OR "Back Ache" OR "Back Pain without Radiation" OR "Vertebrogenic Pain Syndrome" OR "Syndrome, Vertebrogenic Pain" OR "Vertebrogenic Pain Syndromes" OR "Back Pain with Radiation" OR "Torticollis" OR "Wryneck" OR "Cervical Dystonia" OR "Spasmodic Torticollis" OR "orticollis, Psychogenic" OR "Intermittent Torticollis") AND
#3	TS=("randomized controlled trial"[MeSH Terms] OR "randomized controlled trial" OR "controlled clinical trial" OR "Randomized Clinical Trial" OR "randomized trial" OR "randomized" OR "randomized crossover trial" OR "crossover trial" OR "placebo" OR "randomly" OR "trial"[Title] OR "Clinical Trials as Topic"[Mesh:NoExp] OR "Random Allocation")
#4	TI=("systematic review and meta-analysis" OR "Review" OR "systematic review" OR "meta-analysis" OR "systematic review meta-analysis" OR "systematic review with meta-analysis" OR "Synthesis" OR "Consensus" OR "Systematic Reviews as Topic"[Mesh:NoExp])
	#1 AND #2 AND #3 NOT #4

Cochrane CENTRAL

Search	Query
#1	(MeSH descriptor: [Manipulation, Osteopathic] explode all trees) OR (MeSH descriptor: [Manipulation, Spinal] explode all trees) OR (MeSH descriptor: [Musculoskeletal Manipulations] explode all trees) OR (MeSH descriptor: [Osteopathic Physicians] explode all trees) OR (MeSH descriptor: [Osteopathic Medicine] explode all trees) OR ("osteopathic manipulative procedure" OR "osteopathic manipulative technique" OR "osteopathic manipulative treatment" OR "osteopathic manipulative therapy" OR "osteopathic manipulative medicine" OR "osteopathic manipulation" OR "Osteopathic Manipulation Treatment" OR "osteopathic manual therapy" OR "osteopathic manual treatment" OR "OMT" OR "osteopathic treatment" OR "osteopathic therapy" OR "spine manipulation" OR "spinal manipulation procedure" OR "spinal manipulation technique" OR "spinal manipulation therapy" OR "spinal manipulative technique" OR "spine manipulation" OR "spinal manipulation" OR "spinal manipulative therapy" OR "musculoskeletal manipulation" OR "musculoskeletal manipulations" OR "osteopath" OR "osteopathic medicine" OR "osteopathy" OR "osteopathic research" OR "osteopathic care" OR "osteopathic intervention" OR "atlanto-occipital joint manipulation" OR "high velocity low amplitude spinal manipulation" OR "high velocity low amplitude" OR "high-velocity low-amplitude" OR "HVLA" OR "spinal mobilization*" OR "spinal mobilisation*" OR "joint mobilization" OR "joint mobilisation*" OR "joint manipulation*" OR "facial manipulation" OR "somatic dysfunction" OR "spinal mobilization*" OR "spinal mobilisation*" OR "joint mobilization" OR "joint mobilisation*" OR "joint manipulation*" OR "facial manipulation" OR "somatic dysfunction" OR "spinal mobilization" OR "spinal mobilisation" OR "joint mobilization" OR "joint mobilisation" OR "joint manipulation" OR "maitland mobilisation" OR "mulligan mobilisation" OR "mulligan mobilization" OR "oscillatory mobilization" OR "oscillatory mobilisation" OR "snags" OR "nags" OR "mwm" OR "mobilization with movement" OR "chiropractic" OR "chiropractic practice" OR "chiropractic manipulation" OR "Chiropractic Spinal Adjustment*" OR "chiropractic spinal manipulation" OR "Chiropractic Adjustment*" OR "cheirotherapy" OR "chiropraxia" OR "chiropraxis" OR "chirotherapy" AND
#2	"Neck Pain" OR "Neck Pains" OR "Neck Ache" OR "Neck Aches" OR "Cervicalgia" OR "Cervicalgias" OR "Cervicodynia" OR "Cervicodynias" OR "Neckache" OR "Neckaches" OR "Cervical Pain" OR "Posterior Cervical Pain" OR "Posterior Neck Pain" OR "Anterior Cervical Pain" OR "Upper Spine Pain" OR "Anterior Neck Pain" OR "Back Pain" OR "Backache" OR "Back Ache" OR "Back Pain without Radiation" OR "Vertebrogenic Pain Syndrome" OR "Syndrome, Vertebrogenic Pain" OR "Vertebrogenic Pain Syndromes" OR "Back Pain with Radiation" OR "Torticollis" OR "Wryneck" OR "Cervical Dystonia" OR "Spasmodic Torticollis" OR "orticollis, Psychogenic" OR "Intermittent Torticollis"

#1 AND #2 AND limit: Trials

EMBASE	
#1	('osteopathic manipulation'/exp OR 'manipulation, osteopathic':ti,ab,kw OR 'osteopathic manipulation':ti,ab,kw OR 'osteopathic manipulative medicine':ti,ab,kw OR 'osteopathic manipulative procedure':ti,ab,kw OR 'osteopathic manipulative technique':ti,ab,kw OR 'osteopathic manipulative therapy':ti,ab,kw OR 'osteopathic manipulative treatment':ti,ab,kw OR 'spine manipulation'/exp OR 'manipulation, spinal':ti,ab,kw OR 'spinal manipulation':ti,ab,kw OR 'spinal manipulation procedure':ti,ab,kw OR 'spinal manipulation technique':ti,ab,kw OR 'spinal manipulation therapy':ti,ab,kw OR 'spinal manipulative procedure':ti,ab,kw OR 'spinal manipulative technique':ti,ab,kw OR 'spinal manipulative therapy':ti,ab,kw OR 'spine manipulation':ti,ab,kw OR 'musculoskeletal manipulation'/exp OR 'musculoskeletal manipulation':ti,ab,kw OR 'musculoskeletal manipulations':ti,ab,kw OR 'osteopathic medicine'/exp OR 'osteopathic medicine':ti,ab,kw OR 'osteopathy':ti,ab,kw OR 'osteopathic physician'/exp OR 'doctor of osteopathic medicine':ti,ab,kw OR 'osteopath':ti,ab,kw OR 'osteopathic physician':ti,ab,kw OR 'osteopathic physicians':ti,ab,kw OR 'osteopathic manual therapy':ti,ab OR 'osteopathic manual treatment':ti,ab OR 'osteopathic treatment':ti,ab OR 'osteopathic therapy':ti,ab OR 'osteopathic care':ti,ab OR 'osteopathic intervention':ti,ab OR 'atlanto-occipital joint manipulation':ti,ab OR 'high velocity low amplitude spinal manipulation'/exp OR 'high velocity low amplitude':ti,ab OR hvla:ti,ab OR 'spinal mobilization'/exp OR 'joint mobilization'/exp OR 'joint mobilisation':ti,ab,kw OR 'joint mobilization':ti,ab,kw OR 'joint manipulation*':ti,ab OR 'facial manipulation':ti,ab OR 'somatic dysfunction'/exp) "spinal mobilization':ti,ab OR "spinal mobilisation':ti,ab OR "joint mobilization':ti,ab OR "joint mobilisation':ti,ab OR "joint manipulation':ti,ab OR "facial manipulation':ti,ab OR "somatic dysfunction':ti,ab OR “spinal mobilization':ti,ab OR “spinal mobilisation':ti,ab OR “joint mobilization':ti,ab OR “joint mobilisation':ti,ab OR “joint manipulation':ti,ab OR “maitland mobilisation':ti,ab OR “mulligan mobilisation':ti,ab OR “mulligan mobilization':ti,ab OR “oscillatory mobilization':ti,ab OR “oscillatory mobilisation':ti,ab OR “snags':ti,ab OR “nags':ti,ab OR “mwm':ti,ab OR “mobilization with movement':ti,ab) OR 'chiropractic manipulation'/exp OR 'chiropractic manipulation':ti OR 'manipulation, chiropractic':ti OR 'chiropractic spinal manipulation':ti OR 'chiropractic'/exp OR 'cheirotherapy':ti OR 'chiropractic':ti OR 'chiropraxia':ti OR 'chiropraxis':ti OR 'chirotherapy':ti OR 'chiropractic adjustment':ti OR 'chiropractic practice'/exp OR 'chiropractic practice':ti) OR 'chiropractic spinal adjustment*')
	AND
#2	‘Neck Pain’ OR “Neck Pains” OR “Neck Ache” OR “Neck Aches” OR ‘Cervicalgia” OR “Cervicalgias” OR “Cervicodynia” OR “Cervicodynias” OR ‘Neckache” OR “Neckaches” OR “Cervical Pain” OR “Posterior Cervical Pain” OR ‘Posterior Neck Pain” OR “Anterior Cervical Pain” OR “Upper Spine Pain” OR ‘Anterior Neck Pain” OR “Back Pain” OR “Backache” OR “Back Ache” OR “Back Pain without Radiation” OR “Vertebrogenic Pain Syndrome” OR “Syndrome, Vertebrogenic Pain” OR “Vertebrogenic Pain Syndromes” OR “Back Pain with Radiation” OR “Torticollis” OR “Wryneck” OR “Cervical Dystonia” OR “Spasmodic Torticollis” OR “orticollis, Psychogenic” OR “Intermittent Torticollis*'
#3	('randomized controlled trial'/exp OR 'controlled trial, randomized':ti OR 'randomised controlled study':ti OR 'randomised controlled trial':ti OR 'randomized controlled study':ti OR 'randomized controlled trial':ti OR 'trial, randomized controlled':ti OR 'controlled clinical trial'/exp OR 'clinical trial, controlled':ti OR 'controlled clinical comparison':ti OR 'controlled clinical drug trial':ti OR 'controlled clinical experiment':ti OR 'controlled clinical study':ti OR 'controlled clinical test':ti OR 'controlled clinical trial':ti OR 'randomized crossover trial':ti OR 'crossover procedure'/exp OR 'cross over clinical study':ti OR 'cross over clinical trial':ti OR 'cross over comparison':ti OR 'cross over design':ti OR 'cross over method':ti OR 'cross over procedure':ti OR 'cross over study':ti OR 'cross over test':ti OR 'cross over trial':ti OR 'cross-over studies':ti OR 'crossover clinical study':ti OR 'crossover clinical trial':ti OR 'crossover comparison':ti OR 'crossover design':ti OR 'crossover method':ti OR 'crossover procedure':ti OR 'crossover study':ti OR 'crossover test':ti OR 'crossover trial':ti OR 'double blind cross over study':ti OR 'double blind crossover study':ti OR 'procedure, crossover':ti OR 'randomization'/exp OR 'random allocation':ti,ab OR 'randomisation':ti,ab OR 'randomization':ti,ab OR randomized:ti,ab OR 'placebo'/exp OR 'placebo':ti,ab OR 'placebo gel':ti,ab OR 'placebos':ti,ab OR randomly:ti,ab OR 'clinical trial'/de OR 'clinical drug trial':ti,ab OR 'clinical

	trial':ti,ab OR 'major clinical trial':ti,ab OR 'trial, clinical':ti,ab) NOT ('systematic review'/de OR 'review, systematic':ti OR 'systematic review':ti) NOT ('meta analysis'/de OR 'analysis, meta':ti OR 'meta analysis':ti OR 'meta-analysis':ti OR 'metaanalysis':ti) NOT ('consensus'/exp OR 'consensus':ti) NOT ('case report'/exp OR 'case report':ti) NOT ('case study'/exp
#4	OR 'case series':ti OR 'case studies':ti OR 'case study':ti OR 'large case series':ti)
	#1 AND #2 AND #3 NOT #4

Eligibility Criteria

As inclusion criteria, we included randomized clinical trials (RCTs), published no more than fifteen years ago, which addressed the application of mobilization techniques or HVLA techniques in the cervical spine of patients with CCD and whose HR had been evaluated. The studied population was patients of any gender, ethnicity and age, with the presence of pain or dysfunctions in the skull (posterior, temporal and facial region) and cervical spine (between vertebrae C1 and C7) acute or chronic, assessed by any pain scale. As a criterion for comparing data, those that presented pre- and post-intervention assessments were considered. Articles that applied other interventions such as myofascial techniques, stretching and exercises were excluded, as well as studies on patients with hypertension and other comorbidities other than musculoskeletal in the spine. Furthermore, articles that applied mobilizations or HVLA to the thoracic and/or lumbar spine, as well as the application of cranial and visceral techniques were excluded.

Finally, we considered the references of eligible articles to screen other publications relevant to the study, respecting the inclusion and exclusion criteria, and which were not found in pre-established databases. Studies were selected according to criteria around the Population, Intervention, Comparator, Outcome(s) of interest, and Study design (PICOS framework) (chart 2).

Chart 2: Inclusion and exclusion criteria

Inclusion	Exclusion
Population	
Human research	Animal research
Patients of any gender, ethnicity, and age with a confirmed clinical diagnosis of CCD. • Any type of headache (cranial or facial pain). • Cervical pain (acute or chronic).	Healthy populations. Neurological diseases/dysfunctions (except migraine). Heart and respiratory diseases. Concussions or traumas. Endocrine, metabolic, and digestive system diseases. Cancer and degenerative and progressive diseases. Other musculoskeletal disorders.
Intervention	
MTT were characterized by mobilizations or HVLA techniques of the cervical spine. **Definition:** **Mobilization:**	Myofascial techniques (myofascial release). Articulation techniques. Massage. Muscle energy techniques.

Mobilization techniques are consisting of moving the vertebrae in the direction of their restriction, through oscillatory movements, with the intention of increasing their mobility. intended to improve tissue extensibility; increase range of motion; induce relaxation; mobilize joints; modulate pain; and reduce soft tissue swelling, inflammation, or restriction and improving function in patients with a wide variety of diagnoses. We consider the mobilizations applied on cervical vertebrae from C1 to C7. Maitland and Mulligan methods are examples of mobilizations. **HVLA techniques:** HVLA techniques employ a rapid use of force over a short duration, distance, and/or rotational area within the anatomical range of motion of a joint to engage the restrictive barrier in one or more planes of motion to elicit the release of restriction. HVLA techniques promote similar effects to mobilization techniques. We consider the HVLA techniques applied on cervical vertebrae from C1 to C7. Osteopathic and chiropractic manipulations are examples of HVLA.	Stretches. Tractions. Use of activators for joint manipulations. Strain counterstrain techniques. Craniosacral therapy. Cranial techniques. Visceral techniques. Acupuncture. Exercises. Cognitive behavioral therapies. Electrothermophototherapy. Medications such as analgesics, anti-inflammatories and corticosteroids. Any other method used in physiotherapy to gain range of motion, relax muscles and reduce pain.
Control interventions	
Any kind of control intervention (i.e., sham, usual care, pharmacological therapy, other care etc.) or no intervention. **Definition:** 1.a Sham (defined as all interventions mimicking "true" but modifying at least one aspect considered relevant by manual therapy concepts. 1.b Other care with known effectiveness (equivalence or superiority trials) (Standard care or other treatment included pharmacological therapies, relaxation, physical therapies, and so on). 1.c "No treatment" required that neither experimental nor standardized treatment could be initiated during the trial period.	-
Outcomes	
Due to the predicted high heterogeneity of outcome measures, we included all studies reporting the effectiveness of MTT interventions as measured with any type of score and/or scale. ***Time frame:*** We considered follow-up durations as short-term (≤3 months post-intervention), medium-term (3 months to ≤6 months) and long-term (>6 months). If a study has provided data at multiple time points within a single follow-up duration, then the data of the last follow-up point was used. If studies provided data on more than one measure for an outcome, we prioritized the most common measure used in the included studies of this systematic review.	-

Study Design	
1 Randomized controlled trials. 2 Randomized cross-over trials (For cross-over design, only the first phase of intervention was analyzed, and between-group difference was assumed to be identical to trials with parallel-group design).	3 Guidelines, letters, editorials, commentaries, unpublished manuscripts, dissertations, government reports, books or book chapters, conference proceedings, meeting abstracts, lectures and addresses, consensus development statements, or guideline statements. 4 Studies in which the effect of MTT could not be isolated (e.g, studies where osteopathic intervention was included in a multimodal program of care).
Language	
Any language.	Only if the translation was unfeasible for the research group.
Date of publication	
Articles published no more than fifteen years ago.	Articles published more than fifteen years ago.
Trial Registries	
Only those which are completed, and we had not picked up in other searches.	Currently recruiting or not recruiting.
Country	
Around the world	-

Note: CCD, craniocervical dysfunctions; MTT, manual therapy techniques; HVLA, high-velocity low-amplitude techniques.

Data Extraction and Synthesis

Data from the included studies were extracted in standardized data extraction sheets. The following study information was extracted: study design, participants, total number of participants (n), region where MTT was applied, type of intervention, comparisons, outcome, risk of bias, adverse events, attrition details, conflicts of interest and sources of funding. For data synthesis, the average of the differences between the groups was used. For articles in which the data was not complete, without confidence interval (CI) values, we performed the conversion using the following formula: $x \pm (Z * s / \sqrt{n})$, where, x is the sample mean, Z is the Z score, s is the sample standard deviation and n is the sample size. All tabulated data was plotted in an excel table where it was possible to view the individual values of each article. To assess the possible causes in case of heterogeneity of the studies we consider diferences in study design, intervntions, population, effect modifiers and outcomes.

Assessment of Certainty of Evidence and Methodological Quality

The analysis of the certainty of evidence in the articles was carried out using the GRADE)[28,29], which classifies four levels of quality (high, moderate, low and very low). For classification of high-quality evidence, the presence of consistent results among at least 75% of participants in studies with low risk of bias was considered; consistent, direct and accurate data; and no publication bias provided.

Evidence of moderate quality classified when one of these domains was not met. For low-quality evidence, at least two of the domains should not be met. Finally, for very low-quality evidence, three of the domains should not be met and the results given as very uncertain.

The absence of evidence occurred when no randomized studies that addressed this result were identified. Studies with a sample size of less than 300 were of very low quality, as were those with a PEDro score of less than 6. The criteria for downgrading the level of evidence depended on the presence of five factors: limitations (due to risk of bias); consistency of results; openness (e.g. whether the participants are like those about whom conclusions are drawn); precision (i.e., enough data to produce short CIs); and others (e.g., publication bias). The level of quality of evidence was increased if large effects or a "dose-response" were seen based on the analysis of RTCs. In this way, we classify the evidence quality results using four levels: "high", "moderate", "low", or "very low. The statements for the communication of results are in line with the GRADE working group recommendations[30]. A detailed table of GRADE criteria is shown in chart 3. The GRADEpro® Guideline Development Tool program was used to classify the studies.

The methodological quality of the selected articles was assessed using the PEDro scale, through the website https://search.pedro.org.au/search[31], in which the articles analyzed were scored based on the following criteria: eligibility; random allocation; secret allocation; similarity of groups; blind participation; blind therapists; blind assessors; size of results; intention-to-treat analysis; intergroup statistical comparison; and precision and variability measures. The first item (eligibility criteria) is not considered in the total score as it is related to external validity. The total score on the PEDro scale ranges from 0 to 10 points; higher scores mean greater methodological quality. This scale has good levels of validity and reliability[32–34].

Chart 3. Criteria for GRADE downgrade

GRADE Domain	Criteria used in this review
Risk of bias	Downgraded by one level if 50% of studies or 50% of n-randomised had high risk of bias, or 75% of studies or 75% of n-randomised was from studies with some concerns. Downgraded by two levels if all studies had high risk of bias
Inconsistency	Downgraded by one level if substantial heterogeneity was present. For example, effect estimates varied widely across studies, 95% CI had showed minimal or no overlap, I^2>50%, or the prediction interval showing treatment effects favouring both directions.
Indirectness	Downgraded by one level if any evidence supporting the meta-analysis came from studies not directly related to the PICOS criteria.
Imprecision	Downgraded by one level if the 95% confidence interval of the effect estimate includes no effect or the sample size <800 in total (<400 per group).
Publication bias	Downgraded by one level if evidence of asymmetry in the funnel plots, or statistical evidence (p<.05) from the modified Eggers test.

RESULTS

Study Selection

A total of 3,464 potentially relevant records were retrieved. After the removal of duplicates and exclusion of records by title and abstract and full-text screening, we included 3 reports in this review (Figure 1).

Study Characteristics

The review included 3 articles that evaluated the effects of HVLA techniques or mobilization on the cervical spine of patients with craniocervical pain.

Zago, et al (2023)[35], conducted a crossover study with the aim of evaluating the effects of HVLA technique in cervicothoracic junction in HR, in subjects with C7-T1 dysfunction..Twelve male subjects were randomized into two groups: HVLA and Sham. HVLA group received a single HVLA for C7-T1 dysfunction, while the sham group received a simulated HVLA. HR was measured pre, immediately after and ten minutes after the application of the interventions. Immediately after the application of the interventions, a statistically significant increase was observed immediately after the application of HVLA technique, of 9 beats per minute (bpm) [$p < 0.0001$] when compared to the sham group.

Win, et al (2015)[36], conducted a randomized crossover clinical trial, where they allocated 10 asymptomatic patients and 10 patients with acute neck pain. The authors performed an HVLA technique in the upper and lower cervical spine. HR values were collected before and after the application of the interventions. In the volunteers, when submitted to the HVLA technique in the upper cervical spine, HR did not change its value, remaining at 67 beats bpm. In the group of patients with neck pain, when they received the HVLA technique in the upper cervical spine, HR values went from 64±5 bpm to 62±4 bpm. On the other hand, when they received the HVLA technique in the lower cervical spine, the HR values went from 69±11 to 70±10 bpm.

La Touche, et al (2013)[37], performed three sessions in 32 patients with orofacial pain. The patients were randomized into two groups: the treatment group, which received anteroposterior joint mobilizations between C0-C3, with a frequency of one mobilization per second at 0.5 hertz (Hz) for six minutes. The mobilizations were applied in three two-minute intervals, with 30 seconds of rest between them; on the other hand, the comparison group received a sham technique, where the position of the hands was maintained in the region and for the same time as the effective mobilization technique.

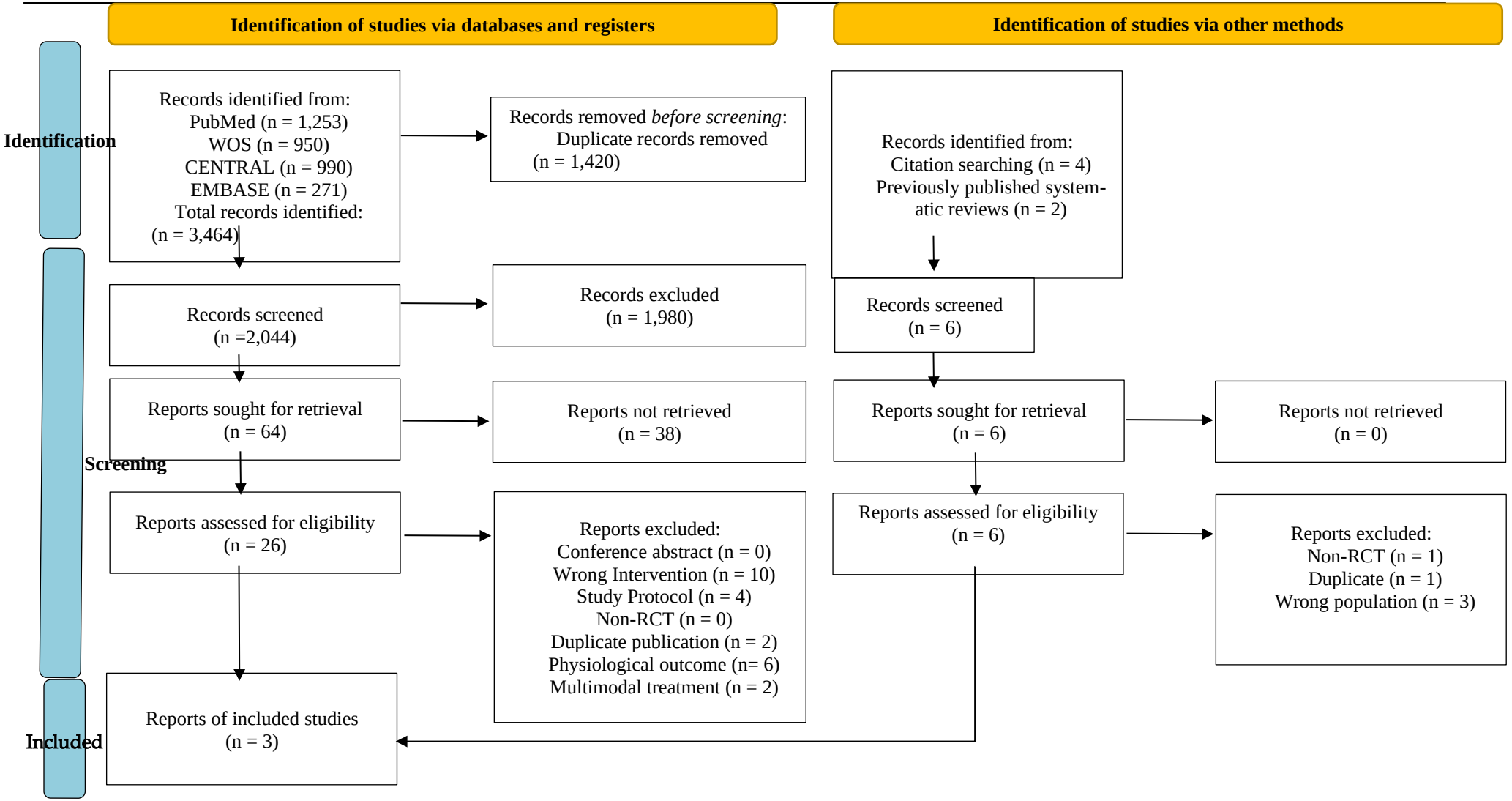

Figure 1: PRISMA flow diagram of study identification, screening, eligibility assessment, and inclusion. (Abbreviation: RCT, randomized controlled trial, WOS, Web of Science).

The authors observed that the treatment based on cervical mobilization applied at a rate of 0.5 Hz contributed significantly to the activity of the SNS in the short term. The authors also evaluated changes in the SNS, whose reflection was measured through changes in skin conductance, respiratory rate and HR. In the first session, the pre-intervention HR values in the treatment group were 69.56±6.3 bpm, followed by post-treatment values of 73.16±5 bpm. In the sham group, pre-intervention values were 67.87±7.35 bpm and post-treatment values were 63.81±7.56 bpm. In the second session, the treatment group presented pre-intervention values of 71.25±4.39 bpm and post-intervention values of 75.1±2.88 bpm.

On the other hand, in the sham group, pre-intervention values were recorded as 67.31±6 bpm and post-intervention values of 63.31±6.73 bpm. In the third session, the treatment group presented pre-intervention values of 72.05±6.84 bpm and post-intervention values of 77.12±4.12 bpm, while the sham group obtained pre-intervention values of 69.37±5.09 bpm and post-intervention values of 66.12±7.01 bpm. Therefore, the authors observed a statistically significant increase in HR in the group that received mobilizations ($p<0.001$).

Heterogeneity of Studies

Overall, the studies showed heterogeneity, especially in relation to the diagnosis of the participants, with Zago, et al recruiting patients with joint dysfunction in C7-T1, Win, et al selecting participants with neck pain and healthy while, La Touche, et al, recruited patients with cervico-craniofacial pain.

The interventions were also different between the studies, with application of HVLA techniques in two studies, however, in different regions of the cervical spine, while the other study applied mobilization technique. Regarding methodological quality, there were also differences between the studies. All these factors made the analysis quite heterogeneous, making a meta-analysis inappropriate. The summary of the studies data is in Table 1.

Table 1. Included studies comparing manual therapies techniques versus comparator groups.

Studies, (year)	Description of protocol									
	Design	Intervention	Comparator	Duration	Frequence	Washout	n	*p*	PEDro	GRADE
Zago et al., (2023)	CO	HVLA technique in C7-T1	Sham technique in C7-	One application	1 session, once a week	7 days	12	<0.001	9	Very low
Win, et al., (2015)	CO	HVLA technique in C1-C2	HVLA technique in C6-C7	One application	1 session, once a week	7 days	20	>0.05	5	Very low
La Touche, et al., (2013)	RCT	Anteroposterior mobiliza-	Sham technique in C0-	6 minutes, 3 intervals of 2 minutes.	1 oscillation per 2 seconds	N/A	32	<0.001	7	Very low

Assessment of Methodological Quality and Certainty of Evidence

To assess the methodological quality of the included studies, we used the PEDro scale. Analysis of the article Zago, et al[35], showed that it was not possible to blind the therapists in the clinical trial, however, the other criteria of the methodological scale were met. Therefore, this study was classified as having high methodological quality, or "Excellent".

Regarding the study by Win, et al[36], there was no record of concealed allocation, blind subjects, blind therapists, intention-to-treat analysis and between group comparisons. Therefore, this article was classified as of low quality or "Poor". Regarding the study La Touche, et al[37], we did not observe blind therapists, Intention-to-treat analysis or between group comparisons.

Therefore, this article was classified as having moderate methodological quality or "Fair". The classification of the study by Win, et al[36], was available on the PEDro website, while the studies by Zago, et al[35] and La Touche, et al[37], underwent an inspection based on the classification system available on the PEDro platform, where the researchers carried out the training available on the platform itself. For these articles, there was full agreement between the authors during these stages of classification. Scale scoring details for each article are in table 2.

Table 2. Classification of the methodological quality of articles

	PEDro scale item	Zago, et al (2023)	Win, et al (2015)	La Touche, et al (2013)
1	Eligibility	Yes	Yes	Yes
2	Random allocation	1	1	1
3	Concealed alloction	1	0	1
4	Baseline comparability	1	1	1
5	Blind subjects	1	0	1
6	Blind therapists	0	0	0
7	Blind assessor	1	1	1
8	Adequate follow-up	1	1	1
9	Intention-to-treat analysis	1	0	0
10	Between group comparisons	1	0	1
11	Point estimated variability	1	1	0
	Score	9/10	5/10	7/10
	Quality	Excellent	Poor	Fair

Note: PEDro, Physiotherapy Evidence Database

Regarding the GRADE criteria, Zago, et al[35], found consistent data, low risk of bias, and no publication bias. The study by Win et al. showed inconsistent data, as it did not present a 95% CI or an effect size calculation for clinically relevant differences. In addition, the study presented a moderate risk of bias. In the study by La Touche et al[37]., we did not detect any inconsistent data or publication bias. In addition, the study was considered to have a low risk of bias. The three articles presented a very low (less than 300), which automatically downgraded them to the level of evidence as very low.

Characteristics of Patients with Craniomandibular Dysfunctions

A total of 64 patients were included in these three studies. Zago, et al[35] included 12 men diagnosed with dysfunctions in the C7-T1 region, through specific mobility tests for the cervical spine. La Touche, et al[37], recruited 32 patients, 21 women and 11 men, with the presence of pain in the cervical spine or in the masticatory muscles with the presence of bilateral trigger points in the masseter, temporalis, upper trapezius and suboccipital muscles.

These were diagnosed through the presence of a palpable muscular tense band in the muscles accompanied by a tender or hypersensitive point within the tense band; local contraction response provoked by rapid palpation of this tense band and reproduction of referred pain in response to compression of the trigger point[38].

Win, et al[36], included 20 participants in their study, of which 10 were asymptomatic and the other 10 presented cervical pain. In total, the sample consisted of 11 men and 9 women, with the group of patients with cervical pain consisting of 5 men and 5 women, while the asymptomatic group consisted of 6 men and 4 women. Acute mechanical cervical pain was defined as pain in the cervical region for which it is not possible to identify a specific pathological cause of pain, and the duration of pain is not greater than 6 weeks, with or without pain in the upper limbs, which may or may not interfere with activities of daily living[39].

Manual Therapy Techniques

HVLA techniques were applied in 2 of the studies[35,36]. The HVLA technique consists of pushing the hypomobile joint to its limit of movement and performing a rapid impulse in the direction of the restriction. One of the studies applied the technique in the region of the C7-T1 vertebrae[35], while the other applied it in the region of C1-C2[36]. Both studies applied only one technique, with a 7-day washout period before applying the next intervention. On the other hand, the other study[37] applied an oscillatory mobilization technique between the C0 and C3 vertebrae. The mobilization technique consists of propelling the vertebra in the anteroposterior direction in an oscillatory manner, with one oscillation every 2 seconds (0.5 hertz). The technique was applied for six minutes, with three two-minute intervals with 30 seconds between them.

DISCUSSION

The results of this review indicate a high to moderate methodological quality, but a very low level of evidence across the studies included. Nevertheless, the findings suggest that the application of MTT, specifically HVLA and mobilization techniques, can elicit responses in the ANS, particularly affecting HR in both the upper cervical (C0-C3) and lower cervical (C7-T1) regions. Notably, Zago et al. reported clinically significant effects following HVLA application at C7-T1, with a Cohen's D of 1.03[35].

Regarding the autonomic response promoted through the application of MTT on the cervical spine, it is known that reflex sympathoexcitatory responses can occur when there is mobilization at any level of the spine[40], however, the literature does not support the effects of sustained manual techniques or with natural apophyseal sliding. In this sense, a study recently concluded that some types of mobilizations probably produce an immediate and short-term statistically significant increase in the sympathetic nervous activity of the skin, when compared to a simulated procedure, which is in line with our results. The hypotheses generated in most studies that evaluate the effects of manual therapies on the modulation of the ANS are based on anatomy, since a large part of the sympathetic and parasympathetic innervation of organs such as the heart emerges from the cervicothoracic segment[41].

On the other hand, the application of HVLA techniques in the cervicothoracic region can produce effects on the ANS, which can cause changes in systolic blood pressure, diastolic blood pressure, HR and local or systemic arterial flow.

HRV also respond to manual stimuli in the cervicothoracic spine, however, most of these studies analyzed data from healthy individuals and, in this sense, we believe that the neuronal response pathways of manual stimuli on the spine may be different compared to individuals with musculoskeletal dysfunctions in the spine, considering the increased nociceptive sensitization and the presence of chemical mediators in these patients[42].

Therefore, we believe that there is a need to develop randomized clinical trials that evaluate biochemical markers such as nitric oxide, so that we can make a more direct relationship about the modulation of the ANS after the application of manual techniques on the spine.

The studies had a common limitation, which was the low number of patients recruited, in addition to two of them presenting little description of the data on differences between the groups, such as 95% CI and effect size calculation. These limitations make it difficult to conclude whether the results of this review may be clinically relevant. This review suggests conducting clinical trials with better methodological quality and following the principles of the CONSORT statement. In the study by Zago et al, the technique was applied to the C7-T1 region, and the results may be conflicting as there was stimulation at T1 and not just at the cervical level, as we had predefined in the inclusion criteria.

CONCLUSION

This review concludes that the application of manual therapy techniques on the cervical spine can generate responses in the activity of the autonomic nervous system, modulating heart rate, in patients with craniocervical dysfunctions, but it is not clear whether these changes are clinically relevant. In addition, the application of high-velocity and low-amplitude techniques, as well as mobilization, can generate responses in heart rate regardless of the level at which they are applied. The studies were classified as having low and moderate risk of bias, but with very low quality of evidence.

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