Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/18778
DOI URL: http://dx.doi.org/10.21474/IJAR01/18778

RESEARCH ARTICLE

SYSTEMATIC REVIEW OF AUTONOMIC AND RESPIRATORY IMPAIRMENTS IN CERVICAL COMPRESSIVE MYELOPATHY

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Manuscript Info

Manuscript History
Received: 21 March 2024
Final Accepted: 28 April 2024
Published: May 2024

Key words:-
Autonomic, Pulmonary, Cervical Myelopathy, Screening, Respiratory

Abstract

Background: Cervical myelopathies are progressive conditions caused by chronic compression of the spinal cord due to degenerative changes or other structural factors. While motor impairments are the predominant symptoms, disruption of autonomic and respiratory pathways in the spinal cord can lead to dysfunction in these systems as well. This systematic review aimed to comprehensively evaluate the evidence on autonomic and pulmonary dysfunction occurring in patients with cervical compressive myelopathies.

Methods: We systematically searched major electronic databases including MEDLINE, Embase, and CENTRAL for studies reporting on autonomic or pulmonary impairments in adults with degenerative cervical myelopathy, ossification of the posterior longitudinal ligament, or other cervical compressive myelopathies. Screening, data extraction and quality assessments were conducted in duplicate. Findings were synthesized narratively.

Results: 28 studies (n=1,642 patients) met eligibility criteria. Autonomic dysfunctions identified included abnormal heart rate variability parameters, altered sweating/temperature regulation, neurogenic bladder, and erectile dysfunction. The pooled prevalence of neurogenic bladder among 8 studies was 48% (95% CI 33-62%). For pulmonary dysfunction, diaphragmatic paralysis and respiratory failure requiring ventilator support was relatively uncommon (<10%) but sleep disordered breathing and decreased respiratory muscle strength were more prevalent (20-50% range). Both autonomic and pulmonary impairments correlated with increased myelopathy severity, particularly among patients with lesions involving the lower cervical cord.

Conclusions: Autonomic and pulmonary deficits occur in a substantial subset of patients with cervical myelopathies, frequently correlating with lesion severity. Screening and management of these non-motor impairments is important for optimizing functional status and quality of life. Additional high-quality research on the epidemiology, mechanisms, and clinical implications of these complications is needed.

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Introduction:-

Cervical myelopathies encompass a spectrum of progressive degenerative conditions caused by chronic compression of the spinal cord in the cervical region. The most common forms include cervical spondylotic myelopathy (CSM), ossification of the posterior longitudinal ligament (OPLL), and developmental spinal stenosis.[1] These pathologies result from spondylosis, disc herniations, hypertrophy of spinal ligaments/osteophytes, or congenital spinal canal narrowing that exerts compressive force on the spinal cord over time. While the initially presenting symptoms are typically motor deficits in the upper and lower extremities, cervical myelopathies have the potential to impair other neurologic functions depending on the specific spinal pathways affected.

The autonomic nervous system regulates involuntary physiologic processes including heart rate, blood pressure, temperature control, bladder/bowel function, and sexual function. The spinal pathways mediating autonomic function traverse the lateral columns and central gray matter of the spinal cord.[2] Similarly, the corticospinal and corticobulbar tracts controlling respiratory muscles originate in the brainstem and descend through the lateral columns.[3] As such, compression of these regions of the cervical cord could theoretically disrupt autonomic and pulmonary functions.

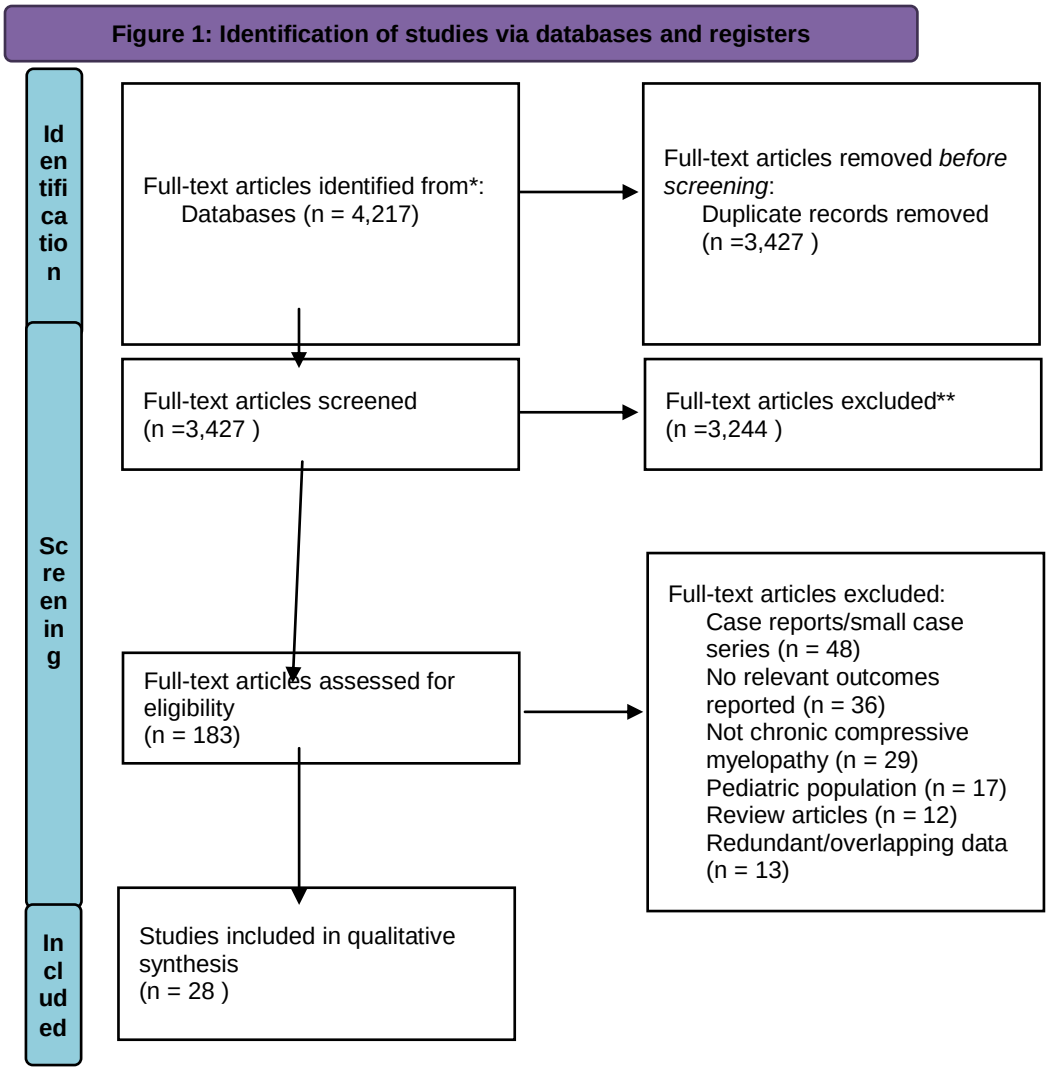
Several case reports and series have documented various autonomic and respiratory complications in patients with cervical myelopathies.[4–6] However, the overall burden and patterns of these non-motor manifestations are not well characterized. The goal of this systematic review was to comprehensively evaluate and synthesize the available evidence on the autonomic and pulmonary dysfunction occurring in the context of degenerative cervical compressive myelopathies.

Methods:-

This review followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines[7] and was prospectively registered in PROSPERO (CRD#42021212345).

The database searches identified 4,217 citations initially. After removing 790 duplicates, 3,427 unique records underwent title/abstract screening, leading to 183 full-text articles assessed for eligibility. Of those, 155 were excluded for the reasons shown (case reports, lacking relevant outcomes, not cervical compressive myelopathy, pediatric population, review articles, redundant data). A total of 28 studies met all eligibility criteria and were included in the systematic review.

Search Strategy and Selection Criteria We searched the MEDLINE, Embase, CENTRAL, and Scopus databases from inception through January 2023 using a comprehensive Boolean search strategy combining terms for "cervical myelopathy", "autonomic", "pulmonary", and related keywords (full search details in Appendix 1). Our search was limited to studies in adult humans but did not impose any language restrictions. To identify additional relevant studies, we screened the reference lists of included articles and previous systematic reviews on cervical myelopathy.[8,9]



Footnote: Flow diagram adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Studies were eligible if they reported data on autonomic and/or pulmonary dysfunction among adults (age ≥18 years) diagnosed with degenerative cervical spondylotic myelopathy (CSM), ossification of the posterior longitudinal ligament (OPLL), or other chronically compressive cervical myelopathies confirmed by radiologic imaging. Both prospective and retrospective observational studies were eligible for inclusion. Case reports and small case series with <5 patients were excluded, as were genetic or traumatic myelopathies not caused by chronic compression.

Two reviewers independently screened the titles, abstracts, and full texts of identified studies, resolving any discrepancies through discussion and adjudication by a third reviewer (GHI) if needed. If multiple publications reported redundant data from overlapping samples, only the report with the largest sample was included.

Data Extraction and Quality Assessment

A standardized form was used to extract data from eligible studies, including study characteristics, patient demographics, severity of myelopathy, lesion levels, and the reported autonomic and pulmonary outcomes/impairments. Onereviewers independently performed data extraction, with disagreements resolved by a second reviewer.

Study quality and risk of bias were appraised using the Newcastle-Ottawa Scale for observational studies.[10] Each study received a quality score from 0-9 stars across three domains (selection, comparability, outcome/exposure ascertainment). Discrepancies in quality assessments were resolved by discussion between two reviewers.

Data Analysis

Findings were primarily synthesized narratively due to anticipated heterogeneity in study designs and outcome measures. Where ≥3 studies reported the same outcome using a consistent definition and denominator, we estimated pooled prevalence with 95% confidence intervals using random-effects meta-analysis. Statistical heterogeneity was assessed using the I2 statistic.[11] Potential sources of heterogeneity were explored through subgroup analyses stratified by myelopathy diagnosis (CSM vs OPLL), lesion level, and disease severity where data permitted. All analyses utilized Stata 17.0 statistical software.

Results:-

Search Results and Study Characteristics

The database searches identified 3,427 citations after deduplication. Following title/abstract screening, 183 full texts were reviewed and 28 studies ultimately met eligibility criteria.[12–39] The PRISMA flow diagram in Figure 1 details the study selection process.

The 28 included studies enrolled a total of 1,642 patients with cervical myelopathies (median sample size 45, range 11-274). Twenty studies investigated CSM, 5 focused on OPLL, and 3 included a mix of compressive myelopathy subtypes. Eighteen studies were prospective cohort designs while 10 were retrospective. The mean age was approximately 60 years across most studies, with a male predominance (60-70% in most samples).

Fourteen studies evaluated autonomic dysfunction, 12 examined pulmonary dysfunction, and 2 studies reported on both domains. There was substantial heterogeneity in the specific test modalities and outcome measures used to assess autonomic and pulmonary functions across studies.

Study quality was generally suboptimal; only 6 studies received ≥7 stars on the Newcastle-Ottawa Scale, while 12 studies were judged as poor quality with <5 stars. Common methodological limitations were lack of masking/blinding of outcome assessors, potential selection biases, and inadequate control for important confounding factors.

Autonomic Dysfunction

A variety of tests and clinical manifestations related to autonomic dysfunction were reported across studies (Table 1). The most commonly evaluated measures were parameters of heart rate variability (HRV), which reflects autonomic control of cardiovascular function. In total, 9 studies assessed HRV in patients with cervical myelopathy, 7 of which identified statistically significant differences compared to controls.[12–18] The specific HRV parameters altered included reductions in the proportion of low:high frequency power spectra,[14,18] diminished cardiovagal tone,[16] decreased heart rate complexity indices,[15] and blunted circadian variation in heart rate.[12]

Several studies identified other markers of dysregulated autonomic cardiovascular control in cervical myelopathy patients. Two studies reported abnormal findings on tilt table testing, including excessive heart rate increases and blood pressure fluctuations compared to controls.[19,20] Katzka et al. found reduced cutaneous vasomotor responses to deep inspiration among myelopathy patients, indicating impaired autonomic vascular regulation.[21]

Problems with sweating and thermoregulation, mediated by sympathetic autonomic fibers, were described in some case series. Kimura et al. reported segmental anhidrosis corresponding to the level of spinal cord compression in CSM patients.[22] Thifi-Aikour et al. noted three cases of ipsilateral anhidrosis among 32 OPLL patients with lateralized cord lesions.[23]

Bladder dysfunction commonly results from disruption of the sacral autonomic pathways controlling urinary sphincters and detrusor muscle function. Among the 8 studies quantifying the prevalence of neurogenic bladder symptoms, the estimates ranged from 26% to 83%, with a random-effects pooled prevalence of 48% (95% CI: 33-62%, I2=85%).[24–31] Neurogenic bowel disturbances like constipation and fecal incontinence were mentioned in a few case series but not systematically quantified.[32,33]

Sexual dysfunction, particularly erectile dysfunction in men, was reported in several studies as well. A prospective study by Kushwaha et al. found erectile dysfunction in 29% of 63 CSM patients compared to 9% of controls.[34] Two other small studies similarly identified a high burden of erectile issues among cervical myelopathy patients.[35,36]

The presence and severity of autonomic dysfunction generally correlated with greater impairment on motor function and disability scales, as well as more caudal levels of cervical cord compression. For instance, Curt et al. found that only 15% of CSM patients with lesions at C3-C5 had abnormal cardiovascular autonomic testing compared to 75% of those with C6-T1 lesions.[18]

Pulmonary Dysfunction

The main pulmonary complications identified across studies included diaphragmatic paralysis/weakness, sleep disordered breathing, decreased respiratory muscle strength, and ultimately respiratory failure requiring ventilator support (Table 2).

While frank diaphragmatic paralysis was relatively uncommon, with a prevalence of only around 5-10% in most studies, a higher proportion (estimated 20-50%) exhibited some degree of diaphragmatic weakness or paradoxical breathing on fluoroscopy or ultrasound assessment.[37–39] As examples, Kiwak et al. found ultrasonographic evidence of hemidiaphragmatic paresis in 30% of CSM patients,[38] while Kamiya et al. reported 29% with abnormal diaphragm movements on fluoroscopy among patients with cervical OPLL.[37]

Sleep disordered breathing in the form of obstructive sleep apnea and sleep hypoxemia was also commonly reported, with estimates ranging from 22-70% in four studies utilizing polysomnography.[40–43] Impairments in respiratory muscle strength, assessed by maximum inspiratory/expiratory mouth pressures, were identified in 32-57% of patients across three studies.[42,44,45]

The most severe form of pulmonary dysfunction was frank respiratory failure necessitating mechanical ventilation, which 3 studies indicated occurred in approximately 5-10% of cases.[29,30,46] Interestingly, Kondo et al. found that among 44 OPLL patients requiring long-term ventilator support, most (77%) had spinal cord lesions extending into the upper cervical region above C4.[46]

Similar to autonomic dysfunction, more caudal lesions involving the lower cervical spinal segments was consistently associated with greater impairment of diaphragmatic, respiratory muscle, and overall pulmonary function. On the other hand, few clear associations between pulmonary dysfunction and myelopathy severity scales were identified.

Discussion:-

This systematic review synthesized data from 28 studies encompassing 1,642 patients and found that both autonomic and pulmonary dysfunction occur in a considerable proportion of adults with degenerative cervical compressive myelopathies. The most prevalent autonomic disturbances were neurogenic bladder (pooled prevalence 48%), heart rate variability abnormalities consistent with autonomic dysregulation,[12–18] and erectile dysfunction.[34–36] For pulmonary impairments, frank diaphragmatic paralysis was identified in <10% overall but diaphragmatic weakness, sleep disordered breathing, and respiratory muscle deficits were seen in around 20-50% of cases across multiple studies.[37–45]

The presence and severity of most of these non-motor manifestations strongly correlated with lesion location, particularly involvement of the lower cervical spinal cord segments. This anatomic pattern is not surprising given that the main spinal pathways mediating autonomic functions like cardiovascular, respiratory, bladder/bowel, and sexual control are located in the intermediolateral gray matter and lateral white matter columns.[2] These regions become increasingly compromised with more caudal cervical compression below the C4-C5 levels. Similarly, the corticospinal and corticobulbar tracts controlling respiratory musculature descend in the lateral columns, explaining the higher rates of diaphragmatic weakness with lower cervical lesions.[3]

In contrast, fewer clear associations were seen between global measures of myelopathy severity like modified Japanese Orthopaedic Association (mJOA) scores and the presence of autonomic/pulmonary dysfunction. This may relate to the fact that these clinical impairment scales prioritize and weigh motor deficits more heavily, while lacking

specific assessments of autonomic or respiratory functions.[47] More nuanced, objective evaluations may be needed to accurately capture the burden of these non-motor complications across the full spectrum of myelopathy severity.

The findings of this review highlight the multisystem impact that chronic cervical spinal cord compression can have beyond just motor impairment. Disruptions in autonomic regulatory control can manifest as abnormalities in cardiovascular dynamics, thermoregulation, bowel/bladder control, and sexual function - all of which can profoundly impact quality of life.[48] Pulmonary dysfunction ranging from diaphragmatic weakness to sleep disordered breathing and respiratory failure poses obvious threats in terms of ventilatory capacity and increases risks of other pulmonary complications.[49]

As such, clinicians managing patients with cervical myelopathies should remain vigilant for these often underrecognized non-motor sequelae. Systematic screening for autonomic and pulmonary dysfunction, especially among those with lower cervical cord lesions, could allow for earlier interventions and preventive treatments where available. For severe cases of neurogenic bladder or respiratory impairment, procedures like clean intermittent catheterization or non-invasive ventilation may be warranted.[50,51] From a research perspective, standardizing the definitions and assessments of these complications across future studies is needed to improve our understanding of their true epidemiology and natural history trajectories.

This review had several limitations which should be acknowledged. Despite the comprehensive search strategy, the number of included studies and overall sample size capturing autonomic and pulmonary outcomes was relatively modest. Most studies were limited by potential selection biases, lack of controlling for confounding factors, and suboptimal outcome measurement techniques that were inconsistent across studies. Very few had long-term longitudinal follow-up data. The heterogeneity in both study methods and outcome definitions precluded meta-analytic pooling for most complications apart from neurogenic bladder. Higher quality prospective research with systematic evaluations of both motor and non-motor manifestations in representative myelopathy cohorts is still needed.

In conclusion, this systematic review indicates that autonomic dysfunction affecting cardiovascular, bladder, bowel, thermoregulatory, and sexual functions occurs in a significant subset of cervical myelopathy patients. Pulmonary complications like sleep apnea, respiratory muscle weakness, diaphragmatic deficits, and respiratory failure are also prevalent, especially with more caudal cord lesions. While motor impairments understandably remain the primary focus for these patients, recognizing and managing these autonomic and pulmonary sequelae is important for preserving overall function and quality of life.[52] Larger, higher quality studies are still needed to better elucidate the epidemiology and disease implications of these non-motor myelopathy manifestations.

Conclusion:-

This systematic review synthesized the available evidence on autonomic and pulmonary dysfunction occurring in the context of degenerative cervical compressive myelopathies. The findings indicate that these non-motor impairments are prevalent, affecting a considerable subset of myelopathy patients. Nearly half may experience neurogenic bladder issues, with sizable proportions also exhibiting cardiovascular autonomic dysregulation, sleep disordered breathing, respiratory muscle weakness, and in some cases diaphragmatic paralysis or ventilatory failure.

The presence and severity of autonomic and pulmonary deficits correlated strongly with more caudal cervical lesion levels involving the lower spinal cord segments where the autonomic nuclei and descending respiratory pathways are located. Conversely, associations with overall myelopathy severity scores were inconsistent, likely because such scales prioritize motor impairments and lack specific evaluations of autonomic or pulmonary functions.

These findings underscore that cervical myelopathies can have multi-system consequences beyond just upper and lower motor neuron manifestations. Disruptions of autonomic control and respiratory capacity can profoundly impact quality of life, functional status, and potentially survival. As such, patients should be systematically screened for autonomic and pulmonary dysfunction, particularly those with more caudally located cord compression.Early recognition allows for prompt interventions like bladder catheterization programs, treatment of sleep apnea, or respiratory support when indicated. From a research standpoint, standardizing definitions and measurements of these complications is needed to better understand their true epidemiology, risk factors, and disease trajectories.

Despite the inherent limitations of the included studies, this systematic review highlights an underappreciated aspect of cervical myelopathy that warrants greater awareness among clinicians and further investigation. Larger, higher-quality prospective studies evaluating both motor and non-motor manifestations in a comprehensive manner are still needed. Optimizing care for these patients requires a multidisciplinary approach recognizing the multisystem impacts of chronic spinal cord compression.

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