## **Current Trends in Degenerative Cervical Myelopathy**

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## Abstract

Advances in patient selection, surgical techniques, and postoperative care have facilitated spine surgeons to manage complex spine cases with shorter operative times, reduced hospital stay and improved outcomes. We focus this article on a few areas which have shown maximum developments in management of degenerative cervical myelopathy and also throw a glimpse into the future ahead. Imaging modalities, surgical decision making, robotics and neuro-navigation, minimally invasive spinal surgery, motion preservation, use of biologics are few of them. Through this review article, we hope to provide the readers with an insight into the present state of art incervical myelopathy and what the future has in store for us.

Keywords: Cervical myelopathy, DTI, ADR, hybrid, laminoplasty, JOA.

### Introduction

Spondylotic myelopathy involving the cervical spine as a result of Degenerative Cervical Myelopathy (DCM) is the most frequent cause of insult to the cervical spine that is non-traumatic in origin.

With age, the cervical spine undergoes degenerative changes including osteophyte formation, which narrows the spinal canal, thereby causing chronic compression and leading to DCM. There has been an increase in the occurrence of DCM and an increased requirement for admission to the hospital due to DCM which is approximately 4.04/100,000 person-years, with the number of patients being managed surgically each year increasing up to 7-fold [1]. However, because of the ambiguous definition and limited studies involving larger populations, the true burden of DCM can be much higher than anticipated [2]. There is a disparity between the rate of degeneration of chronically compressed cervical spinal cord and the degree of neurological worsening, especially in early cases of DCM and effective management strategies are yet to be evolved. The spinal cord has limited regenerative potential with a risk of permanent disability. Early intervention and management are keys to success in the management of early cases of DCM.

As per the population projections of the United Nations, the estimated population of those who were aged 65 years and above was about 703 million in 2019, and it is anticipated to be doubled to 1.5 billion by 2050, thereby accounting for 16% of the world population. Moreover, as indicated by

the World Health Organization (WHO), the rate of aging is progressing at an exponential pace in countries like India. According to statistics by the WHO, the current elderly population estimates 60 million that will be quadrupled by 2050 reaching up to 227 million. Due to the change in the demographics and an escalation in the world aging population, DCM is now prioritized concerning public health. Because of the difficulty in analyzing evolving practices in spine surgery, the main objective of this article is on an area that has shown tremendous evolution recently: DCM [3]. The main objective here is to analyze the recent developments and the future trends in the strategies for the managing DCM.

#### **Materials and Methods**

For the narrative review, the database search was limited to specific keywords: "Recent updates" OR "current trends" AND "DCM" or "cervical myelopathy." We started the search with the abovementioned keywords in the PubMed database. Only English language literature was considered. The initial search yielded 101 articles out of which iblished Date: 31 Mar 2022

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compression.

	ID	FA Mean SDev Size / Min / Max	ADC Mean SDev Size / Min / Max	TraceW Mean SDev Size / Min / Max	Anat Mean SDev Size / Min / Max
	•	477.5 25.5 2 / 452 / 503	1095.0 46.0 2 / 1049 / 1141	78.5 2.5 2/76/81	176.2 29.0 44 / 115 / 260
0	2	470.0 0.0 1 / 470 / 470	1503.0 0.0 1 / 1503 / 1503	28.0 0.0 1/28/28	198.0 5.4 23 / 191 / 214
	3	454.0 0.0 1/454/454	1434.0 0.0 1 / 1434 / 1434	53.0 0.0 1/53/53	173.5 12.0 16 / 154 / 196
	4	608.0 50.0 2/558/658	1114.0 77.0 2/1037/1191	59.5 5.5 2/54/65	148.3 9.7 39 / 129 / 173
0	5	383.7 48.1 3/318/432	1567.0 241.2 3 / 1226 / 1745	27.0 11.7 4/18/47	129.2 8.4 48 / 111 / 151
1. 1. 2. 1. 10	•	277.8 111.1 4/166/454	1738.0 197.2 4 / 1487 / 1946	31.5 5.0 4/27/39	131.3 26.7 73 / 75 / 188

34 articles were relevant to this review and were included in the study. Crossreferences of the included articles were searched and 31 additional articles were added. Additional repeat assessments by two independent reviewers were done for validation and confirmation of the literature review. Key literature pertinent to the present topic has been cited and emphasis has been placed on English literature published in the past 10 years to provide the most current recommendations.

### Review

## Advances in imaging modalities

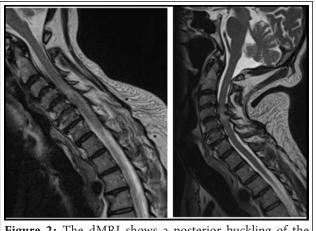
Due to its ability to provide visualization of almost all structures in a high resolution, the investigation of choice in DCM is MRI. The correlation between signal intensity changes on MRI, signs and symptoms, and the outcome of surgery in DCM was analyzed by Nouri et al. who found that T1-weighted hypointensity was the strongest factor that predicted the neurological outcome of DCM post-surgery. It reflected the cavitation and the loss of cells in the gray and white matter, and the degree of cord compression, which could be measured with an array of techniques including maximal spinal cord compression (MSCC), maximal canal compromise, compression ratio, or cross-sectional area [4].

At present, newer imaging modalities such as MR spectroscopy (MRS), magnetization transfer (MT), functional MRI (fMRI), diffusion tensor imaging (DTI), myelin water fraction, and T2\*weighted imaging are being preferred [5] due to the disparity between the MRI changes and the gravity of the disease, which could lead to asymptomatic patients showing severe compromise of the canal on MRI.

fMRI is an MRI sequence that can determine the change in brain activity by detecting changes in blood flow rate to regions of the brain. fMRI measures the rate at which blood flows to the spinal cord at and below the level of compressed segment and information obtained can estimate the retained function, devising patient-tailored rehabilitation programs, assessing the regenerating potential of the injured spinal cord and to assess experimental treatment strategy against the gold standard [6].

Tam et al. claimed that following decompressive spinal cord surgery, fMRI detected the increased cortical activation involving the primary motor cortex, which also translated in significant motor recovery in motor subscores of both upper and lower limbs in the modified Japanese Orthopedic Association (mJOA) score. Thus, they concluded that cortical recruitment can be a marker for recovery of neurology after decompressive spinal cord surgeries [7]. The diffusion of H2O along the spinal cord tracts and across the regions of the brain can be analyzed using DTI, which is a distinctive type of MRI sequence.

Anisotropy suggests that an alteration in the function of neurons could be used as a prognostic marker for patients. Bhosale et al. studied the role of DTI MRI for



**Figure 2:** The dMRI shows a posterior buckling of the ligamentum flavum along with edema of the spinal cord in extension that is not apparent on an MRI taken in flexion.

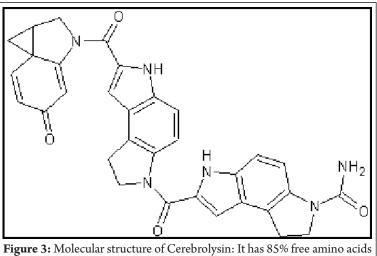


Figure 3: Molecular structure of Cerebrolysin: It has 85% free amino acids and 15% peptides with low molecular weight.

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**Figure 4:** (a, b, c, d): Post-surgical anteroposterior, lateral neutral, and lateral dynamic radiographs of the cervical spine of a 38-year-old female with cervical radiculopathy show replacement of the cervical disc with a restored range of motion.

determining the prognosis of cervical myelopathy patients and found that a positive correlation existed between the fractional anisotropy (FA)/apparent diffusion coefficient (ADC) values measured at the site of MSCC with the pre-operative mJOA score [8]. FA is the marker of acute injury to the spinal cord and patients with increased values of FA at the site of maximal compression have a better prognosis as compared to chronic cord compression which correlates with the focal increase in the values of ADC (Fig. 1).

MT and myelin water fraction help in detecting myelin loss which is seen in DCM.

Another non-invasive technique that evaluates the metabolic cord changes, thereby reflecting the neuronal loss, demyelination, and gliosis is MRS, a technique which does not involve ionizing radiations.

Ellingson et al. analyzed the additive role of DTI and MRS biomarker in DCM. They evaluated the concentration of Nacetyl aspartate (NAA) and choline (Cho) to the concentration of creatinine, along with the ratio of Cho to NAA and suggested that a combination biomarker which involved DTI fiber tract density, mean diffusivity, and Cho/NAA was the best predictor of the mJOA score [9]. The kinetic MRI/dynamic MRI (dMRI) is another development that can be used for detecting innocuous lesions in patients of mild DCM (Fig. 2).

Kolcun et al. summarized the significance of dMRI in early cases of DCM. They evaluated 2661 patients for dynamic spinal cord changes, including changes in canal dimensions, transient cord compression with changes in the head position, and the effect of flexion and extension on the situation of intervertebral disc (IVD). They concluded that dMRI was an important tool to understand the pathophysiology of DCM as well as in pre-operative assessment. dMRI correlates well with the patient's symptoms, especially in early cases of DCM, certain congenital dysplasia, and in flexion-myelopathic diseases such as Hirayama disease [10, 11].

Literature regarding the changes involving the cerebrum in patients with DCM is scarce.



**Figure 5:** Mazor X robotic-guided instrumentation planning shows images in the axial view along with a 3D orientation.

Zdunczyk et al. used navigated transcranial magnetic stimulation (nTMS) to improvise the diagnostic accuracy in DCM by an improvised characterization of the underlying pathophysiology. They identified a decrease in the cortical motor area activity which was seen associated with an increased activity of the supplementary motor area in the patients with DCM and inferred that a change in the parameters of nTMS could be used as a prognostic marker for DCM in the future [12]. Additional research regarding the same would enable us to elucidate the discordance between the clinical picture and radiological findings, and it would also have therapeutic implications. Stimulation of deficient motor areas through TMS to recover motor function is a promising technique. Using laboratory tests as biomarkers to improve diagnostic accuracy and serve as prognostic markers for DCM have generated newfound interest among researchers. Newer biomarkers linked to acute SCI area also identified and some of these could be tried for DCM.

Serum microRNA is a promising

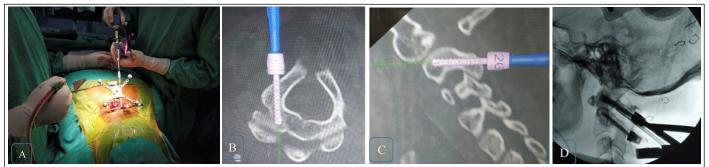


Figure 6: It shows the use of navigation-guided (a) screw insertion in C2 pedicle, axial (b), and sagittal (c) for harms fixation (d) in a 30-year male patient.

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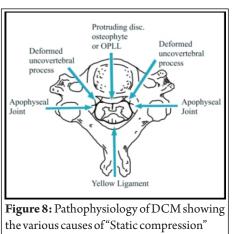
**Figure 7:** Sagittal (a) and (b) axial MRI images of a 36-year male who presented with the right upper limb radiculopathy show discogenic compression. The patient was managed with uniportal posterior endoscopic decompression ©.

biomarker. The expression of these genes is seen following the application of compressive forces on the spinal cord, and these include miR-21 (neural inflammation), miR-34a (neural apoptosis), and miR-10a (OPLL) [13].

# Conservative treatment strategies for mildDCM

Several drugs available are now being investigated for their additional role in DCM to maximize post-operative recovery. One of such drugs that are being investigated is riluzole, a Na+ channel blocker that has shown to decrease the excitotoxicity of glutamate channels in the animal model of CSM, thereby improving outcomes. The drug is approved by the FDA for the management of amyotrophic lateral sclerosis, which has a clinical picture similar to DCM.

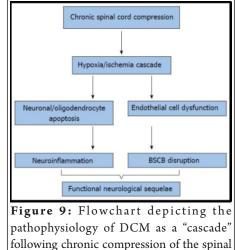
Fehlings et al. conducted a phase three, multicentric, double-blind, RCT to evaluate the role of Riluzole in outcomes



of decompressive spinal cord surgeries in DCM. Preliminary results suggested no additional benefit of riluzole as compared to decompressive surgery concerning mJOA, ASIA score, and Nurick grades but there was a decrease in the post-surgical pain involving the neck and neuropathic pain which persisted for a year [14].

These regenerative therapies used for DCM are currently in their initial stages. An ideal target for these therapies is to put a halt to the chemical cascade responsible for the degeneration.

Attempts are on-going for judging the effectiveness of a combination of surgical modalities and pharmacological drugs offering neuroprotection for maximizing the postsurgical recovery, and here, Cerebrolysin comes into the picture. It offers neuroprotection and consists of 85% free amino acids and 15% biologically active low-molecular-weight



peptides (Fig. 3). Cerebrolysin has shown promising results in conditions associated with neurodegeneration which include Alzheimer's disease, dementia, and head injury. Only a single study exists regarding the part of Cerebrolysin in the conservative management of DCM patients, but there is no literature evaluating its efficacy in surgically managed DCM patients. We did a prospective RCT that analyzed the importance of Cerebrolysin in surgically managed patients of DCM. The patients in the Cerebrolysin group had a better post-operative neurological improvement (66.7%) as compared to the control group (56.7%) but there was

no significant difference. When compared to the placebo, the Cerebrolysin group showed a significant improvement in the function of the hand at 1 year. More importantly, no major adverse reactions to this drug were documented thus proving its safety profile [15].

There is scanty literature regarding the role of steroids in DCM and apart from the anti-inflammatory action of steroids, few other benefits of steroids are determined. Jeyamohan et al. conducted a prospective RCT that assessed the effects of steroids on swallowing, airway, and arthrodesis related to multilevel anterior cervical reconstruction in patients managed with ACDF. One hundred and twelve patients were enrolled in the study and were randomly assigned to receive either saline or dexamethasone. They determined that a perioperative injection of dexamethasone resulted in comparatively lesser edema involving the airways, a decrease in the dysphagia, and a shorter in-patient stay without affecting the rate at which fusion took place [16]. A few other surgeons also used steroidsoaked gel foam for decreasing the softtissue swelling that was seen locally after ACDF. Nonetheless, more extensive series with a longer follow-up are

cord.

required before steroids are routinely included in the management protocol of DCM[17,18].

Villavicencio et al. conducted a singlecenter prospective RCT to assess the ability of injection of local anesthetics in the retropharyngeal space to reduce postoperative dysphagia in anterior reconstructive procedures in cervical degenerative disc diseases (DDCs). The patients undergoing one- or two-level ACDF procedures for cervical DDC were a part of the study and were randomly divided into two groups to receive either 0.5% bupivacaine hydrochloride or 0.9% NaCl solution. They concluded that injecting local anesthetics did not reduce post-operative dysphagia in those who underwent oneor two-level ACDF surgeries [19].

Considering the ability of both gabapentin and pregabalin to treat other forms of neuropathy, they are used for treating the neuropathic pain seen in DCM. Lo et al. conducted an observational study which showed that as compared to the baseline, pregabalin showed more reduction in the pain. They concluded that although pregabalin was successful in ameliorating the pain related to spondylotic radiculopathy as a first-line agent, watchful monitoring is essential to detect the adverse effects, of which somnolence is notable [20].

DDD is a common pathology that acts as a precursor to DCM.

Injectable proteins aiming to promote cellular growth are used in various animal models, and these can be used to put a stop to the progression of DDD [21]. Although the early results have shown promise, the lesser span of the therapeutic effect is a drawback, and hence, additional research regarding the combination of these proteins and a carrier molecule to extend their span of action is required. The aim of gene therapy is to change the intradiscal genetic expression for upregulation of the anabolic cascade along with a simultaneous downregulation of the harmful physiological changes. Matrix metalloproteinase, tissue inhibitor of matrix metalloproteinase, and AD-Sox9 are examples of genes used for gene therapy [22]. Although multiple in vivo models have shown a successful therapeutic expression of these genes causing a delay in the progression of DDD, their success hangs on the discovery of non-viral vectors which could be used as carriers.

The utility of stem cells in slowing the degeneration occurring in advanced DDD is being analyzed, and mesenchymal stem cells are currently the most common lineage used for the same. Multiple studies on the topic of DDD involving the lumbar spine have focused on mesenchymal stem cells and patients have shown a decrease in post-operative pain along with improved MRI findings using stem cells [23].

Wang et al. performed a systematic review and meta-analysis of 22 studies for analyzing the effect of stem cell transplantation and concluded that a deceleration or arrest of the DDD was noted in the IVD of quadruped animals in whom the stem cells were transplanted. Nevertheless, human clinical trials would be necessary to analyze if the similar benefit of stem cells could be obtained in bipedal humans [24].

Although MSCs obtained from the bone marrow and adipose tissue are most frequently used for transplantation, research is being conducted using the MSCs from the umbilical cord Wharton's jelly and results have shown promise [25, 26].

## Advancements in surgical decisionmaking

Surgery in DCM aims for achieving cord decompression, restoring the alignment, and stabilizing the involved segments of the cord. Factors deciding the surgical approach include the patient's age, clinical features, single or multiple level of involvement, alignment of the cervical spine, past surgical procedures, and strength of the bone [27].

A chief element deciding a good postsurgical outcome is the restoration of sagittal balance [28].

The K-line by Fujiyoshi et al. for the evaluation of the spinal and OPLL size as a straight line that joined the midpoints of the spinal canal at C2 and C7 on radiographs of the lateral cervical spine. In the K-line (+) group, OPLL does not exceed the K-line, while in the K-line (-)group, OPLL goes beyond the K-line. The authors stated that in the K-line (-)group, decompression surgery through the posterior approach would not enable an adequate shift of the cord posteriorly, thereby less likely improving the neurology. Taniyama et al. did a modification in the K-line for assessing if the residual anterior cord compression after laminoplasty had a significant positive correlation with the preoperative anterior cord clearance and stated that the modified K-line (mK-line) is a line that joined the midpoints of the spinal cord at C2 and C7 on a T1weighted sagittal MRI. After measuring the minimum interval distance (INT) between mK-line and anterior compressive factors such as disc bulges or osteophytes on the mid-sagittal image, they determined that when the preoperative INT was <4 mm, there was a higher chance of residual anterior cord compression occurring in non-lordotic patients [29].

### Anterior approaches

The current surgical procedure of choice for treating focal DCM is ACDF, which is now being performed on a day care basis due to the emergence of MISS [30]. ACCF helps in anterior decompression of the retrovertebral disease and kyphosis correction. With respect to functional outcome and sagittal alignment, multilevel ACDF is a beneficial procedure when compared to ACCF, while "oblique corpectomy without fusion" is a newer emerging idea [31].

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This approach aims to enable decompression of the ventral spinal cord, with maintenance of > 50% of the body of the vertebra. A claimed advantage of this technique is that it is associated with a decreased risk of adjacent segment disease because of instrumentation, while also achieving functional outcomes similar to ACCF. However, literature comparing oblique corpectomy with ACCF does not exist.

Artificial disc replacement (ADR) preserves motion across the operated segment and decreases the incidence of adjacent level disease but has fewer indicated roles in CSM (Fig. 4).

Although ADR is showing promising results in cases with soft disc and radicular symptoms, with a longer follow-up duration, its revision rate is 7.7%, which is very high with respect to the 2% revision rate of ACDF. Revision ADR has the disadvantages of increased costs to the patient and complications like heterotopic ossification which are seen in as high as 47% of the cases undergoing the procedure [32].

Moreover, as a result of limited usage of ADR in diseases involving >2 levels and the belief of many surgeons that fusion without decompression halts the progression of DCM, the use of ADR in DCM is currently restricted. A recent advance is combining ADR and ACDF forming the hybrid construct, or using ADR to supplement ACDF [33].

Posterior approaches: Although laminectomy is a good option in cases of disease involving multiple levels if performed without instrumented fusion, it can lead to post-laminectomy kyphosis. The procedure has fusion rates of 98% and revision rates even lesser than 1%. [34].

Split or skip laminectomy achieves decompression with preservation of paraspinal muscles and ligaments and has shown promising results for focal pathology [35].

Lou et al. performed a meta-analysis involving four studies with a sample size

of 241 and concluded that concerning the visual analog scale and rates of axial pain and muscle atrophy, skip laminectomy was superior to laminoplasty for the management of DCM[36].

Laminoplasty is a popular modality for OPLL and it does not involve instrumentation while also preventing post-laminectomy kyphosis.

Irrespective of the chosen surgical modality, the main objective of management is decompressing the canal to a diameter of at least 12 mm and restoring the CSF pulsation around the cord. Patients who are stable and have mild myelopathy are treated with conservative modalities, while surgery is needed for those with moderate, severe, or progressive DCM.

Although multiple variables are determining the post-surgical prognosis, studies regarding the significance of intraoperative blood pressure are limited. Studies employing intraoperative neuromonitoring show that raising blood pressures immediately after an observed reduced signal amplitude/increased latency improves the neuromonitoring signals and hence, indirectly, have demonstrated the significance of systemic blood pressure in maintaining the cord perfusion intraoperatively. However, we could not find a consensus among them, with respect to the minimum blood pressure recommendation. Furthermore, the rationale and physiology behind such episodes remain to be understood. Literature on the spinal cord blood flow pattern after an SCI has shown that maintaining a higher mean arterial pressure (MAP) favored better cord perfusion than a hypotensive state. MAP elevation after SCI is routinely done and is recommended as well by the AANS/CNS Joint Committee. The above observations prompted us to understand the significance of elevated MAP during the surgical procedure for the optimization of outcomes and

minimization of complications. Our study concluded that individualization of MAP should be done as per the preoperative average blood pressure and that a higher intraoperative MAP (preoperative MAP + 20 mmHg) during surgery for DCM resulted in comparatively better neurological outcomes [37].

## Future directions in DCM surgery

Computer-assisted navigation (CAN) delivers real-time data which is based on intraoperative radiography and registration points, and MRI coregistration gives output that is beyond the realm of direct vision [38]. Spine assist/renaissance (MAZOR X Stealth Edition Robotics Inc., Orlando, Florida) robot has shown an improved accuracy than fluoroscopic or navigation-guided techniques for the insertion of percutaneous or open pedicle screws [39] (Fig. 5).

CAN has been used for more precise placement of pedicle and lateral mass screws in the cervical spine and for anterior decompression in craniocervical junction cases which are complex, for placing screws in C1-C2, and in surgery of cervical spine tumors which have presented with an abnormal anatomy (Fig. 6).

MIS assisted with robotics and 3D navigation with pre-operative planning has been practiced in surgical intervention in DCM patients. Using robotics with real-time 3D navigation has decreased the number of screw misplacements, decreased the percentage of post-operative neurological deterioration, made spine surgery safer, and has decreased operative time. Diaz-Aguilar et al. reported a case with right hand weakness following right-sided paracentral disc herniation. They performed MIS with robotic-assisted posterior decompression, T1-T2 discectomy with posterior spinal fusion from C7 to T2. There was an immediate post-operative

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neurological recovery of upper limb weakness and post-operative imaging confirmed accurate placement of pedicle screws. They suggested that MIS with robotic assistance largely decreased the risk of screw misplacement and improved patient-related outcomes with lesser post-operative neurological worsening secondary to hardware impingement [40]. Nevertheless, their role in DCM surgery is currently limited.

## **Role of MIS**

Recently, endoscopic approaches are tried for decompression in diseases involving one or two levels [41]. Uniportal or biportal endoscopy for discectomy or foraminotomy is a part of posterior approaches (Fig. 7).

As unilateral biportal endoscopy involves using a viewing portal and a working portal, the degrees of freedom offered by it are more than uniportal endoscopy.

Wan et al. demonstrated posterior percutaneous full-endoscopic cervical discectomy under local anesthesia and managed 25 patients with soft disc herniation causing cervical radiculopathy using this method and showed that the results were promising [42]. Zhang et al. performed cervical microendoscopic laminoplasty (CMEL) in 45 patients, which involved endoscopy-assisted bilateral laminoplasty with retroposition of the spinous process ligament complex and deep extensor musculature along with fixation using bilateral titanium miniscrews and plates. The authors claimed that this newer approach provided a stable reconstruction of an expanded laminar arch with minimal insult to the adjacent soft-tissue structures as compared to open surgical approaches and that the CMEL procedure could be used as an efficient tool for managing DCM[43].

Saringer et al. used cervical anterior foraminotomy (uncoforaminotomy) for managing unilateral cervical radiculopathy which developed as a result of posterolateral disc herniations or spondylotic foraminal stenoses. This achieved a direct decompression of the affected nerve root anteriorly by removing the posterolateral spondylotic spur. The authors claimed that the patients could make an almost immediate return to full activity as there was decreased post-operative pain [44].

There was comparatively lesser damage to the disc and the retained cervical motion segment in the technique of percutaneous endoscopic anterior transcorporeal discectomy which was shown by Du et al. [45].

Using tubular retractors in ACDF enable using smaller incisions which are better cosmetically, use of lesser tractional force, and enhanced shielding of the prevertebral soft tissues from iatrogenic injury [46]. Tunnel corpectomy involves using a similar method, but the benefits of these techniques, with respect to conventional surgery with respect to long-term functional outcomes, are not yet proven [47].

## What's new in implants?

Although plastic surgeons and neurosurgeons have been using "bioabsorbable implants" for craniofacial reconstruction since a long time, the bioabsorbable plating system for ACDF is being used only since the past decade [48]. Although the advantages of these implants include elimination of artifacts on post-operative MRI and the interim stabilization till the graft union takes place or bone healing is seen, the results of these implants in the long term and their comparison with metal implants are not yet researched. ADR prostheses might be developed using polymers and ceramics in the near future and their design would provide a mechanical scaffold, would spare motion, and enable imaging using MRI. It would also better mimic the natural biomechanics of the spine [49].

Hydroxyapatite implant insertion inbetween the laminar bone and the lateral mass, without using sutures are a part of cervical open-door laminoplasty and initial results are promising with lesser operative times and acceptable outcomes [50].

## Newer insights into pathophysiology

Due to the unavailability of animal models, there is a limitation to studying the pathophysiology of DCM [51]. A study of the recently developed animal models which resemble cord compression in humans has led to an improvised comprehension of the pathophysiology of DCM (Fig. 8 and 9) (role of ischemia, inflammation, and apoptosis) [52].

With the progression of age, spondylotic changes occur at the macrovascular level, which compress the lumen of major feeding vessels supplying the spinal cord including the vertebral artery and the anterior spinal artery [53].

Microvascular cord compression leads to stretching and flattening and culminates in decreased vascularity of the lateral pial plexus [54].

Insult to the endothelial cells which is amplified by ischemia disrupts the blood-cord barrier (BCB) and causes the migration of inflammatory cells into cord parenchyma from the peripheral circulation through the disrupted BCB [55]. This activates the microglia and recruits the macrophages (Fig. 9). Initiation of the apoptotic pathway, which involves Fas (TNF receptor superfamily 6) and TNF-alpha and mitogen-activated protein kinases, takes place as a result of ischemia and BCB disruption leading to termination of neurons and oligodendrocytes. Glutamate excitotoxicity plays a role in CSM which is like the damage seen in the cord secondary to trauma. Activating the voltage-gated Na+ channel causes sodium ions influx, which leads to cytotoxic edema causing calcium ion influx from the Na+-Ca2+ exchange pump[56].

This leads to glutamate release into the

extracellular matrix, causing increased local cell apoptosis through excitotoxic means [57].

## Updates in clinical assessment

Although currently, the most widely used tool for assessing the patients of DCM is the mJOA [58], it is less sensitive with poor interobserver reliability. Nurick grading also has a poor sensitivity [59]. Tools such as GAITRite and GRASSP-M have been evolved for surpassing these limitations [60] and multiple studies are being carried out currently regarding shifting these assessment methods for use from the research laboratories to the outpatient clinic.

The "ten-second step test" is a quantitative assessment method described by Yukawa et al. which involves instructing patients to take a step by lifting their thighs parallel to the floor (hip and knee joints in 90° flexion) in the same place without holding onto any object for balance and counting the number of steps taken in 10 s. This test can also be used to assess the functional outcome of decompression surgery. The hand grip and release, triangle step test, and 9-hole peg test are other tests being used.

Technological advances like mobile phones can be used for continuous surveillance that is required to monitor the progression of mild DCM. "Myelopathy.org" is an online initiative and data obtained from Google Analytics shows that even elderly population, which is more susceptible to DCM is comfortable using these online platforms. Machine learning algorithms help in the identification of people with mild symptoms, and those who are candidates for surgery and show a positive response to decompressive surgeries [61].

## Robotics and machine learning algorithms

The treatment of patients with moderateto-severe DCM with a mJOA score of 15

or below is surgery but the treatment of patients who have mild DCM with a mJOA score between 15 and 17 is not yet clearly defined. Fehlings et al. conducted a retrospective subgroup analysis of data which were collected prospectively. One hundred and ninety-three patients with mild DCM who underwent decompressive surgery were enrolled in multicentric AO Spine CSM trials. Short-form-36 (SF-36), mental component summary (MCS), and physical component surgery (PCS) were analyzed at 1 year postoperatively. The changes in the score were dichotomized according to whether the response exceeded the minimally clinically important difference. Division of the data into a training set (75%) and a testing set (25%) was done. Several machine learning algorithms and logistic regression models were trained and optimized using a training set, and the outcome was evaluated using a testing set. The machine learning algorithm (ML) with the greatest area under the curve on the training set was selected. Among the many ML, generalized boosted model and earth models had a good predictive power with significant neurological and symptomatic improvement following decompression surgery as indicated by MCS and PCS score. They also indicated that females with low initial MCS had poor recovery in their MCS score post-surgery than males with similar initial MCS. They concluded that ML models had good predictive power and informed about the phenotypical difference in males and females and their recovery potentials post-surgery in mild DCM cases. They suggested that ML could be used for prediction on recovery potential in mild DCM cases post-surgery [62].

A post hoc analysis of patients with mild DCM enrolled in AOSpine CSM-NA/CSM-I study, who had mJOA scores between 15 and 17 was conducted by Fehlings et al. For separating the patients in two clusters, a k-means clustering algorithm was applied to baseline QOL SF-36 scores. Baseline variables and surgical outcomes (change in SF-36 scores at 1 yr.) were compared between clusters and a k-nearest neighbors (kNN) algorithm was used to assess the ability for classifying patients into the two clusters using significant baseline clinical variables. One hundred and eighty-five patients were eligible and two groups were generated by k-means clustering. The proportion of females in cluster 1 (44% vs. 28%, P = 0.029) and symptoms of neck pain (32% vs. 11%, P = 0.001), gait difficulty (57% vs. 40%, P = 0.025), or weakness (75% vs. 59%, P = 0.041) were more. Although there was no significant correlation between the baseline mJOA and baseline QOL or outcomes, a significantly more improvement in the disability (P = 0.003) and QOL (P < 0.001) scores postsurgery was seen in cluster 1. Cluster classification could be predicted with an accuracy of 71% using a kNN algorithm by neck pain, motor symptoms, and gender alone [61].

# Role of intraoperative ultrasound (IOUS)

At present, the focus is shifting toward the role of IOUS to assess the spinal cord expansion post-decompression and is thought to predict the potential for postoperative neurological gain. Chen et al. evaluated the role of IOUS in the prediction of adequate decompression. Twenty-seven patients undergoing French door laminoplasty were enrolled. mJOA scores were recorded before surgery and postoperatively at 1 year. IOUS images were used for the calculation of the MSCC after sufficient decompression and the patients were divided into adequate (MSCC  $\geq$  0.95) and inadequate (MSCC < 0.95) expansion groups as per the MSCC. They determined that the recovery rate of the mJOA score in the inadequate expansion group was much lower than that of the adequate expansion group

[63].

## Limitations

The current review is narrative in nature and is not a systematic review or a metaanalysis. The search was restricted to the PubMed database only and no other search engine was utilized. We limited the search to English language literature. Hence, although some articles on the current might have been missed, we have tried our level best to summarize all the available literature on current updates in spine surgery.

### Conclusion

Early diagnosis and management are of utmost importance and the management strategy should be personalized to each patient rather than a generalized approach toward DCM. DCM can vary according to degrees of neurological

affection as evident by radiological investigations. As early diagnosis is of paramount importance in DCM cases to prevent neurological worsening, the clinician must be aware of subtle signs and symptoms of early cases of DCM and should investigate thoroughly. With advances in radiology, identification of several chemical biomarkers, and clinical ancillary tests, it should be more advantageous in planning a personalized approach toward each patient. The management strategy, whether to opt for more aggressive surgical decompression or to give a conservative trial, depends on the degree of neurological affection and residual potential for spinal cord regeneration. Patient-specific factors and wishes would play an important role in the eventual treatment modality. Recently, an online poll has been utilized to better understand the needs of patients

who have lived with DCM. This multistakeholder consensus process is termed AO Spine Research objectives and Common Data Elements for DCM (RECODE-DCM) [64].

With a personalized approach, treatment outcomes can be enhanced in all the cases. The operative approach, pre- and post-operative care can be personalized and optimized for achieving favorable patient outcomes [65].

An extensive population of a country like ours will need care at decreased costs, which would thus affect the innovation in our specialty. As it is rightly said, "Change is the law of life," and so it is essential for all the stakeholders involved in innovation including the industry, surgeons, and scientists to work in collaboration for the patients.

**Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the Journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed. **Conflict of Interest:** NIL; **Source of Support:** NIL

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