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Serious Adverse Events and Spinal Manipulative Therapy of the Low Back Region: A Systematic Review of Cases

Jeffrey J. Hebert, DC, PhD
Senior Lecturer; School of Psychology and Exercise Science, Murdoch University, Perth, Western Australia, Australia

Norman Stomski, PhD
Postdoctoral Researcher; School of Health Professions, Murdoch University, Perth, Western Australia, Australia

Simon French, PhD, MPH, BAppSc
NHMRC Research Fellow / Adjunct Senior Lecturer; Primary Care Research Unit, University of Melbourne / Faculty of Heath Sciences, Murdoch University

Sidney M. Rubinstein, PhD
Senior Researcher; Department of Epidemiology and Biostatistics; EMGO+ Institute for Health and Care Research VU University Medical Center

ABSTRACT

Objective: To systematically search the literature for studies reporting serious adverse events following lumbopelvic spinal manipulative therapy (SMT) and to describe the case details.

Methods: A systematic search was conducted in PubMed including MEDLINE, EMBASE, CINAHL and The Cochrane Library up to January 12, 2012 by an experienced reference librarian. Study selection was performed by 2 independent reviewers using predefined criteria. We included cases involving individuals 18 years or older who experienced a serious adverse event following SMT applied to the lumbar spine or pelvis. A serious adverse event was defined as an untoward occurrence that results in death or is life threatening, requires hospital admission, or results in significant or permanent disability. We included studies published in English, German, Dutch and Swedish.

Results: 2046 studies were screened and 41 studies reporting on 77 cases were included. Important case details were frequently unreported. Adverse events consisted of cauda equina syndrome (29 cases, 38% of total), lumbar disc herniation (23 cases, 30%), fracture (7 cases, 9%), hematoma or hemorrhagic cyst (6 cases, 8%), or other serious adverse events (12 cases, 16%) such as neurological or vascular compromise, soft tissue trauma, muscle abscess formation, disrupted fracture healing and esophageal rupture.

Conclusions: This systematic review describes the case details of serious adverse events reported to occur following SMT of the lumbopelvic region. The anecdotal nature of these reports does not allow for causal inferences between SMT and the events identified in this review. Recommendations regarding future case reporting and research aimed at furthering the understanding of SMT's safety profile are discussed.

Key Words: risk, spinal manipulation, lumbosacral region, intervertebral disc displacement, cauda equina syndrome, injury

INTRODUCTION

Spinal manipulative therapy (SMT) is a form of manual therapy commonly used to provide care for people with low back pain and other disorders of the lumbar spine and pelvis.[1] The frequency of SMT use by healthcare providers has increased over the past several decades.[2] SMT is generally recommended by treatment guidelines[3-5] and appears to be a cost-effective therapeutic option for patients with spinal pain.[6]

Previous prospective analyses of harm following lumbopelvic SMT have primarily reported benign and self-limiting events, such as muscle soreness and local discomfort but have not observed and hence reported the occurrence of serious adverse events. Senstad and colleagues[7] investigated the outcomes of a large cohort of chiropractic patients (n=1058) and reported that when SMT was included in the course of care, an adverse reaction was associated with 25% of SMT treatments and 55% of patients reported at least one adverse event. Reactions primarily consisted of short-term local discomfort, headache, and tiredness or radiating discomfort and were classified as mild to moderate in most patients. There were no reports of serious adverse events. In another analysis, Leboeuf-Yde et al.[8] surveyed 66 chiropractors who reported on 625 patients who received 1,858 chiropractic treatments, of which 99% included spinal manipulation. Adverse events were found to be common, benign and usually self limiting within 24 hours. Additionally, the authors reported that adverse reactions with chiropractic treatment were associated with female gender, treatment at first consultation and longer pain duration. Neither study, however, reported a serious adverse event associated with SMT.

Recent systematic reviews of randomized controlled trials, cohort studies and a patient survey have failed to identify a single serious adverse event following lumbopelvic SMT.[9-13] However, the reporting of harms in the primary literature is generally poor[14] and case reports of serious

adverse events following lumbopelvic SMT have been described. Examples of serious adverse events following lumbopelvic SMT include cauda equina syndrome,[15] lumbar disc herniation,[16] fracture[17] and spinal haematoma.[18] Gouveia and colleagues[19] undertook a systematic review of adverse events following chiropractic treatment that included all articles reporting on adverse events associated with chiropractic treatment. While the authors identified several reports of serious adverse events following lumbopelvic SMT, they implemented a limited search strategy and excluded adverse events following therapy performed by other types of healthcare providers.

Although the incidence of serious adverse events following lumbopelvic SMT is thought to be extremely low,[20] such events represent a potentially important source of morbidity. Improved knowledge of SMT risk with respect to serious adverse events has potential to inform clinical decision-making and understanding the circumstances surrounding such events would serve as a first step in this process. Therefore, the purpose of this study was to systematically search the literature for cases reporting serious adverse events following lumbopelvic SMT and to describe the case details.

METHODS

Types of studies and participants

Case reports, case series and studies utilizing other designs to report original, individual case details were included. Identified cases involved individuals 18 years or older who experienced a serious adverse event following SMT applied to the lumbar spine or pelvis. We included studies published in English, German, Dutch and Swedish.

Types of interventions

The intervention of interest was SMT applied to the lumbar spine or pelvis. The terminology reported in the literature to describe SMT and other manual therapy procedures has been described as problematic,[21] with some calling for a clear distinction between spinal mobilization and spinal manipulation.[22,23] Consequently, we considered SMT to include both spinal manipulation and spinal mobilization, although we attempted to distinguish between these two approaches when extracting data. We operationally defined spinal manipulation as a therapeutic procedure involving the use of a high-velocity low-amplitude thrust, while spinal mobilization was defined as a non-thrust therapeutic procedure involving low-velocity passive joint movements. Cases involving SMT applied while the patient was under anaesthesia were excluded.

Types of outcome measures

The outcomes of interest in this systematic review were serious adverse events. No widely adopted definition of serious adverse event exists in the rehabilitation literature. We defined a serious adverse event as an untoward occurrence that results in death or is life threatening, requires hospital admission, or results in significant or permanent disability.[24] Examples of serious adverse events resulting from lumbopelvic SMT could include disc herniation, cauda equina syndrome, fracture, dislocation, or hematoma/hemorrhagic cyst.

Search methods for identification of studies

A comprehensive search was conducted by an experienced reference librarian in the following databases from inception to January 12, 2012: PubMed including MEDLINE, EMBASE, CINAHL(via EBSCO), and The Cochrane Library(via Wiley). Search terms included MeSH

terms in PubMed, EMtree terms in EMBASE, and CINAHL Headings in CINAHL as well as free text terms. We used free text terms only in The Cochrane Library. The search syntax developed for PubMed is presented in Table 1. No time or language restrictions were applied. The reference lists of included studies were also examined.

Selection of studies

Two review authors independently examined the title and abstract of studies identified by the search strategy and excluded those studies not meeting the selection criteria. Next, the full text of reports thought to fulfil the selection criteria were retrieved and assessed. Disagreements between the review authors regarding study inclusion were resolved by consensus, and if necessary a third review author was consulted. All review authors were experienced in conducting systematic reviews.

Data extraction

We extracted the following information, when available: clinician-related (discipline, country of origin, years in practice), participant-related (age, gender) as well as clinical case details (indication for manual therapy, manual therapy technique, adverse event description including time from SMT to the adverse event, contributing factors and clinical outcome). When the country of origin was not identified, we reported the primary author's country as identified by their affiliation. Given that there are no widely accepted criteria for judging the quality of adverse event reporting and the current studies' objective of describing case details, we did not assess the risk of bias in the included studies.

RESULTS

Selection of Studies for Inclusion

Figure 1 describes the study selection process.[25] The literature search generated a total of 2512 references: 1083 in PubMed, 1224 in EMBASE.com, 70 in CINAHL and 135 in The Cochrane Library. An additional 29 references were identified by searching the references of selected papers. After removing duplicate references, 2046 records remained. Following the title and abstract screen, 117 articles were obtained for full-text review and 41 studies[15-18,26-62] involving 77 cases were included.

Description of Cases

Table 2 describes the case details for all included studies. Reporting was frequently incomplete as evidenced by the suboptimal case details of the included studies. This was most notable with reporting related to the descriptions of SMT technique, the pre-SMT presentation of the patient, the specific details of the adverse event, time from SMT to the adverse event, factors contributing to the adverse event and clinical outcome.

The most commonly reported adverse events were signs and symptoms consistent with cauda equina syndrome (29 cases, 38% of total) and lumbar disc herniation (23 cases, 30% of total). Additional adverse events consisted of fracture (7 cases, 9%), hematoma or hemorrhagic cyst (6 cases, 8%), or other serious adverse events (12 cases, 16%) including neurological or vascular compromise, soft tissue trauma, muscle abscess formation, disrupted fracture healing and esophageal rupture.

Most cases were reported from Europe (35, 46%) and North America (32, 42%), with few cases from Australia (7, 9%) and Asia (3, 4%). Of the reported patient demographic data, the mean(standard deviation) patient age was 50.1(15.9) years and 41% were female. Of the 61

cases with available data on the patient's pre-SMT presentation, 58 (95%) appeared to have signs or symptoms originating from the lumbopelvic region (e.g., low back pain, sciatica), while the indication for lumbopelvic SMT in the remainder of cases was for pain in other regions (e.g., neck pain, mid back pain) or other complaints (e.g., dyspnea) .

Of the 50 cases reporting clinician type, 40 (80%) identified the SMT provider as a chiropractor, 3(6%) an osteopath, 2(4%) a doctor or physician and 5(10%) another type of healthcare provider or non-professional. Approximately half (49%) of the cases reported information regarding the time to onset of the adverse event following SMT; 29 (76%) of these cases occurred within 24 hours of SMT. Sixty-three cases (82% of total) reported information describing treatment for the adverse event, of which 53 (84%) involved some type of surgical intervention. Fifty-three cases (69% of total) reported some information related to the patient's clinical outcome and of those, 34 (64%) reported favorable clinical outcomes (i.e., no major functional impairment) following treatment. No information was available on years of experience of the healthcare practitioner

DISCUSSION

We conducted a comprehensive systematic review of cases describing serious adverse events following lumbopelvic SMT. Of the 77 cases involving a serious adverse event following lumbopelvic SMT, cauda equina syndrome and lumbar disc herniation accounted for the majority. Important details of most cases were frequently missing or poorly reported. These results have clinical and research related implications.

Clinical Relevance

Given the mechanical nature of SMT, it is intuitive to think that disc herniation and cauda equina syndrome could result from this therapy. This presumption is supported by some cases we

identified in which there appears to be a strong temporal relationship between SMT and the onset of signs and symptoms of these conditions. Based on these cases alone, one clinical recommendation could be to avoid the use of SMT when there is potential for disc herniation or cauda equina syndrome. However, it is unreasonable to make such a recommendation based solely on knowledge derived from anecdotal cases. An accurate judgement regarding the value of any therapy requires knowledge of additional domains such as: 1) clinical effectiveness, 2) cost effectiveness, and 3) details of the therapies' risk profile including estimates of adverse event incidence and the magnitude of risk relative to other treatment options.

Recent evidence supports the clinical and cost effectiveness of lumbopelvic SMT when applied to patients with non-specific low back pain.[3,4,6] However, the existence of a subgroup of patients for whom SMT is most appropriate may be important when considering the therapy's risk profile. Preliminary evidence suggests that SMT's clinical effect may in part be moderated by changes in back muscle function[63,64] and recent research suggests that those patients who are most likely to experience improved muscle function[65] or clinical outcome[66,67] following SMTcan be identified by information from the history and physical examination. Implementing this evidence to inform clinical decision-making and directing SMT to those patients most likely to experience benefit, has potential to reduce the probability of exposure and harm.

In addition to low back pain, current evidence suggests that SMT is likely to benefit patients with known lumbar disc herniation,[68,69] with randomized trials reporting SMT to be superior to sham[70] and equivalent to microdiscectomy.[71] Conversely, it seems improbable that patients experiencing cauda equina syndrome would benefit from SMT. Cauda equina syndrome is a rare sequela of lumbar disc herniation, with only 0.12% of herniations resulting in this disorder.[72] Nevertheless, cauda equina syndrome is a serious condition that requires urgent surgical

intervention.[73] Therefore, clinicians should be diligent in screening patients for and maintain a high index of suspicion for cauda equina syndrome when patients present with one or more of the following signs or symptoms : (1) bladder and/or bowel dysfunction (2) reduced sensation in the saddle area or (3) sexual dysfunction with possible neurologic deficits of the lower limb.[74]

With respect to serious adverse events, a detailed understanding of SMT's risk profile will be difficult to achieve. Previous attempts to prospectively estimating the incidence of these events have been unsuccessful as no serious events were identified and therefore this rate is assumed to be extremely low.[7,8,75,76] Furthermore, incidence estimates derived from case studies are unlikely to be valid representations of the true rate of serious adverse events following SMT and should be interpreted with caution.

However, additional knowledge of SMT's risk profile is gained from analyses of comparative safety between SMT and other treatment options. Carnes *et al*.[9] undertook a meta-analysis of randomized controlled trials which, in part, examined the relative risk (RR) of mild to moderate adverse events (no major adverse events were identified) when manual therapy was compared to other therapeutic options. Their results demonstrated a similar risk of adverse events occurring from manual therapy as compared to exercise (RR[95% CI] = 1.04[0.83,1.31]) and a lower level of risk with manual therapy (high-velocity manipulation) when compared to drug therapy (RR[95% CI] = 0.05[0.0,0.20]). Similarly, Oliphant[77] estimated lumbar manipulation to be safer than non-steroidal anti-inflammatory drugs among patients with lumbar disc herniation.

Recommendations for future research and reporting

Additional research is needed to enhance our knowledge of serious adverse events reported to follow lumbopelvic SMT. While anecdotal evidence is of limited value, additional case

reporting may be beneficial given our limited knowledge of these rare adverse events. However, future case reporting should strive to ensure that a detailed and accurate account of the case is presented. In this literature, one known reporting issue relates to the inaccurate representation of provider type and treatment. Specifically, the terms "chiropractor", "chiropractic" and "chiropractic manipulation" are problematic with respect to their misuse in the biomedical literature, where any healthcare worker who provides SMT is labelled as a chiropractor regardless of their clinical training.[78-80] Additional instances of suboptimal case reporting identified in this review include the details of the patient's presentation prior to SMT, SMT technique, time to the adverse event, contributing factors and long-term clinical outcome.

One possible explanation for the lack of detailed reporting is that many cases appear to be authored by clinicians, such as spine surgeons, who are responsible for the care of patients following occurrence of the serious adverse event. In these instances, the clinicians may have little knowledge of or interest in the details of the manual therapy or the patient presentation prior to SMT. Therefore, seeking additional information directly from the SMT provider has potential to improve the quality of case reporting and further our understanding in this area.

For instance, little is known about the safety profile of different SMT techniques. While SMT is often considered to be a singular approach, it is a collection of poorly described methods that may differ with respect to their safety profile.[22] A review of the manual therapy techniques reported in Table 2 reveals that generic terminology such as "back manipulation" frequently represents the extent of reporting. Furthermore, some technique descriptions were unusual and inconsistent with what is taught in modern education programs teaching manual therapy. For example, Livingston[45] includes the following patient description of a manual therapy treatment received 2 years prior: "He stated that he lay on a table and the chiropractor stood on a high

stool and jumped onto his back with both knees". While it is possible such unusual descriptions accurately describe the treatment provided, they raise the question of mistaken reporting. Accurate and comprehensive reporting of SMT technique details, obtained directly from the SMT provider, would likely enhance reporting and may serve as a first step toward understanding the comparative safety of these methods.

Parties interested in additional recommendations for publishing adverse event reports should refer to the guidelines endorsed by the International Society for Pharmacoepidemiology and the International Society of Pharmacovigilance.[81] While these guidelines were developed for the purpose of enhancing case reports describing suspected adverse effects of drugs and medical products, many of the recommendations are relevant to reporting of adverse events following SMT.

Although case reports make a modest contribution to scientific knowledge, they represent a level of scientific evidence that is inappropriate for making causal inferences. Ultimately, our understanding of lumbopelvic SMT risk will be enhanced through high-quality clinical research. Future research efforts should aim to further explore the potential association between lumbopelvic SMT and the types of adverse events reported here as well as identify accurate estimates of incidence using methodology ensuring low risk of bias and confounding. Ideally, this would involve prospective investigations of large population-based patient cohorts. Previous[7,8,82-84] and current[85] research efforts have undertaken a prospective approach to examine the adverse events associated with SMT. However, as previously discussed, prospective studies have failed to identify a serious adverse event following lumbopelvic SMT. Accordingly, prospective study designs may not be feasible in this context.

Retrospective study designs such as cohort, case-control, and "case only" approaches[86] including case-crossover and self controlled case series designs offer a more efficient method of assessing the risk of rare events. However, an inherent source of bias in retrospective study designs is their inability to identify the temporal sequence of exposure to a potential risk factor (e.g., SMT) and the outcome of interest (e.g., serious adverse event). Therefore, with retrospective study designs, it is not possible to know whether a person is free from the outcome of interest at the time of exposure. Incorrect temporal judgements can result in confounding due to protopathic bias.[87] This form of bias occurs when a treatment for the first symptoms of a disease or injury appear to cause the outcome and is a potential source of confounding in any retrospective study, including the cases identified in this review. For example, Fisher[31] reported on a 32 year old female who "was given an adjustment to her lower spine". Prior to SMT exposure, the patient had suffered from severe, bilateral radicular leg pain and progressive left leg weakness. Following the SMT, the patient went on to develop saddle anesthesia and bowel and bladder incontinence leading to a diagnosis of cauda equina syndrome. Due to the retrospective nature of this report, it is unknown whether the patient was already experiencing the early signs of cauda equina syndrome (e.g., bilateral lower extremity pain and progressive motor deficit) prior to SMT exposure.

Researchers seeking to understand the potential relationship between neck manipulation, vertebrobasilar artery dissection, and stroke have encountered a similar challenge. Early case control studies identified a relationship between vertebrobasilar artery stroke and previous exposure to neck manipulation.[88,89] Subsequently, Cassidy *et al.*[90] conducted a case-control and case-crossover study investigating the potential relationship between vertebrobasilar artery stroke and visits to both chiropractors and primary care physicians. Their results replicated the previous studies in that an association between vertebrobasilar artery stroke and visits to a

chiropractor was identified. However, Cassidy *et al*. also identified an association between vertebrobasilar artery stroke and visits to primary care physicians. Since common symptoms of vertebrobasilar artery dissection include neck pain and headache,[91] the authors concluded that the increased risk of vertebrobasilar artery stroke associated with visiting a chiropractor or primary care physician is likely due to patients with dissection related headache and neck pain seeking care prior to the onset of stroke. Therefore, cases of vertebrobasilar artery stroke following neck manipulation may be inappropriately attributed to exposure to neck manipulation when the symptoms of dissection (e.g., headache, neck pain) were present prior to treatment (i.e., these associations may result from protopathic bias). A similar research approach investigating lumbopelvic SMT may help elucidate whether this therapy should be included in the causal pathway of the types of adverse events identified in this review.

Finally, the development of surveillance tools allowing the widespread and systematic reporting of adverse events following SMT may provide a valuable contribution to knowledge in this area. Early attempts at developing such approaches have been undertaken[92] and these efforts should be encouraged. Accurate estimates of incidence and the exploration of possible risk factors or predictors of serious adverse events are likely to enhance clinical decision making for healthcare providers and help patients to make informed healthcare decisions.

Study strengths and limitations

This study has several strengths and limitations. The search process included a comprehensive examination of 4 databases by an experienced reference librarian and the selection of studies was undertaken by 2 independent reviewers using predefined criteria.

Among studies included in this review, the quality of reporting was generally lacking with potentially important case details frequently not described. Additionally, due to the inherent nature of case reports and other anecdotal reporting, it is not possible to make inferences regarding cause and effect. Therefore, it is not known whether the serious adverse events identified in this review were caused by lumbopelvic SMT or whether the association between therapy and event was incidental (i.e., the result of natural history, protopathic bias or other source of confounding).

CONCLUSION

We identified 77 cases involving a serious adverse event following lumbopelvic SMT. Important information such as SMT description, pre-SMT presentation of the patient and adverse event details were lacking. Cauda equina syndrome and lumbar disc herniation accounted for the majority of adverse events. In addition, we identified cases of spinal fracture, haematoma, haemorrhagic cyst and other serous adverse events. Two thirds of cases had a favorable clinical outcome. Additional high-quality research is needed to better estimate the incidence of adverse events associated with lumbopelvic SMT and to elucidate the relationship between this therapy and the types of adverse events reported in this systematic review.

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Table 1. Search syntax for PubMed

Search syntax	Items found
1. Search terms related to spinal manipulative therapy: "Musculoskeletal Manipulations"[Mesh:NoExp] OR "Manipulation, Spinal"[Mesh] OR "Manipulation, Chiropractic"[Mesh] OR "Manipulation, Osteopathic"[Mesh] OR "Spinal Manipulation"[tiab] OR "Spinal Manipulative"[tiab] OR "lumbar Manipulation"[tiab] OR "chiropractic"[tiab] OR ("manual therapy"[tiab] AND (back[tiab] OR lumbar[tiab] OR spine[tiab] OR spinal[tiab]))	5740
2. Search terms related to Serious adverse events: "adverse effects"[Subheading] OR "complications"[Subheading] OR "adverse effects"[tiab] OR "adverse effect"[tiab] OR "adverse events"[tiab] OR "adverse event"[tiab] OR "adverse reactions"[tiab] OR "adverse reaction"[tiab] OR "side effects"[tiab] OR "undesirable effects"[tiab] OR "injurious effects"[tiab] OR "side effect"[tiab] OR "undesirable effect"[tiab] OR "injurious effect"[tiab] OR complication*[tiab] OR "Intervertebral Disk Displacement"[Mesh] OR "Intervertebral Disk"[tiab] OR "Intervertebral Disc"[tiab] OR "Herniated Disc"[tiab] OR "Herniated Disk"[tiab] OR "prolapsed Disc"[tiab] OR "prolapsed Disk"[tiab] OR "disk prolapse"[tiab] OR "disc prolapse"[tiab] OR "Spinal Fractures"[Mesh] OR fracture*[tiab] OR Radiculopath*[tiab] OR Polyradiculopathy[mesh] OR radiculit*[tiab] OR monoradiculopath*[tiab] OR polyradiculopath*[tiab] OR "cauda equina syndrome"[tiab]	3428604
3. 1 AND 2	1260
4. 1 AND 2 NOT: ("addresses"[Publication Type] OR "biography"[Publication Type] OR "comment"[Publication Type] OR "directory"[Publication Type] OR "editorial"[Publication Type] OR "festschrift"[Publication Type] OR "interview"[Publication Type] OR "lectures"[Publication Type] OR "legal cases"[Publication Type] OR "legislation"[Publication Type] OR "news"[Publication Type] OR "newspaper article"[Publication Type] OR "patient education handout"[Publication Type] OR "popular works"[Publication Type] OR "congresses"[Publication Type] OR "consensus development conference"[Publication Type] OR "consensus development conference, nih"[Publication Type]) NOT (animals[mh] NOT humans[mh])	1083

Table 2. Case descriptions

Cite	Country	Age (y), Sex, SMT Indication	Details of Manual Therapy	Clinician Type	Adverse Event (nature and location)	Possible Contributing Factors	Time From SMT To Adverse Event	Outcome
CES or signs/symptoms suggestive of CES (n = 29)								
Dan[27]	Australia	49, M, LE pain/ numbness, urinary urgency, impotence	Lumbar manipulation	?	Loss of bladder sensation, L5/S1 disc herniation	CES signs prior to SMT	?	L5-S1 laminectomy improved clinical status with persistent limb numbness.
Dan[27]	Australia	72, M, sciatica.	"Forceful back manipulation"	?	Worsened sciatica and urinary frequency.	Organized thrombus at site of old L5 fracture	Immediate	L5 laminectomy.
Fischer[29]	USA	32, FM, LBP, bilateral LE pain and weakness	Lower spine adjustment	Chiropractor	Saddle numbness, urinary retention, bowel incontinence	L5 congenital deformity	Following day	L5-S1 surgery with excellent clinical outcome with almost complete return to normal
Gallinaro[30]	Italy	24, FM, LBP	Manipulation	?	CES, L5/S1 disc sequestration.	-	Immediate onset, with progression over 2 days	Surgery with improved pain but continued bowel/bladder symptoms.
Haldeman[31]	USA	31, M, LBP	"Activator" and side-lying pelvic manipulation.	Chiropractor	CES	Achondroplasia with thoracolumbar central stenosis	Immediate onset with progression over 3 days.	L1-S1 laminectomy with persistent bowel/bladder symptoms and LE weakness.
Haldeman[31]	USA	62, M, LBP and radicular leg pain	Prone and side-lying lumbopelvic manip-ulation and traction.	Chiropractor	CES, L4-L5 disc herniation.	-	?	L4-L5 laminectomy with persistent deficits and catheterization requirement.
Haldeman[31]	USA	36, FM, LBP and radicular leg pain.	Cervical and lumbar spine manipulation.	Chiropractor	CES, L4-L5 disc herniation.	Increasing radicular pain associated with persistent cough.	1 day	Surgical decompression and hemilaminotomy with persistent deficits and catheterization requirement.
Hensell[34]	Germany	39, M, lumbar radiculopathy	?	Chiropractor?	CES	Presented initially with sciatica	Immediate	Surgical decompression; several years later continued paralysis of the bladder.
Hipp[35]	Germany	35, FM, LBP with recent exacerbation	"chiropractic treatment"	?	CES	Ependymoma	?	Decompression
Hooper [36]	Australia	55, M, LBP	Back manipulation	Chiropractor	Lumbar disc extrusion with LE motor deficit, loss of anal tone, genital numbness and bladder dysfunction	Patient regarded as "mentally disturbed"	?	Lumbar laminectomy, with persistent LE weakness
Jackson[38]	UK	?, M, ?	Back manipulation for disc lesion	?	CES, large L4-L5 central disc protrusion	?	?	Recovery of bladder function
Jackson[38]	UK	?, M, ?	Back manipulation for disc lesion	?	CES, large L4-L5 central disc protrusion	?	?	Recovery of bladder function
Jennett[39]	UK	?, ?, sciatica	Back manipulation	?	Cauda equine paralysis	?	Immediate	?
Lehman[41]	UK	50, M, LBP	Spinal manipulation	Chiropractor	CES, L3-L4 disc sequestration	-	8 hours	Laminectomy, with persistent left ankle weakness
Lehman[41]	UK	36, M, LBP	Manipulation with lumbar spine hyperextension	Chiropractor	CES, L4-L5 disc herniation	-	Within 3 hours	Laminectomy with persistent bladder incontinence requiring catheterization, S2-S4 sensory impairment.
Malmivaara [44]	Finland	42, M, right buttock tightness	Chiropraxis; thrusting the right thigh into extension/abduction.	?	CES	-	Immediately	Patient recovered without treatment. No CES signs after 2 months. LBP persisted for 1 year.
Markowitz [45]	USA	38, M, recurrent L5-S1 disc herniation	Chiropractic manipulative type treatment	Chiropractor	CES , L5-S1 disc sequestration	Previous L5-S1 discectomy with recurrent disc herniation prior to SMT	24 hours	S1 discectomy/laminectomy with residual ankle weakness and bowel/bladder dysfunction
Oppenheim	USA	39, M, LBP	Spinal manipulation	Chiropractor	CES, L5-S1 disc herniation	-	Immediate	Discectomy with excellent outcome.

Cite	Country	Age (y), Sex, SMT Indication	Details of Manual Therapy	Clinician Type	Adverse Event (nature and location)	Possible Contributing Factors	Time From SMT To Adverse Event	Outcome
15								
Oppenheim[15]	USA	32, M, LBP and leg pain	Spinal manipulation	Chiropractor	CES, L4-L5 disc herniation		?	Discectomy with excellent outcome.
Poppen[48]	USA	?, ?, ?	Manipulation	Osteopath	Complete paraplegia associated with intervertebral disc herniation	?	Immediate	?
Poppen[48]	USA	?, ?, ?	Manipulation	Osteopath	Complete paraplegia associated with disc herniation	?	Immediate	?
Powell[49]	USA	42, M, sciatica	Spinal manipulation therapy	?	Severe bilateral leg pain, urinary hesitancy	Chemo-nucleolysis and lumbar disc herniations prior to SMT	?	L4-L5, L5-S1 discectomy with excellent outcome.
Richard[50]	USA	41, FM, back pain, leg pain, paresthesias	Pressure applied over the sacrum	Chiropractor	CES, L4-L5 disc herniation	-	Immediate	L4-L5 laminectomy, L5-S1 foraminotomy. Continued bladder dysfunction and LE numbness.
Rydell[52]	Sweden	32, M, LBP and sciatica	Flexion mobilization of thoracolumbar spine	Napropath	Lumbar disc herniation and bowel/bladder dysfunction	Congenital spinal stenosis	Within hours	Lumbar discectomy with continued leg pain, numbness, weakness and mild bladder dysfunction.
Rydell[52]	Sweden	70, FM, LBP	Manipulative treatment of L4-L5	Chiropractor	Paraplegia, bladder incontinence	-	Immediate weakness, paraplegia after one week	Rehabilitation with improvement, persistent bladder dysfunction
Shephard [53]	UK	?, ?, ?	Manipulation	?	CES	?	?	?
Slater[55]	UK	28, FM, LBP	"vigorous" manipulation	Chiropractor	L4-L5 disc sequestration, altered bladder sensation	-	"Within hours"	L4-L5 discectomy with excellent outcome but persistent LBP
Solheim[56]	Norway	77, M, LBP	Lumbar manipulation therapy	Chiropractor	Partial CES due to spinal epidural hematoma in the L3–L4 region.	anticoagulation therapy, previous L3 compression fracture	Immediate with progression over 3 or 4 days	Surgical evacuation of hematoma via L3 and L4 laminectomies. Improvement with residual bladder dysfunction and sensory abnormalities.
Tamburrelli[14]	Italy	42, M, back pain and S1 radiculopathy	Spinal manipulation	Chiropractor	CES, L5-S1 extrusion.	Previously diagnosed L5-S1 disc herniation	Within 12 hours	L5 laminotomy, L5-S1 discectomy. Improved, but with persistent bowel dysfunction, impotence, LE pain, paresthesias and mild sensory deficit.
Lumbar Disc Herniation (n = 23)								
Dvorak[28]	Switzer-land	?, ?, ?	Lumbar spine HVLA manipulation	?	Disc herniation with progressive radicular syndrome	-	?	Surgery with complete recovery
Dvorak[28]	Switzer-land	?, ?, ?	Lumbar spine HVLA manipulation	?	Disc herniation with progressive radicular syndrome	-	?	Surgery with complete recovery
Dvorak[28]	Switzer-land	?, ?, ?	Lumbar spine HVLA manipulation	?	Disc herniation with progressive radicular syndrome	-	?	Surgery with complete recovery
Dvorak[28]	Switzer-land	?, ?, ?	Lumbar spine HVLA manipulation	?	Disc herniation with progressive radicular syndrome	-	?	Surgery with complete recovery
Dvorak[28]	Switzer-land	?, ?, ?	Lumbar spine HVLA manipulation	?	Disc herniation with progressive radicular syndrome	-	?	Surgery with complete recovery
Dvorak[28]	Switzer-land	?, ?, ?	Lumbar spine HVLA manipulation	?	Disc herniation with progressive radicular syndrome	-	?	Surgery with complete recovery
Dvorak[28]	Switzer-land	?, ?, ?	Lumbar spine HVLA manipulation	?	Disc herniation with progressive radicular syndrome	-	?	Surgery with unknown recovery

Cite	Country	Age (y), Sex, SMT Indication	Details of Manual Therapy	Clinician Type	Adverse Event (nature and location)	Possible Contributing Factors	Time From SMT To Adverse Event	Outcome
Gallinaro[30]	Italy	34, FM, LBP	Chiropraxis manipulation	?	Worsened LBP with leg pain, L5/S1 disc herniation	-	?	Surgery
Gallinaro[30]	Italy	41, FM, LBP	Manipulation	?	L5/S1 disc herniation	-	?	Surgery
Gallinaro[30]	Italy	50, FM, LBP	Manipulations	?	L4/L5 disc herniation	-	?	Surgery
Hansis[33]	Germany	38, M, L5-S1 disc protrusion	?	?	Disc prolapse	?	Immediate	Surgery
Hipp[35]	Germany	61, M, LBP, sciatica	Chiropractic adjustment	?	Lumabr disc herniation with sensorimotor deficit	Hemangioma	?	?
Hipp[35]	Germany	32, FM, LBP, sciatica	Manual treatment	?	L4/5 disc herniation, peroneal muscle weakness	?	?	Discectomy
Hipp[35]	Germany	56, M, LBP, sciatica	Chiropractic treatment	?	L3/4 disc herniation , quadriceps muscle weakness	Osteochondrosis	?	Disecetomy
Hooper[36]	Australia	46, M, sciatica	Back manipulation	"Doctor"	L4-L5 disc extrusion	Patient regarded as "mentally disturbed"	Initially improved, LE weakness the next day	L4-L5 laminectomy and physiotherapy with minimal residual LE weakness.
Modde[46]	USA	50, M, ?	Manipulation	Chiropractor	Prolapsed lumbar disc	?	?	Surgery
Oppenheim[15]	USA	35, FM, LBP	Spinal manipulation	Chiropractor	L4-L5 disc herniation.	-	Immediate	Discectomy with excellent outcome.
Oppenheim[15]	USA	48, FM, neck and back pain	Spinal manipulation	Chiropractor	L4-L5 disc herniation	-	?	Conservative care with excellent outcome.
Oppenheim[15]	USA	47, M, LBP	Spinal manipulation	Chiropractor	L4-L5 disc herniation	-	?	Discectomy with excellent outcome.
Oppenheim[15]	USA	37, FM, LBP	Spinal manipulation	Chiropractor	L5-S1 disc herniation	-	?	Discectomy with excellent outcome.
Oppenheim[15]	USA	45, FM, neck pain	Lumbar manipulation	Chiropractor	L4-L5 disc herniation	-	?	Conservative care with excellent outcome.
Oppenheim[15]	USA	58, M, LBP	Spinal manipulation	Chiropractor	L4-L5 disc herniation	-	?	Discectomy with excellent outcome.
Ryan[51]	Australia	55, M, LBP	"Manipulation."	Chiropractor	L2-L3 disc herniation	-	"acute onset"	L3 partial laminecomy/discetomy with good clinical outcome
Fracture (n = 7)								
Austin[24]	UK	55 , FM, LBP and sciatica	"spinal manipulation"	Lay manipulator	L2 compression fracture with near total paraplegia, saddle anesthesia and sensory loss below L2 dermatome	Adenocarcinoma with spinal metastasis	Day of SMT	L1-3 laminectomy with good outcome.
Haldeman[16]	USA	82, FM, knee and leg pain	Clinician claimed SMT not performed while patient claimed SMT was performed	Chiropractor	L5 compression fracture	Multiple falls and frequent memory loss	?	Hospitalization due to multiple medical problems.
Haldeman,[16]	USA	73, FM, back pain	Manipulation	Chiropractor	Multilevel thoracolumbar compression fractures.	Severe osteoporosis and multiple medical problems. Previous L1 compression fracture.	?	Patient treated with medication, bracing and pool therapy.
Haldeman,[16]	USA	61, FM, back stiffness	Manipulation	Chiropractor	L3 compression fracture	Severe osteoporosis, long-term prednisone use	?	Continued deterioration with additional compression fractures and LE numbness noted in months subsequent to cessation of SMT.

Cite	Country	Age (y), Sex, SMT Indication	Details of Manual Therapy	Clinician Type	Adverse Event (nature and location)	Possible Contributing Factors	Time From SMT To Adverse Event	Outcome
Hansis[33]	Germany	45, M, "fixation" L3 to L5	"Chirotherapy", "pulled on the low-back"	?	L4 fracture	Osteoporosis	During treatment	Recovered.
Livingston[42]	Canada	82, M, ?	"Rough treatment"	Chiropractor	L3 body fracture	?	?	?
Livingston[43]	Canada	82, M, LBP and leg numbness	"forceful direct pressure on his lumbar spine"	Chiropractor	L3 compression fracture	Prostate carcinoma with spinal metastasis	?	Pain improved with stilbestrol
Hematoma/Hemorrhagic Cyst (n = 6)								
Dabbert[26]	USA	54, FM, LBP	"adjustments and roller exercises"	Chiropractor	Spinal hematoma	Anticoagulant medication	Within 5 days	T7-L1 laminectomy with improved clinical status and continued deficits at 1 postoperative month.
Ruelle[17]	Italy	64, FM, LBP	HVHA technique with knee against the lower back and firm twisting of the patient's pelvis.	Chiropractor	T9-T11 epidural hematoma with cord compression	-	Within 2 hours	T9-T11 laminectomy and surgical evacuation with excellent outcome.
Shvartzman[54]	Isreal	49, M, posterior thigh spasms, LE sensory deficit	"chiropractic Treatment"	Chiropractor	Hemorrhagic cyst	-	?	T11-L2 laminectomy
Stewart-Wayne[58]	UK	55, M, sciatica	Spinal Manipulation	Osteopath	Iliopsoas haematoma with femoral neuropathy	Anticoagulation therapy with warfarin sodium.	After SMT with progression over 4 days.	Conservative management. Improved clinical status with residual LE muscle wasting and weakness.
Wang[60]	Australia	82 FM, sciatica	Lumbosacral manipulation	?	Extradural haemorrhagic synovial cyst. Pain exacerbation and LE numbness and paraesthesia.	Multilevel degenerative changes with canal stenosis.	Within 24 hours	L3-L5 laminectomy and cyst and hematoma removal with excellent outcome.
Wang[60]	Australia	76, FM, buttock pain	Lumbar manipulation.	?	Hemorrhagic synovial cyst with resultant lumbar canal stenosis and exacerbation of pain.		Immediate	L4-L5 laminectomy and cyst removal with excellent outcome.
Other (n = 12)								
Balblanc[25]	France	67, FM, LBP	Vertebral manipulation	Traditional healer	Symmetric distal LE sensory and motor loss, possibly due to cauda equine or conus medularis injury.	-	Transient increase in LBP. Impaired LE function after 10 days.	Rehabilitation and vitamin B supplementation. Improved clinical status and continued deficits.
Haldeman[32]	USA	87, M, dyspnea, mid back pain, aching in the thighs.	Upper thoracic and lower lumbar "adjustment," hip flexion and extension	Chiropractor	Ruptured rectus femoris muscle	-	?	?
Huang[37]	Taiwan	51, M, LBP with LE pain and parasthesias	Manipulation directed at the lumbopelvic/ thigh region and massage	Physio-therapist	Rupture of soft tissue tumour at anterior proximal thigh	Extra-adrenal myelolipoma with extensive chondro-osseous metaplasia.	Immediate thigh swelling with development of soft tissue mass over 6 months	Surgical tumour resection
Kornberg[40]	USA	44, M, LBP	"deep, painful manipulation"	Chiropractor	Distal aortic occlusion	Lumbar artery aneurysm	Within 1 week	Vascular surgery with uneventful postoperative course.
Livingston[43]	Canada	31, M, LBP	Practitioner jumped from a stool onto patient's back with both knees	Chiropractor	"extreme pain", leg pain, leg weakness	-	Directly following SMT	Conservative treatment with "gentle traction-rotation of the lumbar spine" with improved pain and neurological status

Cite	Country	Age (y), Sex, SMT Indication	Details of Manual Therapy	Clinician Type	Adverse Event (nature and location)	Possible Contributing Factors	Time From SMT To Adverse Event	Outcome
Livingston [43]	Canada	"young", M, ?	Direct pressure chiropractic manipulation	Chiropractor	Left foot numbness, loss of ankle reflex	Sciatica present prior to SMT	?	?
Modde[46]	USA	58, FM, LBP and hip pain	Manipulation with leg flexed	Chiropractor	Disruption of pre-existing hip fracture healing	Hip fracture prior to SMT	?	Total hip arthroplasty
Modde[46]	USA	58, M, ?	Spinal manipulation	Chiropractor	Paralysis from waist down	Bladder cancer with spinal metastasis	?	?
Morandi[47]	France	49, FM, LBP	Lumbar vertebral manipulation	Physician	Spinal cord ischemia with paraplegia below T12 level.	-	Worsened LBP, then bilateral LE paresthesias, paraplegia within 36 hours	No improvement in neurological status (Frankel grade A).
Oppenheim [15]	USA	32, M, LBP	Spinal manipulation	Chiropractor	Myelopathy, thoracic syrinx and swollen cord.	-	?	Surgery with shunt placement, good outcome.
Sozio[57]	USA	47, FM, LBP	Practitioner applied the majority of his weight to patient's thoracic and lumbar spine while patient was prone.	Chiropractor	Esophageal rupture (Boerhaave's syndrome)	-	Approximately 1 day	Surgical esophageal repair with mediastinal drainage via thoracotomy. Uneventful recovery.
Sun[59]	Taiwan	33, M, LBP and Left sciatica	Vigorous manipulation	Chinese Kong Fu practitioner	L4/L5 paraspinal muscle abscess	Lumbar canal stenosis, L4/L5 disc herniation	Less than 7 days	Surgical debridement/abscess drainage, L4/L5 laminectomy and foraminotomy and IV antibiotic therapy. Resolution of infection without neurologic deficits.

CES, cauda equina syndrome; M, male; FM, female; LE, lower extremity; SMT, spinal manipulative therapy; LBP, low back pain; HVLA, high velocity low amplitude; HVHA, high velocity high amplitude.