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CERVICAL INJURIES AND TREATMENT (HJ KIM, SECTION EDITOR)

Degenerative cervical myelopathy

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Abstract Cervical myelopathy is the most common cause of acquired spinal cord compromise. The concept of degenerative cervical myelopathy (DCM), defined as symptomatic myelopathy associated with degenerative arthropathic changes in the spine axis, is being introduced. Given its progressive nature, treatment options have to be chosen in a timely manner. Surgical options include anterior discectomy and fusion (ACDF), anterior corpectomy and fusion (ACCF), arthroplasty (in highly select cases), posterior laminectomy with/without fusion, and laminoplasty. Indications for each should be carefully considered in individual patients. Riluzole, a sodium-glutamate antagonist, is a promising option to optimize neurologic outcomes post-surgery and is being examined in the CSM-Protect Randomized Controlled Trial. Preoperative risk assessment is mandatory for prognostication. Sagittal alignment is known to play an important role to optimize surgical outcome. Guidelines for optimal management of DCM are in process. In principle, all but the mildest cases of DCM should be offered surgery for optimal outcome.

Keywords Degenerative cervical myelopathy · Non-surgical treatment · Surgical treatment · Approach · Adjuvant therapy · Prognosis

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Introduction

Degenerative cervical myelopathy (DCM) is a leading cause of acquired spinal cord compromise [1]. Aside from various other underlying conditions, degenerative change to the vertebral column is by far the leading cause of DCM. Degeneration can happen in many locations in the spinal column, including arthropathy of facet joints and/or intervertebral discs as well as ligamentous aberration (hypertrophy, calcification, or ossification) in the ligamentum flavum and/or posterior longitudinal ligament (Fig. 1). We are introducing the comprehensive concept of DCM defined as symptomatic cervical myelopathy associated with a broad variety of degenerative changes of the extradural spinal tissues [2, 3•]. The major conditions falling under the umbrella term DCM have been previously well known as cervical spondylotic myelopathy (CSM) and ossification of the posterior longitudinal ligament (OPLL).

Establishing the standard of care for DCM is extremely important in our aging societies, given its increased prevalence in the elderly population. On the other hand, there are a number of controversies with regards to the management of DCM. Considerable numbers of studies with contradictory results are found in the literature and guidelines have yet to be developed. In the present paper, we reviewed the studies published in the last 3 years focusing on the treatment options and prognosis, and update the current strategies for the management of DCM.

Non-surgical treatment

Non-surgical treatments, also described as conservative treatments, currently used in the management of DCM include physical therapy, spinal injection, immobilization by collars, and cervical traction. Evidence for the efficacy of non-surgical treatment for DCM is scarce. Rhee et al. and Ghobrial et al. separately published systematic reviews with regard to non-

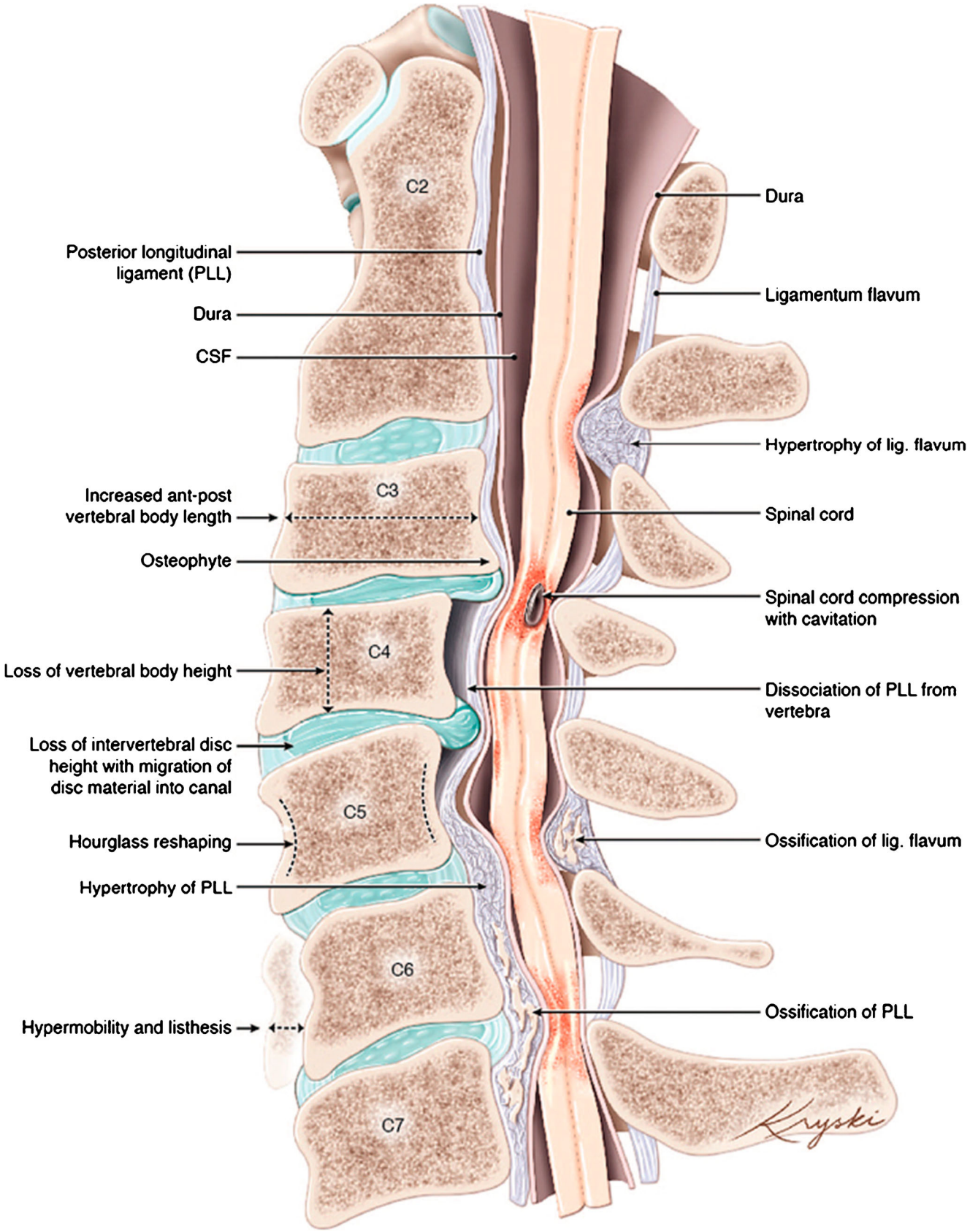

Fig. 1 An artistic depiction of the pathobiology of degenerative cervical myelopathy [3•]. Medical illustration by Diana Kryski (Kryski Biomedia), reused with permission. *PLL* indicates posterior longitudinal ligament, *CSF* cerebrospinal fluid

surgical management, and both concluded that the effectiveness may be greatly dependent on the individuals [4•, 5]. In particular, there is weak evidence that non-surgical treatment has some role in the management of mild myelopathy. Kadanka et al. performed a small randomized controlled trial and showed surgical outcome was not superior in mild myelopathy patients [6], but no further studies have been published and more research in the area is warranted. For moderate to severe myelopathy, surgery is generally the only treatment option given its progressive nature [7, 8]. Risk stratification of symptom progression at the early stage of presentation is also important in order to understand which cases are more likely to progress and are thus more likely to benefit from early intervention.

Surgical treatment

Anterior approach versus posterior approach

The fundamental strategies for the operative management of DCM are well established and most of them entail decompression with or without fusion of the spinal column. However, consensus has not been met in terms of whether surgical approach should be made from the anterior or posterior direction. As spinal cord compromise is caused by various lesions in DCM, compression may occur anteriorly (disc, osteophyte, or OPLL), posteriorly (hypertrophy or ossification of ligamentum flavum), and the concept of decompression performed from the side of major compressive factors seems to be straightforward and well accepted. For example, it may be that superior outcomes result from anterior decompression for OPLL with more than 60 % of canal occupying ratio [9–12]. However, DCM can frequently be associated with multiple degenerative lesions and compression can be circumferential. One of the advantages of posterior surgery is the ease of accessing multilevel compression [13]. Therefore, determining the approach is not always straightforward. Common anterior approach surgeries include discectomy and fusion (ACDF), corpectomy and fusion (ACCF), and arthroplasty, while laminectomy with or without fusion and laminoplasty are used for posterior surgery. Two illustrative cases are shown for anterior approach (Fig. 2) and posterior approach (Fig. 3). Although previous literature did not have a consensus on the superiority of one approach over another [14, 15], more recent meta-analyses have shown that multilevel anterior surgery up to three levels is superior to posterior surgeries in some aspects including post-operative outcome and alignment but also that anterior surgery is associated with higher rate of reoperation [13, 16–19, 20•]. Overall surgical complication rates were also reported to be higher in anterior surgery than in posterior surgery, but the spectrum of complications is very different between the two groups and it should be interpreted with caution. Comparative studies are limited, and the conclusions drawn are mixed likely because of their selection biases [21–25]. Further investigations by multicenter prospective controlled trials are warranted.

Anterior decompression and fusion versus arthroplasty

Smith and Cloward first developed anterior decompression with disc removal [26, 27]. Today, it usually entails putting a graft in the disc space and adding a plate for fixation. However, for a single level lesion, disc replacement can be a good alternative to fusion surgery. Instead of conventional ACDF, by inserting the prosthesis in the disc, its motion sparing technique can theoretically avoid adjacent segment degeneration and could be potentially promising for younger patients. Long-term outcomes for arthroplasty are still under investigation, and the implant related costs appear to be higher in comparison to anterior fusions. Both prospective [28–33] and retrospective studies [34–36] have been reported, and meta-analyses showed that disc replacement is equivalent or superior to fusion surgery [37–41]. Its superiority in cost-effectiveness is still questionable [42–44] and long-term studies will be needed. Of note, arthroplasty is principally an option in patients with DCM who have minimal spondylosis and cord compression from a soft disc herniation—this is an unusual clinical scenario.

Anterior fusion by discectomy versus corpectomy

For a multilevel stenosis, ACCF can be considered instead of multiple ACDF. With the same surgical approach as ACDF, ACCF entails vertebral body resection with disc removal at both ends as well as reconstruction by a strut graft instead of using a spacer in the disc space in ACDF. Corpectomy is especially useful in cases of bony compression at the level of the vertebral body. It also enables wide decompression and provides a satisfactory amount of autograft. Compared to multilevel ACDFs, ACCF fusions rely on bony healing at two interfaces adjacent to the graft and, theoretically, may lead to higher fusion rates. However, there may be a higher rate of complications with a corpectomy including excessive bleeding and graft dislodgement. For these reasons, its superiority has not been established. Only a small number of retrospective analyses have been done [45–50], and no randomized trials have been reported. Several meta-analyses indicated that ACDF is associated with less surgical complications and better post-operative alignment [51–55].

Laminectomy with or without fusion versus laminoplasty

The laminoplasty procedure was originally developed by Japanese surgeons as an effective treatment option for congenital cervical stenosis [56, 57]. Its aim is to expand and

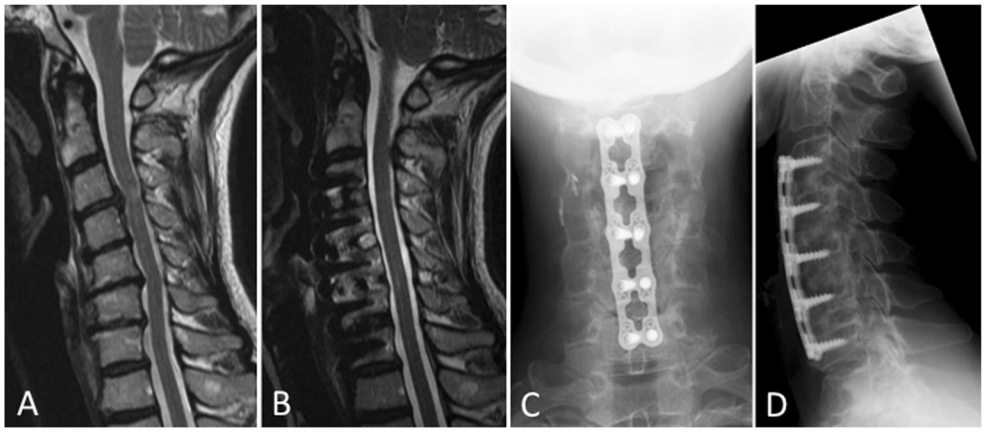

Fig. 2 An illustrative case of anterior surgery. Multiple level spinal cord compression by degenerative discs with mild kyphosis was treated by 4-level anterior cervical discectomy and fusion (C3-7). Optimal decompression was achieved in each level and the post-operative alignment was lordotic by the reconstruction. **a** Preoperative T2 weighted MRI sagittal image, **b** post-operative T2 weighted MRI sagittal image, **c** post-operative antero-posterior radiograph, **d** post-operative lateral radiograph

reconstruct the posterior arch and to prevent post-operative kyphosis (a frequent complication seen post-laminectomy) [58]. Disadvantages of laminoplasty are the technical difficulty in foraminal decompression, potential neurological damage, and higher cost when utilized with the implants. Lately, a newer modification of conventional laminectomy known as "skip laminectomy" which involves preserving muscle attachments to the spinous processes has been introduced, and its effectiveness has been compared with laminoplasty [59–61]. Based on these facts, literature reviews have concluded that the superiority of laminoplasty has not been justified [62, 63].

Laminectomy with instrumented fusion is more commonly performed in North America. Using the same but wider exposure than laminoplasty, fixation is usually achieved by lateral mass screw fixations in the subaxial spine and occasionally also pedicle screw fixations in the upper thoracic spine. It results in the loss of post-operative mobility in the cervical spine as compared to laminoplasty, but it more effectively prevents post-operative kyphosis. Therefore laminectomy and fusion is preferred over laminoplasty in those with preoperative kyphosis or potential instability [64–66]. Otherwise, its selection is usually based on surgeons' preference and comparative studies are very limited [67, 68]. Recent systematic reviews have indicated that they are equally effective with similar post-operative outcome, but laminectomy and fusion may result in better alignment in the long term [69–71].

Complications

Complications specific to surgeries for DCM include dysphagia, pseudarthrosis, C5 palsy, and axial pain. Numerous risk factor analyses have been published recently [72••].

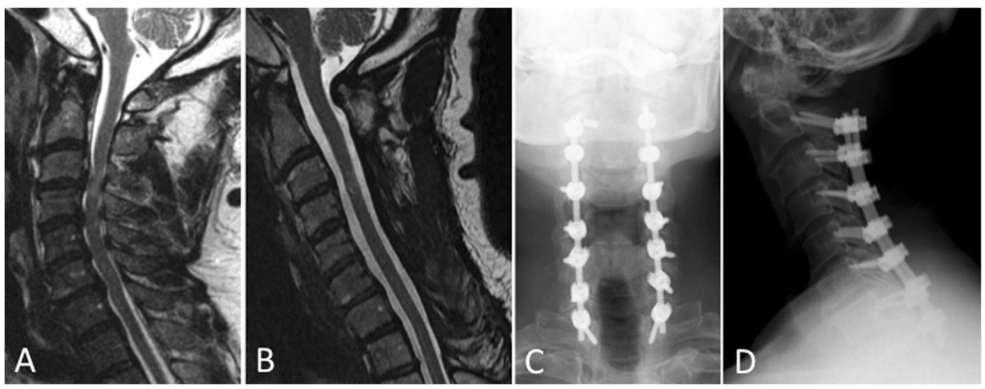

Fig. 3 An illustrative case of posterior surgery. Multiple level spinal cord compression by degenerative discs and ligamentum flavum hypertrophy was treated by posterior laminectomy and fusion (C2-T1). Solid fixation were achieved at both ends of the construct by C2 pars screws and T1 pedicle screws. **a** Preoperative T2 weighted MRI sagittal image, **b** post-operative T2 weighted MRI sagittal image, **c** post-operative antero-posterior radiograph, **d** post-operative lateral radiograph

Dysphagia is a well-known complication after anterior surgeries [73]. Multilevel surgery and bone morphogenetic protein have been raised as risk factors [74, 75]. Newer low profile implants and perioperative steroid administration were shown to be effective in reducing dysphagia by reducing retropharyngeal edema [76, 77]. Non-union rate after ACDF has been reported to be 2.6 %, and use of autograft resulted in better fusion rates in comparison to allograft [78]. C5 palsy is reported both in anterior and posterior surgery, although the risk is higher in posterior laminectomy and fusion [79]. The other risk factors include preoperative foraminal stenosis, OPLL, and asymmetric decompression [80–82]. C5 palsy may be preventable by prophylactic foraminotomy [83]. Axial pain is commonly reported as a posterior neck and scapular pain after laminoplasty. Attempts have been made to decrease the rate by preserving the muscle attachments to the spinous processes [84, 85].

In addition to these, cervical spine surgery can cause rare but devastating complications due to its anatomical proximity to critical structures. Esophageal injury is one of these and can be caused by direct injury or by forceful retraction during the anterior approach. It can also occur as a late complication related to malpositioned screws or plates. Unless treated adequately in a timely fashion, it results in fatal infections including mediastinitis [86]. In a cross-sectional study led by the Cervical Spine Research Society, another complication, vertebral artery injury, was found to occur in 0.07 % of their members' cases both with anterior and posterior surgeries [87]. Vertebral artery injury can also be associated with aberrant vasculature and thus careful radiographic preoperative planning is warranted. Although direct injury to the carotid artery is extremely rare, the meticulous hemostasis of its branches is required in order to avoid hematoma formation. In terms of neurological structures, the recurrent laryngeal nerve and the sympathetic chain are at risk. Transient hoarseness after the anterior approach is almost universal in patients after this surgery, but permanent vocal cord palsy can also occur, related to the recurrent laryngeal nerve. The right side approach may increase risk of this complication while decuffing of the endotracheal tube may decrease the risk [88]. Damage to the sympathetic chain can cause Horner's syndrome, which is characterized by ptosis, meiosis, and anhidrosis.

Adjuvant therapy

Neuroprotective agents may become a common mode of augmenting surgical treatment. Riluzole is an anticonvulsant that functions as a sodium-channel blocker. It is thought to attenuate the ischemia-related excitotoxicity in spinal cord injury models. A phase I trial for traumatic spinal cord injury has already been published, and it showed the preferable recovery in those who received riluzole at 90 days after admissions [89]. Although there are certain differences in pathobiology from traumatic spinal cord injury, ischemia due to the anterior vessel compressions and the deformation in microangiostructure are also the main mechanisms of neural damage in DCM and it is reasonable to extrapolate its effectiveness in these populations. It has already been shown to have promising results in a rodent model of CSM [90, 91]. Fehlings et al. have started a multicenter double-blinded randomized controlled trial to assess the potential neurological benefits as a complementary strategy to surgical decompression [92•]. They are enrolling patients with degenerative-related spinal cord compression and a modified Japanese Orthopaedic Association (mJOA) score of less than 14 who underwent surgical decompression, and randomly assigning to the riluzole group or the placebo group. The riluzole group receives a dose of 50 mg every 12 h for 14 days preoperatively and 28 days post-operatively. The comparison of neurological recovery will be made at 6 months post-operatively using mJOA as a primary outcome.

Prognosis and outcomes

Predictors of outcome

Since the surgical indication for DCM is determined based on the clinical symptoms and the radiographic findings as well as patients' characteristics and demands, it is important for the surgeons to be able to predict the outcome and offer the best solutions at the appropriate timing for each patient. Although multiple studies have been published, the clinical predictors for poor outcome after decompression surgery were similar in many of them. Worse preoperative neurological status (baseline mJOA), gait impairment, smoking, older age, psychiatric comorbidities, and longer duration from the onset of symptoms to surgical treatment have been flagged [12, 93, 94••, 95–101]. Tetreault et al. created a prediction model using the covariates raised above in 278 patients enrolled in the AOSpine CSM North American study and validated this in 479 patients in AOSpine CSM International study [94••, 98, 102]. Radiographically, T2 signal hyperintensity on MRI and more than 60 % of occupying ratio in OPLL are also noted [12, 103–105].

Importance of sagittal balance/alignment on treatment/outcomes

Cervical sagittal alignment with optimal lordosis has been known to be associated with post-operative quality of life in fusion surgery, but it is now revealed that it also affects the severity of myelopathy symptoms and post-operative outcomes after the decompression [106]. Kyphosis is thought to play an important role in the development of DCM by spinal cord tethering by the dentate ligaments and nerve roots,

and also by angiostructural change [107]. Indeed, Smith et al. and Mohanty et al. showed that mJOA correlated with C2-C7 sagittal vertical axis in preoperative patients [108, 109]. Preoperative kyphosis has also been identified as a risk factor for inferior surgical outcomes both in anterior and posterior surgery [12, 65, 110, 111, 112•]. Although it is still unclear whether post-operative realignment has a positive impact on the outcome, we should note that post-operative outcome was better after anterior surgery for DCM with kyphosis in Shamji et al.'s study [112•]. Aggressive realignment by posterior reconstruction should be avoided since it can result in the foraminal compression whereas anterior reconstruction increases disc height and opens the foramens.

Future directions

Establishing the standard of care for DCM is challenging. First, the pathology of DCM consists of multiple factors, each of which is may have an ideal approach and the treatment modality has to be chosen differently. Second, diversity in patients backgrounds is increasing, especially considering the aging society prevailing internationally. Their goals and demands have to be carefully considered depending on the risks associated with the treatment options they possess. Finally, we now have more surgical options due to the development of newer techniques and technologies. Numerous authors have advocated that they all showed the promising results in individual studies, but comparative evidence and long-term results are still lacking. Furthermore, the optimal timing for the surgical intervention is unclear. Given that duration of the symptoms has a negative impact on the surgical outcome, timely intervention is mandatory to obtain the optimal results. Clear thresholds of symptoms and durations should be determined so that surgeons can make evidence-based decisions. Efforts are being made to establish the management guideline for DCM. The expert meetings have been led by Fehlings et al. under the auspices of AOSpine North America and the Cervical Spine Research Society. These guidelines are expected to make a significant contribution to help all health care providers involved in care of DCM to provide the best management.

Conclusions

Despite considerable progress having been made in terms of deeper understanding of cervical myelopathy and development of safe and effective treatment options, there still remain many controversies with regard to optimal management of cervical myelopathy. Surgeons have to be aware of pros and cons of each strategy and its prognosis and should be able to propose the best possible care for the individual patients. To choose the optimal treatment in a timely fashion, the establishment of guidelines is strongly indicated.

Compliance with ethical standards

Conflict of interest So Kato and Michael Fehlings declare that they have no conflict of interest.

Human and animal rights and informed consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
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