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RESPIRATORY MECHANICS

Association Between Diaphragmatic Paralysis and Ipsilateral Cervical Spondylosis on MRI

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Abstract

Purpose Diaphragmatic paralysis (DP) is an important cause of dyspnea with many underlying etiologies; however, frequently no cause is identified despite extensive investigation. We hypothesized that cervical spondylosis (CS), as manifest by cervical neuroforaminal stenosis on magnetic resonance imaging (MRI), is an underrecognized cause of unilateral DP.

Methods A retrospective study was performed assessing cervical spine imaging utilization in the investigation of unilateral DP, and the contribution of CS to its pathogenesis. To assess the relationship between CS and DP, comparison was made between severity of ipsilateral and contralateral foraminal stenosis on cervical spine MRI in individuals with idiopathic DP, and to controls with DP of known etiology.

Results Record searches identified 334 individuals with DP who were classified as idiopathic ($n=101$) or DP of known etiology ($n=233$). Of those with idiopathic DP, only 37% had undergone cervical spine imaging. Cervical spine MRIs, available for 32 individuals from the total cohort identified ($n=15$ idiopathic DP, $n=17$ DP of known etiology), were reviewed and severity of CS graded (0–2). In idiopathic DP, CS was significantly more severe (grade 2 stenosis) on the side of DP at C3–C4 (73% affected vs 13% unaffected side; $p=0.031$) and C4–C5 (60% affected vs 20% unaffected side; $p=0.0039$), while no difference was observed in DP of known etiology. Overall severity of CS across all cervical spine levels was significantly worse in idiopathic DP *versus* those with DP of known etiology.

Conclusions In unilateral idiopathic DP, severity of CS is associated with DP laterality and is an underrecognized cause of diaphragmatic dysfunction. We propose that evaluation of 'idiopathic' DP should routinely include cervical spine imaging, preferably by MRI.

Keywords Diaphragm · Paralysis · Phrenic nerve · Cervical spondylosis

Abbreviations

CS	Cervical spondylosis
DP	Diaphragmatic paralysis
EMG	Electromyography
i2B2	Informatics for integrating biology and the bedside
MRI	Magnetic resonance imaging
NCS	Nerve conduction studies
PFT	Pulmonary function tests

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Introduction

The diaphragm, the principle muscle of respiration, is innervated by the phrenic nerve which arises from cervical nerve roots C3, C4, and C5. Injury to these nerve roots and/or the phrenic nerve may lead to diaphragmatic dysfunction and paralysis [1]. Diaphragmatic dysfunction has a variety of etiologies which may be grouped based on the site of the lesion including upper motor neuron lesions (cerebrovascular accident, infection, multiple sclerosis), lower motor neuron (spinal cord injury, poliomyelitis, amyotrophic lateral sclerosis)/phrenic nerve lesions (neck or chest trauma, surgical damage, compression by tumor, inflammatory processes, e.g., vasculitis), and muscular lesions (myasthenia gravis, muscular dystrophy, inflammatory myositis), with some processes affecting multiple sites [1–3]. Frequently, despite extensive investigation, the cause is not identified.

Once diaphragmatic paralysis (DP) is diagnosed, a search for the underlying etiology should be pursued. In addition to a detailed medical history and clinical examination focused on identifying etiologies of DP, workup typically includes pulmonary function testing (PFT) to assess the physiological impact of DP. There is no standard approach to imaging of the neck and chest to evaluate for potential causes [1]. Additionally, electromyography (EMG) of the diaphragm and phrenic nerve conduction studies (NCS) may be useful in differentiating neuropathic and myopathic etiologies of DP [4].

Cervical spondylosis (CS) is an age-related degenerative condition of the cervical spine characterized by degeneration of the intervertebral discs, uncovertebral and cervical facet joints, and frequent osteophyte formation [5, 6]. CS is common and increases in frequency with advancing age, with evidence of degenerative disease present in 57% of asymptomatic individuals over the age of 40 years on magnetic resonance imaging (MRI) [7]. The spinal level most commonly affected is C5–C6 followed by C6–C7 and C4–C5. Degenerative changes may be asymptomatic or lead to neck pain, radiculopathy, and less commonly myelopathy [5, 8]. Cervical radiculopathy in CS results from compression of the cervical nerve roots in the region of the neural foramen resulting in neck pain with radiation to the arm, weakness, paraesthesia, and loss of sensation in a dermatomal pattern [9–11]. As the phrenic nerve arises from cervical nerve roots C3–C5, it is vulnerable to compression in CS. Several case reports have linked CS with radiculopathy to DP [12–16], and cervical spondylotic myelopathy can lead to respiratory dysfunction and DP [17–19]. While one study of individuals with DP undergoing phrenic nerve reconstruction attributed 13% of cases to CS [20], in contrast another series of unilateral DP cases did not link any cases to CS [21].

To date, individual cases of diaphragmatic dysfunction and paralysis associated with CS have been reported in the literature; however, larger studies investigating this association have not been performed. To address this, we performed a retrospective case–control study assessing the use of cervical MRI in the investigation of idiopathic DP and comparing the severity of ipsilateral CS as manifest by cervical foraminal stenosis on cervical spine MRI in individuals with idiopathic DP to those with DP related to a known etiology to determine if there was an association between CS severity and ipsilateral DP.

Materials and Methods

Study Population

Ethical approval was obtained from the Weill Cornell Medicine (WCM)/New York-Presbyterian Hospital institutional review board (protocol number 1607017374). Individuals were identified from pulmonary clinics and utilizing the 'Informatics for Integrating Biology and the Bedside' (i2B2) system searching terms from the ICD-9 519.4 'disorders of the diaphragm' diagnosis code including 'diaphragm paralysis,' 'diaphragmatic paresis,' and 'diaphragm disorder.' Comprehensive review of the electronic medical records (EMR) of all identified individuals was performed to identify and characterize cases of true DP. Only those with evidence of DP and MRI cervical spine imaging available for review were included in the final study cohort.

Clinical and Radiological Evaluation

Clinical Characterization

The EMR of all patients with a diagnosis of unilateral diaphragmatic paralysis were reviewed by 2 independent clinicians (SO'B and BG) to confirm the diagnosis of DP and to exclude other causes of an elevated diaphragm including hiatal hernia, diaphragmatic eventration, or sub-phrenic masses. Individuals were then classified into two clinical categories: "idiopathic DP" or "DP of known etiology" when a recognized etiology was present to explain their DP. Known etiologies included prior history of thoracic surgery or trauma, history of neck trauma, presence of multiple sclerosis, or neurodegenerative disorders. In cases of disagreement regarding clinical category assignment, cases were subsequently reviewed jointly and adjudicated. Detailed data collection including demographics, medical history and physical examination, relevant laboratory test results, and PFT when available was undertaken for a subgroup of individuals who had undergone cervical MRI.

MRI Grading

Imaging was performed on closed system superconducting magnets on high-field strength 1.5 or 3 Tesla MRI systems. Studies performed on open magnets at less than 1.5 Tesla were excluded. Examinations performed at Weill Cornell and outside uploaded cervical spine examinations were considered for review if axial T2 spin echo sequences met minimum imaging requirements of 4 mm or thinner slice thickness and < 10% interslice gap. Axial T2 weighted spin echo sequences were used for grading the cervical neuroforamen according to methods described by Kim et al. [22]. Briefly, a grade 0 was given if neuroforaminal stenosis was absent; grade 1 if the narrowest width of the neuroforamen was the same or less than (but > 50%) the width of the extraforaminal nerve root; grade 2 if the neuroforaminal width was < 50% the width of the extraforaminal nerve root (Fig. 1). Cervical MRI examinations were excluded from analysis if there was excessive motion artifact which limited grading. A board-certified radiologist with a certificate of added qualification in neuroradiology (JLC) and radiology resident (JCH) reviewed the imaging examinations independently and were both blinded to the clinical history and laterality of DP.

Statistical Analysis

All statistics were computed using Graphpad Prism version 7.0. For the primary end point of the severity of cervical foraminal stenosis on the affected *vs* unaffected side, comparisons were made by evaluating the percentage of patients with severe (Grade 2) stenosis compared to those with mild or no stenosis (Grade 0–1) using a Wilcoxon matched-pairs signed rank test. The Mann–Whitney *U* test was used to compare phenotypes (idiopathic DP vs DP of known etiology), while comparisons of foraminal stenosis severity across different clinical groups was performed using the Kruskal Wallis Test. For comparison of clinical characteristics, Chi-square and unpaired t tests were used as appropriate. Cohen's kappa was used to assess inter-rater agreement of cervical spine MRI grading.

A power calculation was performed indicating that $n = 18$ subjects per group were required for an 80% power to detect a significant difference in the rate of cervical stenosis in idiopathic DP versus DP due to a known etiology. This calculation was based on a historical prevalence of 20% cervical stenosis in asymptomatic populations and an estimated prevalence of 65% in patients with idiopathic DP [23].

Results

Comprehensive review of all those with a diagnosis of DP identified in our institution through assessment of pulmonary outpatient attendees and an i2b2 search identified 334 patients with a diagnosis of diaphragmatic paralysis. For inclusion in the study, all subjects were required to have DP as evidenced by an elevated hemidiaphragm on chest imaging. Thirty-four percent of subjects underwent either a sniff test or a chest ultrasound confirming the presence of DP, while a further 31% had DP confirmed based on diaphragmatic EMG. Subjects were then classified as either DP of known etiology ($n = 233$, 70%) or idiopathic DP ($n = 101$, 30%). Records were then reviewed to assess whether concurrent imaging of the cervical spine (CT or MRI) was performed. In DP of known etiology 18% of individuals had undergone imaging of the cervical spine (CT 6%, MRI 13%) while in idiopathic DP, imaging was performed in 37% of patients (CT 12%, MRI 25%; $p = 0.0002$).

Of the 55 patients with DP had undergone MRI of their cervical spine, 23 were excluded for reasons including incorrect diagnosis [($n = 9$); i.e., another explanation for elevated diaphragm was present such as pleural effusion/

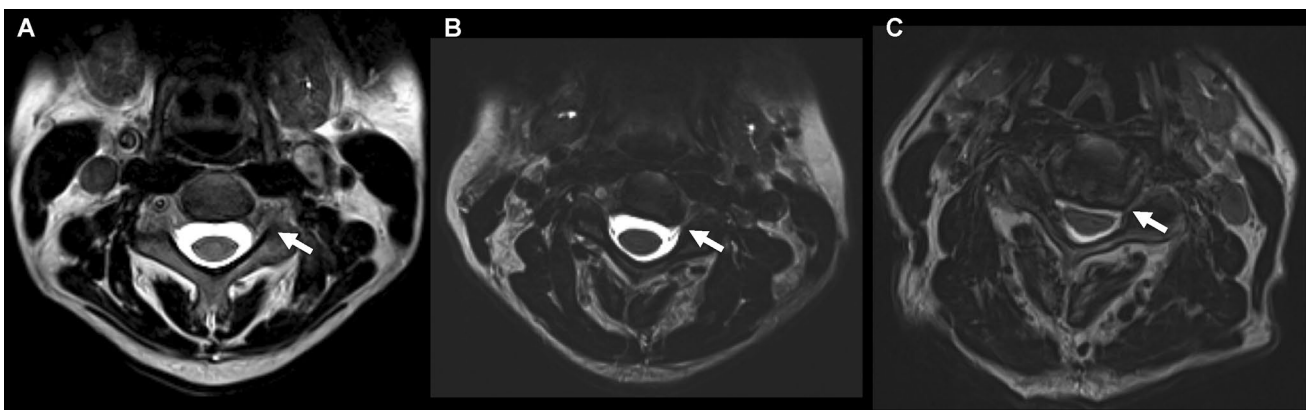

Fig. 1 Magnetic resonance imaging (MRI) grading of cervical spine neuroforaminal stenosis. High-resolution axial T2 SPACE images of the cervical spine illustrating grade 0 (**a**), grade 1 (**b**), and grade 2 (**c**) stenosis of the left C3–C4 neuroforamen (arrow) in three study subjects

mass ($n=3$), prior lung resection ($n=2$), transient ($n=2$), scoliosis ($n=1$), and focal eventration ($n=1$)], bilateral DP ($n=2$), inadequate clinical information ($n=4$), and MRI unavailable for review ($n=8$). The remaining 32 subjects underwent detailed analysis of available clinical and radiological data. Review of these individuals yielded $n=15$ cases of idiopathic DP and $n=17$ with DP due to a known etiology including prior thoracic surgery or malignancy, cervical surgery, trauma, and neurological disease (Supplemental Fig. 1).

Individuals with idiopathic DP were significantly older than those with DP due to a known etiology (67.9 ± 11.2 years vs 57.6 ± 12.7 years, $p=0.02$, Table 1). Females were in the minority in both idiopathic DP (13%) and DP of known etiology (35%), $p=0.31$. The most common presenting complaint in both individuals with idiopathic DP and those with DP of known etiology was dyspnea (60% vs 41%, $p=0.29$), while DP was discovered incidentally in 25% of those with idiopathic DP and 31% of controls ($p=0.09$). Neck pain reported by 52.9% of subjects with idiopathic DP and 20% of those with DP of known etiology ($p=0.056$). There was no significant difference in the presence of pulmonary or neurologic symptoms (e.g., numbness or weakness) between groups. The right hemidiaphragm was paralyzed in 53% of those with idiopathic DP versus 71% of those with DP of known etiology ($p=0.17$).

Severity of cervical spine spondyloarthritic disease was graded based on degree of neuroforaminal stenosis from

Table 1 Demographics of idiopathic and non-idiopathic diaphragmatic paralysis (DP) cases

Parameter	Idiopathic DP	Known etiology DP	*p* value
n	15	17	
Gender (M/F) *n* (%)	13 (86.7)/2 (13.3)	11 (64.7)/6 (35.3)	0.31
Age at diagnosis (years)	67.9 ± 11.2	57.4 ± 12.7	**0.02**
Body mass index (kg/m^2)	27.2 ± 4.8	27.9 ± 5.3	0.68
Symptoms			
Dyspnea *n* (%)	10 (66.7)	12 (70.6)	0.88
Other pulmonary symptoms *n* (%)[a]	12 (80)	8 (47)	0.05
Neck pain *n* (%)	10 (66.7)	9 (52.9)	0.43
Neurological symptoms *n* (%)[b]	9 (60)	10 (58.8)	0.94
Smoking history			
Current/ex-smoker *n* (%)	9 (52.9)	10 (66.7)	0.43
Duration of smoking (pk yr)	45.6 ± 59.2	41.6 ± 26.5	0.89
Pulmonary function parameters[c,d]			
FVC	65.6 ± 14.7	78.4 ± 32.6	0.36
FEV1	69.2 ± 19.9	79.9 ± 43.1	0.47
FEV1/FVC	76.8 ± 10.9	79 ± 4.6	0.56
TLC	70.2 ± 25.3	80.1 ± 23.4	0.4
DLCO	95.5 ± 19.1	83.4 ± 19.9	0.22
Side of DP (left/right) *n* (%)	7 (46.7)/8 (53.3)	4 (23.5)/13 (76.5)	0.17
Sniff test performed	6 (40)	2 (11.8)	0.15
Ultrasound performed	4 (1.1)	0 (0)	0.08
Diaphragm EMG	8 (82.7)	5 (29.4)	0.17
Indication for cervical spine MRI *n* (%)			
Neck pain	3 (20)	9 (52.9)	0.06
Neurological symptoms/signs	6 (40)	5 (29.4)	0.80
Diaphragmatic paralysis	3 (20)	1 (5.9)	0.50
Other/unknown	3 (20)	2 (11.8)	0.88

Data are presented as mean ± standard deviation, *p* values of numeric parameters calculated using a 2-tailed Student's *t* test with unequal variance, *p* value of categorical parameters calculated using a chi-square test

NA not applicable, *DP* diaphragmatic paralysis, *EMG* electromyography, *MRI* magnetic resonance imaging

[a]Other pulmonary symptoms: dyspnea on bending, orthopnea, cough, sputum, wheeze

[b]Neurological symptoms: arm pain ± weakness, arm numbness, arm paraesthesia

[c]Pulmonary function testing parameters are given as % of predicted value with the exception of FEV1/FVC, which is reported as % observed; *FVC* forced vital capacity, *FEV1* forced expiratory volume in 1 s, *TLC* total lung capacity, *DLCO* diffusing capacity

[d]Available in 59% of subjects

0–2 at cervical spine levels C2–C3 through to C7–T1 as described above [22]. Figure 1 provides examples of each severity grade in study participants. Of the 15 cases with idiopathic DP, CS was significantly more severe on the side of DP (affected side) compared to the unaffected side at C3–C4 (73% vs 13% with grade 2 severity, respectively, $p = 0.031$) and C4–C5 (60% vs 20%, $p = 0.0039$) spinal levels (Supplemental Fig. 2b, c). There was no significant difference in the severity of cervical foraminal stenosis on the affected *vs* non-affected side at C2–C3, C5–C6, or C6–C7 spinal levels (Supplemental Fig. 2a, e, f; $p > 0.05$ for all comparisons). For the 17 patients that had a known explanation for DP, there was no significant difference between the severity of the cervical foraminal stenosis of the affected side in comparison to the unaffected side at all levels, from C2–T1 (Supplemental Fig. 2). Cohen's kappa for cervical spine MRI grading was 0.68, indicating moderate agreement between observers.

At C3–4, C4–5, and C5–6, there was significantly higher levels of CS on the affected side in the idiopathic group compared to the control group with known causes of DP (Table 2), suggesting this population had overall more advanced cervical spine disease.

Discussion

Diaphragmatic dysfunction and paralysis are underrecognized causes of dyspnea, where the underlying etiology is frequently difficult to determine. We report a study of 334 individuals with DP at a single institution, 32 of whom underwent detailed assessment and evaluation of cervical MRI. Of these 15 individuals were classified as 'idiopathic' DP and 17 as DP due to a known etiology. Evaluation of cervical spine MRI in the idiopathic DP group revealed significant concordance between severity of CS, as evidenced by cervical foraminal stenosis, and laterality of DP at C3–C4 and C4–C5. The phrenic nerve originates in the most medial part of the gray matter in the C3–C5 cervical ventral horn, with the C4 root believed to supply the main bulk of the nerve fibers of the phrenic nerve [24], adding to the biologic plausibility of the finding.

In contrast, in individuals with DP of known etiology who had undergone MRI of the cervical spine there was no association between laterality of DP and severity of CS. In addition, overall severity of cervical foraminal stenosis across C3–C5 cervical spinal levels was greater in idiopathic DP compared to the controls, supporting the hypothesis that these groups represented separate entities. Of note, several of the individuals in the idiopathic DP group had cervical foraminal stenosis grading of 0 at the C3–C4 and C4–C5 levels, implying that for these patients, CS was not likely the etiology. For those patients, there remain other undetermined causes of DP, other than CS.

Prior case reports have suggested that CS and cervical manipulation can lead to phrenic nerve root injury and subsequent DP [12–16, 25, 26]. However, there is no standardized approach to the investigation of patients presenting with unexplained DP to determine its relationship to cervical nerve root injury. Importantly, though significantly more patients with idiopathic DP underwent cervical spine imaging (CT or MRI), they still comprised only 37% of those with idiopathic DP. Of those with idiopathic DP and MRI imaging of the cervical spine, 73% had severe (grade 2) CS on the ipsilateral side, possibly representing the etiologic mechanism for their DP and suggesting that there may be significantly more cases in the total population of unexplained DP who had not undergone cervical spine imaging.

These findings suggest that CS is an important and under recognized cause of 'idiopathic' DP and raises the intriguing prospect of identifying cases of DP due to phrenic nerve root injury that are potentially reversible. Future investigations should focus on whether the phrenic nerve is salvageable in cases of impingement due to CS. This could theoretically be achieved by nerve conduction and electromyography studies to assess if the nerve remains viable. If so, it is also conceivable that patients may benefit from laminectomy and decompression of the

Table 2 Distribution of patients with diaphragmatic paralysis (DP) according to cervical spondylosis score and cervical spine level for the two groups

Level	Idiopathic DP[a]			DP of known etiology[a]			*p* value[b]
Cervical spondylosis score	2	1	0	2	1	0	
C2–C3	0	3	12	1	2	14	0.65
C3–C4	10	1	4	3	5	9	**0.03**
C4–C5	9	5	1	4	8	5	**0.04**
C5–C6	9	5	1	3	6	8	**0.01**
C6–C7	4	4	7	3	3	11	0.40
C7–T1	1	3	11	0	3	14	0.64

[a]Idiopathic DP ($n = 15$); known etiology ($n = 17$)

[b]*p* value calculated by Mann–Whitney *U* test

nerve root with possible restoration of diaphragmatic function. There are reports of patients improving or restoring diaphragmatic function after cervical laminectomy [20, 27].

An important limitation of this study is its retrospective nature, making it difficult to definitively exclude secondary causes of DP. Our review was limited to the available clinical data and it is possible that additional components of the medical history were not documented in the EMR potentially resulting in subjects being misclassified as idiopathic DP. Additionally, there are many common potential underlying causes for DP. To circumvent this issue, individuals with a history of any condition associated with DP (e.g., diabetes mellitus, West Nile virus, multiple sclerosis) [1, 28] were included in the non-idiopathic group; however, it is difficult to be certain if these coexisting conditions were in fact the cause of the diaphragmatic dysfunction in all cases. Also, CS may be contributory in the control group and worsen their DP. Lastly, the diagnosis of diaphragmatic paralysis was presumed on the presence of an elevated hemidiaphragm without another explanation (e.g., prior lung resection, pleural effusions, scoliosis); not all subjects had documented sniff tests or ultrasound demonstrating a lack of movement of the diaphragm.

Another limitation is the small sample size and single institution nature of the study. DP is relatively rare with 334 patients identified over a 12-year period at our institution through a thorough search of DP-related diagnosis codes. Of the 334 cases initially identified, only 79 had cervical imaging performed, of these 55 had an MRI of the cervical spine (25 had CT of the cervical spine). As MRI of the cervical spine is the preferred modality for grading the severity of cervical spondylosis [29], only those with MR imaging were included in the study. As this is a single center study, investigation practices may not be reflective of those in other institutions. Additionally, by only including patients who had undergone a cervical MRI, we likely increased the probability of identifying individuals with CS already a relatively common condition that increases with age, in the control group. Despite this potential bias, we identified significantly more severe CS is the idiopathic DP group.

Finally, while this study demonstrates an association with cervical foraminal stenosis and DP, proving causality which would require additional functional testing such as nerve conduction and electromyography studies. Overall, these findings support the hypothesis that cervical spondylosis is the likely etiology behind a significant number of cases of 'idiopathic' DP. In new cases of DP, we believe the phrenic nerve should be imaged in its entirety, from the nerve root via cervical MRI, through its course in the chest cavity by brachial plexus and chest cross-sectional imaging.

Conclusions

Cervical spondylosis is an important and underrecognized cause of diaphragmatic paralysis, and hence evaluation of the cervical spine with MRI should be considered in the investigation of individuals presenting with diaphragmatic dysfunction and paralysis without a clear cause.

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Author contributions SO'B: Conceived study, identified study subjects, collected clinical data, performed data analysis, prepared manuscript. JCH: Reviewed and graded radiology images. JLC: Reviewed and graded radiology images, contributed to preparation manuscript. BTC: Reviewed subject, performed and interpreted EMG and NCS, contributed to manuscript preparation. BDG: Conceived study, identified study subjects, collected clinical data, performed data analysis, prepared manuscript.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

References

1. McCool FD, Tzelepis GE (2012) Dysfunction of the diaphragm. N Engl J Med 366(10):932–942. https://doi.org/10.1056/NEJMra1007236
2. Laghi F, Tobin MJ (2003) Disorders of the respiratory muscles. Am J Respir Crit Care Med 168(1):10–48. https://doi.org/10.1164/rccm.2206020
3. Qureshi A (2009) Diaphragm paralysis. Semin Respir Crit Care Med 30(3):315–320. https://doi.org/10.1055/s-0029-1222445
4. Jammes Y, Budin-Poirier C, Bregeon F (2010) Electromyographic tools to assess hemidiaphragm paralysis. Clin Physiol Funct Imaging 30(2):107–115. https://doi.org/10.1111/j.1475-097X.2009.00911.x
5. Shedid D, Benzel EC (2007) Cervical spondylosis anatomy: pathophysiology and biomechanics. Neurosurgery 60 (Supp1 1):S7–13. https://doi.org/10.1227/01.NEU.0000215430.86569.C4
6. Tracy JA, Bartleson JD (2010) Cervical spondylotic myelopathy. Neurologist 16(3):176–187. https://doi.org/10.1097/NRL.0b013e3181da3a29
7. Boden SD, McCowin PR, Davis DO, Dina TS, Mark AS, Wiesel S (1990) Abnormal magnetic-resonance scans of the cervical spine in asymptomatic subjects. A prospective investigation. J Bone Jt Surg Am 72(8):1178–1184

8. Kalsi-Ryan S, Karadimas SK, Fehlings MG (2013) Cervical spondylotic myelopathy: the clinical phenomenon and the current pathobiology of an increasingly prevalent and devastating disorder. Neuroscientist 19(4):409–421. https://doi.org/10.1177/1073858412467377
9. Abbed KM, Coumans JV (2007) Cervical radiculopathy: pathophysiology, presentation, and clinical evaluation. Neurosurgery 60 (1 Suppl 1):S28–34. https://doi.org/10.1227/01.NEU.0000249223.51871.C2
10. Kuijper B, Tans JT, Schimsheimer RJ, van der Kallen BF, Beelen A, Nollet F, de Visser M (2009) Degenerative cervical radiculopathy: diagnosis and conservative treatment A review. Eur J Neurol 16(1):15–20. https://doi.org/10.1111/j.1468-1331.2008.02365.x
11. Harrop JS, Hanna A, Silva MT, Sharan A (2007) Neurological manifestations of cervical spondylosis: an overview of signs, symptoms, and pathophysiology. Neurosurgery 60 (1 Supp1 1):S14–20. https://doi.org/10.1227/01.NEU.0000215380.71097.EC
12. Buszek MC, Szymke TE, Honet JC, Raikes JA, Gass HH, Leuchter W, Bendix SA (1983) Hemidiaphragmatic paralysis: an unusual complication of cervical spondylosis. Arch Phys Med Rehabil 64(12):601–603
13. Hayashi H, Kihara S, Hoshimaru M, Hashimoto N (2005) Diaphragmatic paralysis caused by cervical spondylosis Case report. J Neurosurg Spine 2(5):604–607. https://doi.org/10.3171/spi.2005.2.5.0604
14. Keelan E, Kidney J, Judge EP (2017) An unusual case of orthopnea. Clin Med (Lond) 17(3):245–247. https://doi.org/10.7861/clinmedicine.17-3-245
15. Reddy YN, Josephson RA (2014) Osteoarthrosis causing altered mental status: a case report. J Med Case Rep 8:401. https://doi.org/10.1186/1752-1947-8-401
16. Daniil ZD, Malagari K, Zakynthinos EG, Kapotsis GE, Roussos C, Papiris SA (2004) An unusual cause of dyspnea in a 77-year-old man. Chest 125(2):770–774. https://doi.org/10.1378/chest.125.2.770
17. Ishibe T, Takahashi S (2002) Respiratory dysfunction in patients with chronic-onset cervical myelopathy. Spine 27(20):2234–2239. https://doi.org/10.1097/01.BRS.0000029251.16654.53
18. Fregni F, Conceicao Souza GE, Taricco MA, Mutarelli EG (2004) Phrenic paresis and respiratory insufficiency associated with cervical spondylotic myelopathy. Acta Neurochir 146(3):309–312; discussion 312. https://doi.org/10.1007/s00701-003-0201-4
19. Yu E, Romero N, Miles T, Hsu SL, Kondrashov D (2016) Dyspnea as the presenting symptom of cervical spondylotic myelopathy. Surg J (New York, NY) 2(4):e147–e150. https://doi.org/10.1055/s-0036-1597664
20. Kaufman MR, Elkwood AI, Brown D, Cece J, Martins C, Bauer T, Weissler J, Rezzadeh K, Jarrahy R (2017) Long-term follow-up after phrenic nerve reconstruction for diaphragmatic paralysis: a review of 180 patients. J Reconstr Microsurg 33(1):63–69. https://doi.org/10.1055/s-0036-1588018
21. Elefteriades J, Singh M, Tang P, Siegel MD, Kenney B, Pandey A, Kopf GS (2008) Unilateral diaphragm paralysis: etiology, impact, and natural history. J Cardiovasc Surg 49(2):289–295
22. Kim S, Lee JW, Chai JW, Yoo HJ, Kang Y, Seo J, Ahn JM, Kang HS (2015) A new MRI grading system for cervical foraminal stenosis based on axial T2-weighted images. Korean J Radiol 16(6):1294–1302. https://doi.org/10.3348/kjr.2015.16.6.1294
23. Ko S, Choi W, Lee J (2018) The prevalence of cervical foraminal stenosis on computed tomography of a selected community-based korean population. Clin Orthop Surg 10(4):433–438. https://doi.org/10.4055/cios.2018.10.4.433
24. Banneheka S (2008) Morphological study of the ansa cervicalis and the phrenic nerve. Anatomical science international 83(1):31–44. https://doi.org/10.1111/j.1447-073X.2007.00201.x
25. Heffner JE (1985) Diaphragmatic paralysis following chiropractic manipulation of the cervical spine. Arch Intern Med 145(3):562–564
26. Schram DJ, Vosik W, Cantral D (2001) Diaphragmatic paralysis following cervical chiropractic manipulation: case report and review. Chest 119(2):638–640. https://doi.org/10.1378/chest.119.2.638
27. Weiss C, Witt T, Grau S, Tonn JC (2011) Hemidiaphragmatic paralysis with recurrent lung infections due to degenerative motor root compression of C3 and C4. Acta Neurochir 153(3):597–599. https://doi.org/10.1007/s00701-010-0880-6
28. Leis AA, Stokic DS (2012) Neuromuscular manifestations of west nile virus infection. Front Neurol 3:37. https://doi.org/10.3389/fneur.2012.00037
29. Bono CM, Ghiselli G, Gilbert TJ, Kreiner DS, Reitman C, Summers JT, Baisden JL, Easa J, Fernand R, Lamer T, Matz PG, Mazanec DJ, Resnick DK, Shaffer WO, Sharma AK, Timmons RB, Toton JF, North American Spine S (2011) An evidence-based clinical guideline for the diagnosis and treatment of cervical radiculopathy from degenerative disorders. Spine J 11(1):64–72. https://doi.org/10.1016/j.spinee.2010.10.023