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TITLE PAGE

Thoracic adverse events following spinal manipulative therapy: a systematic review and narrative synthesis

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ABSTRACT

Objectives: Spinal manipulative therapy (SMT) is widely used by manual therapists to manage spinal complaints. Notwithstanding the perceived relative safety of SMT, instances of severe thoracic adverse events (AE) have been documented. An evidence synthesis is required to understand the nature, severity and characteristics of thoracic AE following all SMT. The primary objective of this study was to report thoracic AE following SMT and secondly to report patient characteristics to inform further research for safe practice.

Methods: A systematic review and data synthesis was conducted according to a registered protocol (PROSPERO CRD42019123140). A sensitive topic-based search strategy for key databases, grey literature and registers used study population terms and key words, to search to 12/6/19. Two reviewers were involved at each stage. Using the Oxford Centre for Evidence-based Medicine (CEBM) the level evidence was evaluated with grade presented for each AE. Results were reported in the context of overall quality.

Results: From 1013 studies identified from searches, 19 studies, (15 single case studies, 4 and case series) reporting 21 unique thoracic AE involving the spinal cord tissues [non vascular (n=7), vascular (n=6)], pneumothorax or hemothorax (n=3), fracture (n=3), esophageal rupture (n=1), rupture of thoracic aorta (n=1), partial pancreatic transection (n=1). Reported outcomes included fully recovery (n=8), permanent neurological deficit (n=5), and death (n=4).

Conclusion: Although causality cannot be confirmed, serious thoracic AE to include permanent neurological deficit and death have been reported following SMT. Findings highlight the importance of clinical reasoning, including pre-thrust examination, as part of best and safe practice for SMT.

Keywords: spinal manipulative therapy, thoracic, adverse events, systematic review

INTRODUCTION

Thoracic spinal manipulative therapy (SMT), involving a single high velocity amplitude thrust technique is a recommended best practice management option for individuals with neck pain who have been appropriately screened for contraindications to the use of SMT [1, 2]. Evidence from systematic reviews of clinical trials support thoracic SMT as an effective treatment option for acute, sub-acute and chronic neck pain [3, 4, 5] and shoulder pain [6, 7], with a recent high quality systematic review with meta-analysis supporting the use of thoracic SMT over thoracic or cervical mobilization for improving pain and disability in participants presenting with mechanical neck pain [3]. Clinical reasoning in practice includes examination to establish the existence of factors, which may contraindicate use of certain techniques where AE are of concern. An AE being an 'untoward medical occurrence' in a patient subjected to an intervention.[8] Although AE are rare, and causality linked to SMT not established, they have been associated with use of SMT [9, 10]. Despite many trials of thoracic SMT failing to report AE data [11], of the 14 studies included in a recent review, 9 reported AE and side effects (SE) [13]. SE are minor, reversible and short lived and AE are considered moderate to severe, last longer and importantly may require medical management (e.g. spinal cord injury or hemothorax) [12, 13]. It is of note that across the existing trials of thoracic SMT (n=885 participants), no AE were reported [3]. This is perhaps a consequence of pre-trial training and involvement of expert practitioners delivering trial interventions.

Current evidence suggests that around half of all patients experience SE after SMT, with AE rarely occurring [14, 15]. Life-changing AE such, as stroke or spinal cord injury, cannot be ignored [18, 19] and further research is required to inform safe and best practice. Currently literature shows that the thoracic spine is the most commonly manipulated spinal region, and, thoracic SMT perceived safe by >91% USA physical therapists [16]. Moreover from a

trial that compared cervical and thoracic SMT for patients with acute neck pain more SEs were reported in the thoracic SMT group [17]. A recent survey reported that just 40% of UK physiotherapists use pre-thoracic SMT examination [18]. A review of 134 case reports revealed that almost half of AE following cervical manipulation could have been prevented with pre-thrust examination; thus, a further consideration of pre-thrust examination is needed [9]. Knowledge of the severity and nature of thoracic AE; including patient characteristics, is required to inform clinical reasoning and safe practice using SMT. Recognizing the poor specificity of SMT [19], a focus solely on thoracic spine SMT may exclude evidence where SMT for the neck or low back results in an thoracic AE. A comprehensive review is required to inform a clinical reasoning framework for the thoracic spine. This would support the development of a region specific clinical reasoning framework, akin to that which has been developed and implemented globally for the cervical spine [20]. A systematic review published in 2015 reported 10 unique cases of AE [10] following thoracic SMT. With a focus on thoracic SMT, some methodological limitations and, recent scoping searches identifying other cases, a rigorous updated review of thoracic AE following SMT is now required. Results from this evidence synthesis highlights the importance of clinical reasoning and will inform the development of a clinical practice framework for safe practice for SMT involving the thoracic spine.

Objectives

The primary objective was to synthesize evidence of thoracic AE following SMT (cervical, thoracic and lumbar spine), documenting their severity and nature. The secondary objective was to describe the characteristics of patients who have experienced a thoracic AE.

DESIGN AND METHODS

This systematic review and narrative synthesis was designed in accordance with the Centre for Research and Dissemination Guidelines [21] and Cochrane Handbook [22]. The review is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [23]. An *a priori* protocol informed by PRISMA-P [24] was registered with the International Prospective Register of Systematic Reviews (PROSPERO number: CRD42019123140).

Eligibility criteria

Using the SPIDER search concept tool eligibility criteria were defined by the research team [25].

Inclusion criteria:

S - the sample population included adults >16 years;

PI - the phenomenon of interest was thoracic AE following SMT;

D - all types of observational study designs were included (survey, single case studies, cohort and case-control studies);

E - the type and nature of thoracic AE, the presence of risk factors, the SMT technique/s used and the time to the onset of symptoms were evaluated;

R - research data included quantitative and narrative findings.

Exclusion criteria :

AEs occurring without SMT, systematic or literature review articles, modelling and simulation studies, non-English publications.

Information sources

A comprehensive search of databases [PubMed, Medical Literature Analysis and Retrieval System Online (MEDLINE), Excerpta Medica dataBASE (EMBASE), Allied and

Complementary Medicine (AMED), Cumulative Index of Nursing and Allied Health (CINAHL), Physiotherapy Evidence Database (PEDro) and Index to Chiropractic Literature (ICL)] was conducted from database inception to 12/6/19 with strategies tailored for each database. Grey literature searching included British National Bibliography for Report Literature, Dissertation Abstracts, Index to Scientific and Technical Proceedings, National Technical Information Service and the System for Information on Grey Literature. Other sources comprised Google Scholar, subject specific journals (e.g. Manual Therapy) and reference lists of included articles and relevant systematic reviews.

Search strategy

Extensive scoping searches informed the search strategy. The following controlled vocabulary and keyword combined terms were utilized: 'musculoskeletal manipulations', 'spinal manipulation', 'thrust', 'manual therapy', 'musculoskeletal manipulation', 'adjustment', chiroprac*', 'osteopat*', physiotherap*' AND 'adverse reaction', 'adverse event', 'side effect', 'side effect', 'harm', 'complication', 'safety' OR 'spinal injury', 'pneumothorax', 'hematoma', 'epidural haematoma', 'fracture', 'ischemia'. Unique search strategy and alternative spellings were used for each database. An example of the search strategy for Medline is illustrated in S1 table.

Study selection

Two reviewers (CP and KK) with expertise in musculoskeletal physiotherapy (postgraduate qualification) and experience of conducting systematic reviews screened the search results independently. Based on inclusion and exclusion criteria, reviewers grouped the studies as eligible, potentially eligible or not eligible. For the eligible and potentially eligible studies, the full texts were reviewed. The third reviewer (NH) had oversight at all stages of the process and mediated in case of disagreement after discussion.

Data collection process and items

The two reviewers (CP and KK) extracted data independently using a bespoke form being designed and reported in the protocol. Where data were missing or clarification was required, the study authors were contacted. Following piloting of the data extraction process, the data extracted from each individual study included: year of publication, study design, medical specialty of the author(s), age, gender, symptoms treated with thoracic spine manipulation, thoracic level manipulated and technique used, thoracic AE occurred, interval to symptoms onset, secondary care management and clinical outcome.

Level of evidence of individual studies

Given the inclusion of studies involving a broad range of study designs, eligible studies were evaluated based on the level of evidence. [26] This ranged from 1a representing a systematic review of randomized control trials through to level 5 representing expert opinion without critical appraisal [26].

Synthesis of results

A narrative synthesis was conducted with results from single case studies and case series tabulated according to thoracic AE. The synthesis allowed sub-classification according to classification of AE (e.g. spinal cord injury: vascular or non-vascular complications, internal organ, fracture etc.). For findings from surveys, reports of thoracic AE were also tabulated as part of the narrative synthesis. As a different study design and with limited detail of patient characteristics, synthesis with case study and series data was not possible.

Level of evidence for each thoracic AE was evaluated using grades of recommendation from the Oxford Centre for Evidence based Medicine to include: A or level 1 studies, B or level 2 or 3 studies, C or level 4 studies and D or level 5 studies. [26].

RESULTS

Study selection

Thoracic AE were reported in 19 studies, (15 single case studies and 4 case series. Twenty-one instances of thoracic AE dating back as far as 1947 up to 2018 were described in single case studies or case series and grouped according to classification of thoracic AE. The PRISMA flow diagram of study selection is shown in Figure 1.

Study characteristics

Most of the studies were single case studies (n=15) with four case series involving six cases and a further 12 cases reported in surveys. Patient presentations being managed with SMT included pain in the thoracic spine (n=3), low back or thoracolumbar region (n=9), neck, chest or upper back (n=5), unknown (n=2), hip (n=1), and for maintenance in an individual with ankylosing spondylitis (n=1). Slightly more male than female cases were reported (males n=12, females n=9) with the age ranging from 17 to 71 years. Reported thoracic AE included non-vascular tissue of the spinal cord or dura (n=7), vascular related to spine (n=6), pneumothorax or hemothorax (n=3), fracture (n=3), esophageal rupture (n=1), rupture of thoracic aorta (n=1) and partial pancreatic transection (n=1). The specific detail of the SMT techniques used were not reported in 14 cases. In two cases, the technique was described 'aggressive', posterior-anterior thrust in four cases, seated traction, 'bear hug', 'back to back lifting' and manipulation under anesthesia. Those performing the techniques included chiropractors (n=16), physical therapists (n=2), osteopath (n=1), lay person (n=1) and was unreported in one case. Secondary care management ranged from surgery (n=15), to medical management (n=3), bed rest and steroids (n=1), and not reported (n=1). In terms of reported secondary care outcomes, (n=12), 11 patients were discharged in good condition, four patients were left with long term neurological deficit, four patients died, and

in two cases the outcome was not reported. One death occurred immediately following SMT. The study characteristics and thoracic AE occurred are detailed in Table 1.

Figure 1. PRISMA flow diagram for systematic reviews

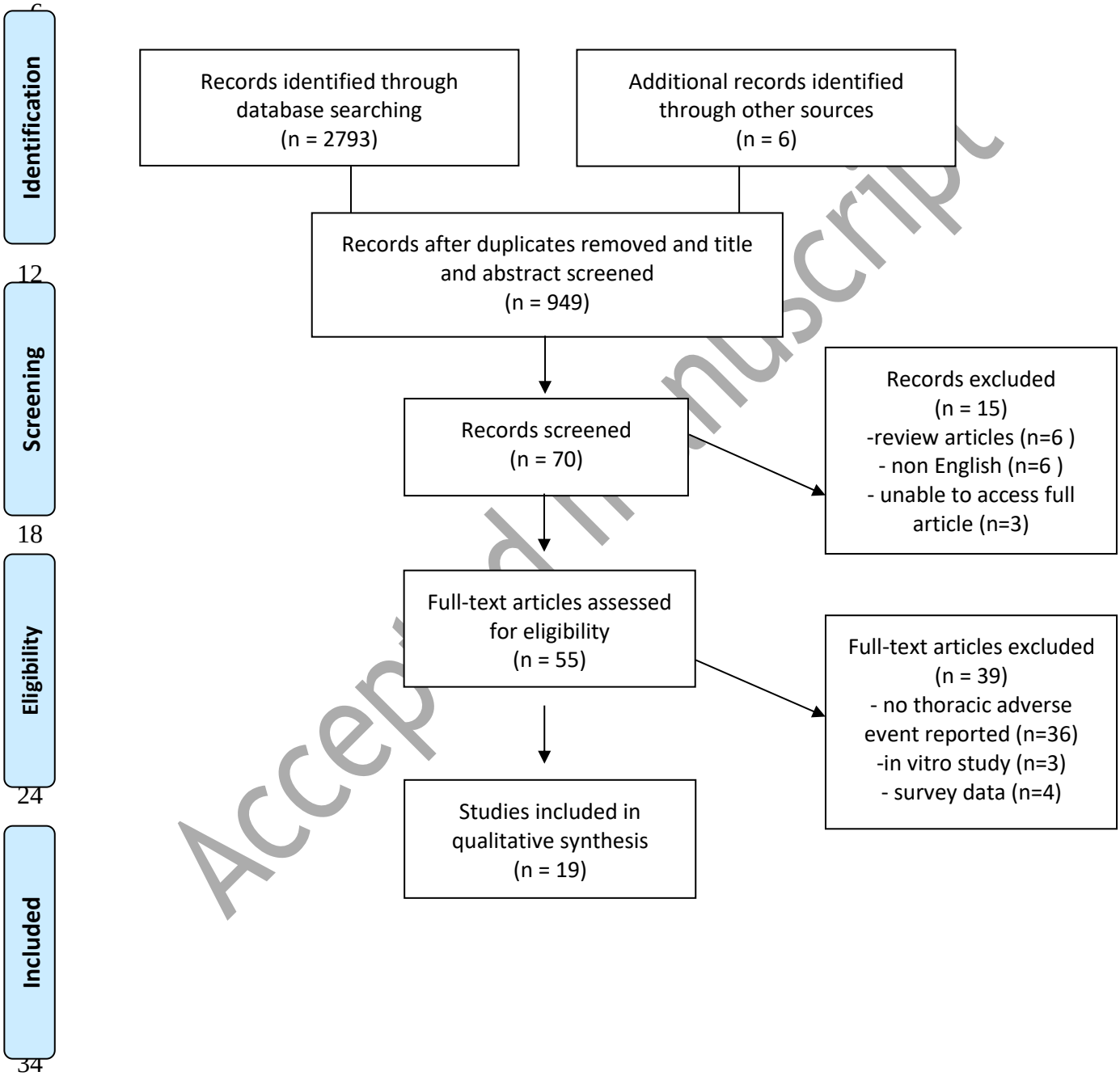

Table 1. Case study and case series studies and participant characteristics

Authors and year	Study design	Age, gender	Sample/ TAE	Patient complaint Patient characteristics	Technique details and Practitioner	Description of thoracic AE	Interval to TAE	Secondary management	Outcome
Pratt-Thomas & Berger 1947 [27]	Case series	31, M	3 /1	Neck and chest pain Good health	Described as having back 'mashed' Chiropractor	Epidural hematoma below T1-2, lead to spinal cord necrosis	Immediate	Not described	Died of sepsis
Livingstone 1971 [28]	Case series	70, M	12 /1	Upper back, mild sternal pain, numbness feet and difficulty urinating Undiagnosed multiple myeloma	Not reported Chiropractor	T8 incomplete block, T9-12 plasmacytoma	Immediate	Myeloma management	Died 3 weeks after from complications
Austin 1985 [29]	Case series	57, M	2 / 1	Thoracic pain Undiagnosed multiple myeloma	Not reported Physiotherapist	Compression fracture T9 in multiple myeloma patient	Immediate	Myeloma management	Not reported
Lanska et al 1987 [30]	Case study	55, M	1	Low back pain Good health	Aggressive rotatory & extension to spine Chiropractor	Myelopathy, T2-3	Immediate	T2-3 costotransversectomy	Mild Brown-Sequard syndrome at 3 months
Ruelle et al., 1999 [31]	Case study	64, F	1	Low back pain No history of hypertension or coagulation disorders	Rotational HVLA technique ?lumbar region Chiropractor	Epidural hematoma. Epidural lesion T9-T11 causing spinal cord compression	Immediate	T9-T11 laminectomy	Complete recovery 1 year
Oppenheim et al 2005 [32]	Case series	60, F	18 /3	Hip pain History of breast cancer	Not reported Chiropractor	T4-5 collapse, cord compression (Paraparesis T5 sensory loss)	Not reported	T4-5 vetebrectomy	Good
		32, M		Low back pain Not reported		Thoracic syrinx, swollen cord (myelopathy)		Shunt surgery	Good

		56, F		Thoracic pain Not reported		T3 pathology, epidural tumor (Paraparesis T4 sensory loss)		Fracture laminectomy	Died one month later
Wang et al 2006 [33]	Case study	44, M	1	Pain in ?right scapular area Good health	Not reported Chiropractor	Cord compression, spinal epidural abscess	<3 hours	Laminectomy T3-6	Moderate paresis left leg at 3 months
Domenicucci el al., 2007 [34]	Case study	52, F	1	2 month history upper cervical and thoracic vertebrae pain Good health	Cervical manipulation Chiropractor	Epidural hematoma C3-T1 with cord compression	Immediate	Laminectomy C3-T1	Complete recovery 6 months
Masneri et al 2007 [35]	Case study	20, F	1	No complaint No history of lung disease or thoracic history	'Bear hug' Lay person	Pneumothorax	Within 24 hours	Chest tube thoracostomy	Discharged after 3 days in good health
Donovan et al 2007 [36]	Case study	32, F	1	Not reported Not reported	PA manipulation of thoracic and lumbar spine in prone Physical Therapist	CSF leak and spontaneous intracranial hypotension due to C8-T5 dural sleeve tear	Immediate	2 epidural blood patches	No symptoms at one year
Sozio and Cave 2008 [37]	Case study	47, F	1	Low back pain No history of esophageal disease and alcohol use, or antecedent of nausea, vomiting, retching or dysphagia	PA manipulation of thoracic and lumbar spine in prone Chiropractor	Esophageal rupture	Within 24 hours	Repair of esophageal perforation	Good
Lee et al 2011 [38]	Case study	38, F	1	Neck and shoulder soreness Good health. No anticoagulation therapy	Not reported Chiropractor	Intraspinal epidural hematoma, T1-6	Immediate	Laminectomy C7-T8	Complete recovery 2 weeks
Lopez-Gonzales and Peris	Case study	45, F	1	Thoracic and LBP Good health	Not reported Chiropractor	Spinal cord ischemia	20 minutes	Best rest and steroid	At 15 day follow up deficits included strength and sensory

Celda 2011 [39]				'had a history of only diffuse, not irradiated middle and LBP'					with pyramidalism. T9 sensory sensory loss.
Hudkins, 2012 [40]	Case study	55, M	1	Chronic low back pain Previous surgery for abdominal gunshot with splenectomy and appendectomy. Hypertension and gout	Not reported Chiropractor	Partial pancreatic transection	Immediate	Distal pancreatectomy	Some complications day 33, but resolved
Struewer et al 2013 [13]	Case study	17, M	1	Thoracolumbar pain No PMH of lung disease or thoracic injury	Seated HVLA mid-thoracic Osteopath	Hemothorax	Within 2 days	Chest tube thoracostomy & thoracoscopic hemostasis	Discharged 7 days later good health
Gardner et al 2013 [41]	Case study	57, M	1	Maintenance for ankylosing spondylitis Ankylosing spondylitis	Manipulation under anesthetic Chiropractor	Hemothorax and oblique fracture from T9 to T11	Within 24 hours	Open reduction and internal fixation	Discharged 12 days later –neurologically intact
Kaczorowska , 2014 [42]	Case study	45, M	1	Chronic low back pain No significant medical history of cardiovascular disease	'spinal adjustment" Chiropractor	Rupture of thoracic aorta (aneurysm)	Immediate		Death
Hdeib et al 2016 [43]	Case study	71, M	1	Back pain PMH: hypertension, hyperlipidemia and benign prostatic hyperplasia. Medication: NSAIDs and daily aspirin	Not reported Chiropractor	Hemorrhagic conversion of a spinal schwannoma at T8 level	Within 24 hours	Thoracic laminectomy	At 6 months follow up anti gravitational strength, walking strength
Skappak and Saude 2018 [44]	Case study	66, M	1	Low back pain PMH: transient ischemic attack, hypothyroidism and transient pancytopenia. No previous traumatic injury.	Not reported Chiropractor	Compression fractures, T11,L1, L2 and L3 in multiple myeloma patient	Within 24 hours	Myeloma management	Not reported

HVLA: high velocity low amplitude thrust, NSAID: non steroid anti-inflammatory drugs, LBP: low back pain, PMH: past medical history

Level of evidence

All evidence sources were graded as level 5 [26] being either single case studies or case series. There was complete (100%) agreement between the two reviewers on the evaluation. Where authors were contacted for additional information or clarification, no responses were received.

Synthesis of results

Synthesis of evidence is presented in Table 3, with the results grouped according to type of thoracic AE. Study designs being predominantly level 5 evidence (case studies and case series) with the overall body of evidence rated as D [26] (See Table 1).

Thoracic adverse events following SMT

Non-vascular thoracic AE. Instances of non-vascular spinal cord injuries following SMT exist (n=7). Participant characteristics were similar for gender with age ranging from 31 to 71 years. The level of the SMT and technique was reported in just two studies. In one instance, an 'aggressive' rotatory and hyperextension manipulation thrust was performed for a patient with LBP [30] and the other a posterior-anterior (PA) technique was targeted at the upper thoracic spine [36]. Onset of thoracic AE was immediate in most cases with one case presenting to the emergency department within three hours with acute paraplegia [43] and one study [19] failing to report time to onset for three reported cases. In terms of medical management, five patients were managed surgically, one conservatively [45] and one received treatment for multiple myeloma [40]. Two patients fully recovered [19, 45], two were left with neurological deficits [43, 42] and three patients were reported to have later died; albeit not directly related to SMT and onset of AE [40, 19] (See Table 3).

Table 3. **Non-vascular AEs, medical management and outcome**

Author and year	Adverse event	Interval to thoracic AE onset	Secondary care management	Clinical outcome
Livingstone 1971 [28]	T8 incomplete block, T9-12 plasmacytoma	Immediate	Myeloma treatment	Developed complications and died 3 weeks later
Lanska et al 1987 [30]	Myelopathy, T2-3	Immediate	T2-3 costotransversectomy	At 3 months follow up mild Brown-Séquard syndrome
Oppenheim et al 2005 [32]	Spinal cord compression due to T4-5 collapse	Not reported	T4-5 vetebrectomy	"Good", however, the patient died 3 years later of unknown reason
Oppenheim et al 2005 [32]	Thoracic syrinx, swollen cord	Not reported	Shunt surgery	"Good"
Oppenheim et al 2005 [32]	T4 pathology, epidural tumor	Not reported	Fracture laminectomy	Died one month later
Wang et al 2006 [33]	Spinal cord compression, spinal epidural abscess	Within 3 hours	Extended laminectomy T3 to T6	At 3 months follow up shown moderate left lower extremity paresis
Donovan et al 2007 [36]	C8-T5 dural sleeve tear	Immediate	2 epidural blood patched administered 1 week apart	No symptoms at 1 year follow up

Vascular spinal AE. There were six cases of vascular thoracic AE following SMT [27, 31, 34, 38, 39, 43]. Participant characteristics were similar for gender, with age ranging from 31 to 71 years. Four cases of immediate epidural hematoma were identified [27, 31, 34, 38] in patients ranging 31-64 years. All but one study reported use of a forceful manipulative technique for complaints in the neck/shoulder region. In a further case, spinal cord ischemia occurred within 20 minutes of SMT in a region with a herniated and calcified disc [39]. In one case, a 70-year old male experienced a hemorrhagic conversion of a spinal schwannoma [43] within a day of receiving SMT. In terms of medical management, four patients underwent surgery, one was treated conservatively [39] and in one case

management was not reported [27]. Three patients recovered completely, two experienced neurological deficits [39, 43] and one patient died of sepsis [27].

***Table 4*. Vascular AEs, medical management and outcome**

Author and year	Adverse event	Interval to thoracic AE onset	Secondary care management	Clinical outcome
Pratt-Thomas and Berger 1947 [27] 31, M	Epidural hematoma below T1-2	Immediate	Not described	Died of sepsis
Ruelle et al., 1999 [31]	Epidural hematoma T9-11	Immediate	Laminectomy from T9-T11	Complete recovery 1 year
Domenicucci et al., 2007 [34]	Epidural hematoma C3-T1	Immediate	Laminectomy from C7 to T8.	Complete recovery 6 months
Lee et al 2011 [38]	Intraspinal epidural hamatoma from T1 to T6.	Immediate	Laminectomy from C7 to T8.	Complete sphincter control and able to walk independently at 2 weeks follow up
Lopez-Gonzales and Peris Celda 2011 [39]	Spinal cord ischemia	20 minutes after the session	Bed rest and steroids	At 15 days follow up the patient had strength and sensory deficit and pyramidalism signs with a T9 sensory loss level were established
Hdeib et al 2016 [43]	Hemorrhagic conversion of a spinal schwannoma at T8 level	Over the course of the day after manipulation	Thoracic laminectomy	At 6 months follow up the patient presented with anti-gravitational strength, walking assisted.

Internal organ injury thoracic AE

Hemothorax: Two single case studies of male patients, aged 57 and 17 years old reported hemothorax the day following SMT [13, 41]. One patient had SMT under anesthetic as a maintenance treatment for ankylosing spondylosis resulting in a complete transversally oriented fracture of the spine and hemothorax [49]. The other case, a previously healthy 17-year-old patient received SMT for thoracolumbar pain [13]. For both cases, subsequent

medical management involving internal fixation for one and chest tube 'thoracostomy' for the other. Both patients were later discharged in good health.

. ***Pneumothorax***. One case of pneumothorax in a 20-year-old female following SMT was reported. The manipulation was described as a 'bear hug' and performed by a layperson [35]. The patient required a chest tube thoracostomy and then discharged after three days in good condition.

Esophageal rupture. One case study reported Boerhaave's syndrome (transmural perforation of the oesophagus) the day after receiving a PA SMT for low back pain in a 47-year old female [37]. The patient required thoracostomy and repair of the esophageal perforation. Despite the high risk associated with this condition, the patient fully recovered.

Partial pancreatic transection. One case of a 55-year old male was reported following SMT for chronic low back pain. The patient underwent a distal pancreatectomy and made a full recovery. His history included surgery for an abdominal gunshot with splenectomy and appendectomy, hypertension and gout [40]. The patient made a full recovery with the authors suggesting a causal link made between the SMT and thoracic AE given the immediacy of occurrence (See Table 5).

Table 5. **Internal organ AEs, medical management and outcome**

Author and year	Adverse event	Interval to thoracicAE onset	Secondary care management	Clinical outcome
Masneri et al 2007 [35]	Pneumothorax	Over the course of the day	Chest tube thoracostomy	Discharged after 3 days in good condition

Sozio and Cave 2008 [37]	Esophageal rupture	Following day after manipulation	Repair of the esophageal perforation with mediastinal drainage	Successful and uneventful recovery
Hudkins, 2012 [40]	Partial pancreatic transection	Immediate	Distal pancreatectomy	Following complications reported day 33, resolved.
Gardner et al 2013 [41]	Hemothorax and oblique fracture from T9 to T11	Over the course of the day	Open reduction and internal fixation of the thoracic spine	Discharged after 12 days and returned to normal activities, neurologically intact
Streuwer et al 2013 [13]	Hemothorax	Over the course of two days	Chest tube thoracostomy and thoracoscopic haemostasis	Discharged after 7 days in good condition

Fracture AE

Compression fractures. Compression fractures were reported in two single case studies involving males 57 and 66 years of age [29, 44]. In both cases, the symptom onset occurred within 24 hours. In one case the back pain intensified [44] while in the other case, the patient experienced spinal instability [29]. Both patients were neurologically intact with no symptoms or signs of spinal cord compression. The patients received care for multiple myeloma and the outcome was not reported in either case.

Oblique spinal fracture. In one case, SMT resulted in a complex spinal fracture. [41] The patient, a 57-year-old male with ankylosing spondylitis received manipulation under anesthetic. He experienced an oblique coronal and transversely oriented fracture and hemothorax (reported earlier) [41]. After the manipulation, the patient reported increased pain, light-headedness and shortness of breath. The patient subsequently underwent chest tube thoracostomy and thoracic spinal fusion. The patient was later discharged neurologically intact and able to return to his normal activities [41] (see Table 6).

Table 6. **Fracture AE, medical management and outcome**

Author and year	Adverse event	Interval to thoracic AE onset	Secondary care management	Clinical outcome
Austin 1985 [29]	T9 compression fracture	After manipulation	Multiple myeloma care	Not reported
Gardner et al 2013 [41]	Hemothorax and oblique fracture from T9 to T11	Over the course of the day	Open reduction and internal fixation of the thoracic spine	Discharged after 12 days and returned to normal activities, neurologically intact
Skappak and Saude 2018 [44]	Compression fractures T11, L1, L2 and L3	Within 24 hours	Multiple myeloma care	Not reported

Other thoracic AE

In one case a ruptured aortic aneurysm occurred in a 45-year old male following 'spinal adjustment' for a complaint of chronic low back pain [42]. No significant medical history of cardiovascular disease was noted and the patient died within minutes.

DISCUSSION

This systematic review synthesizes evidence of instances of thoracic AE in the period following SMT. To the authors knowledge, this is the most comprehensive review to date, including 21 cases published in 19 studies (case studies and case series). Although the evidence was derived from case studies and case series, there are reports of thoracic AE following SMT. Analysis of findings are outlined below with recommendations to inform future safe practice in SMT involving the thoracic region.

Severity and nature of TAE

While the precise detail of the thrust techniques involved was not always clear, we have included instances where thoracic AE was reported following SMT. Findings reflect those of

lumbar spine SMT, with the most commonly reported AEs involving spinal cord or cauda equina injury and less often fractures, internal organ injuries or soft tissue trauma [45]. The most frequently reported thoracic AE across cases involved the spinal cord (n=13). Based on our findings, reported thoracic AE are severe as opposed to moderate. This is likely a reflection of interest or priority rather than prevalence (moderate AE not a priority for publication). All reported cases required some form of medical management, including costly surgical interventions. Cases involving internal organ injuries or fractures had a faster recovery compared to those with spinal cord injuries. Although in four cases the reported outcome was the patient died, only one death occurred immediately following SMT with a ruptured aortic aneurysm [42].

Patient and therapist characteristics

Case reports and case series included twelve males and nine females patients across a wide age range (17 to 71 years). A clear patient profile was not evident given the lack of included detail in the studies. Gender and age were the only characteristics reported in all studies, with demographics comparable to those reported for individuals experiencing AEs following cervical spinal manipulation [46, 47]. The authors have identified cases of thoracic AE in the presence of undiagnosed pathologies (e.g. myeloma [28, 29]) and two cases where the SMT was performed in the presence of documented contraindications [48], specifically a history of cancer [32] and a diagnosis of ankylosing spondylitis [41]. These findings support the importance of clinical reasoning, including evidence informed pre-thrust examination. For a number of cases, detail regarding patient presentation was omitted or insufficient to examine possible contraindications or precautions to performing SMT (e.g. establishing bone health) through a detailed assessment of family history, diet, menstrual status for females, *etc.*

The majority of practitioners were chiropractors, which likely reflect differences in professional practice and relative use of SMT. Level of practitioner experience or advanced training was not reported, which could have usefully provided further insights with respect to the value of specialist training to inform future practice. It is of note that recent published trials of SMT have not reported any instances of thoracic AE. This perhaps reflects involvement of experienced practitioners or specialist training for those involved in trials, as well as ethical oversight and stringent inclusion/exclusion criteria. In routine practice where no clinical screening tools exist, practitioners are required to draw on advanced levels of clinical reasoning, including knowledge of contraindications and precautions to inform their decision to use SMT; as is available for the cervical spine with the internationally informed framework [20].

Causality and SMT forces

Notwithstanding the single instance of death immediately following SMT, the case for determining causality of thoracic AE following SMT is not possible from this review. Studies were published primarily by emergency care physicians or neurosurgeons, with interest in the management of thoracic AE and where details pertaining to pre-SMT clinical examination were not reported. It may seem instinctive to attribute thoracic AE directly to the force of SMT technique although preliminary evidence investigating the gross chest deformation as a reaction of 'typical and standard' SMT suggest that is unlikely for a thrust technique to cause injury or thoracic AE [49]. Many of the included cases involved the spine (rather than ribs) resulting in vascular or non-vascular injury. This could be attributable to a sub-clinical complaint/condition (e.g. osteopenia), or where practitioner peak force exceeded the tolerance of tissues in that specific patient, something which remains unclear. It does however highlight the importance of precision for personalized patient management.

Future directions

Although relatively few cases are reported in the literature, with best practice guidelines supporting the use of thoracic SMT [1, 2] further work is needed to support safe practice. Development of reporting guidelines of single case studies and case series would help ensure inclusion of more precise information in these instances (e.g. age, gender, complaint, pre-thrust examination, technique, and interval to onset of thoracic AE). Future research should make efforts to evaluate any association between the parameters of the SMT and thoracic AE reported with regard to protopathic bias. Furthermore, efforts to promote and engage with reporting systems to allow clinicians to report thoracic AE following SMT without fear of reprisal should be supported. Systematic reporting of thoracic AE may enable allow more accurate estimates of incidence, prevalence and relative risk of thoracic AE.

Strengths and limitations

A strength of this review is use of a registered protocol, comprehensive search strategy synthesizing evidence from case studies and series, and reporting in line with published guidelines. Although a methodologically rigorous review, the lack of reporting guidelines for single case studies and case series has contributed to the poor reporting of included studies. Moreover, the included evidence was low level and included one study involving a 'lay person'. This extensive review, including cases of thoracic AE with all forms of SMT can be used to inform the development of a clinical practice framework, recognizing that Puentedura [10] focused of AE following thoracic SMT. It is important to emphasize that estimates of incidence, prevalence and relative risk of thoracic AE are not possible from this, nor causality established. A further limitation of this review was a lack of response from authors who were contacted for further information.

CONCLUSION

Although relatively few cases of thoracic AE are reported in the literature, best practice guidelines supporting the use of SMT are needed to ensure safe practice. Gaps in the current literature include detailed patient data for those who experience thoracic AE, and a framework to guide clinical reasoning for pre-thrust examination.

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