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A Clinical Practice Guideline for the Management of Patients With Degenerative Cervical Myelopathy: Recommendations for Patients With Mild, Moderate, and Severe Disease and Nonmyelopathic Patients With Evidence of Cord Compression

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Abstract

Study Design: Guideline development.

Objectives: The objective of this study is to develop guidelines that outline how to best manage (1) patients with mild, moderate, and severe myelopathy and (2) nonmyelopathic patients with evidence of cord compression with or without clinical symptoms of radiculopathy.

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Methods: Five systematic reviews of the literature were conducted to synthesize evidence on disease natural history; risk factors of disease progression; the efficacy, effectiveness, and safety of nonoperative and surgical management; the impact of preoperative duration of symptoms and myelopathy severity on treatment outcomes; and the frequency, timing, and predictors of symptom development. A multidisciplinary guideline development group used this information, and their clinical expertise, to develop recommendations for the management of degenerative cervical myelopathy (DCM).

Results: Our recommendations were as follows: (1) "We recommend surgical intervention for patients with moderate and severe DCM." (2) "We suggest offering surgical intervention or a supervised trial of structured rehabilitation for patients with mild DCM. If initial nonoperative management is pursued, we recommend operative intervention if there is neurological deterioration and suggest operative intervention if the patient fails to improve." (3) "We suggest not offering prophylactic surgery for non-myelopathic patients with evidence of cervical cord compression without signs or symptoms of radiculopathy. We suggest that these patients be counseled as to potential risks of progression, educated about relevant signs and symptoms of myelopathy, and be followed clinically." (4) "Non-myelopathic patients with cord compression and clinical evidence of radiculopathy with or without electrophysiological confirmation are at a higher risk of developing myelopathy and should be counselled about this risk. We suggest offering either surgical intervention or nonoperative treatment consisting of close serial follow-up or a supervised trial of structured rehabilitation. In the event of myelopathic development, the patient should be managed according to the recommendations above."

Conclusions: These guidelines will promote standardization of care for patients with DCM, decrease the heterogeneity of management strategies and encourage clinicians to make evidence-informed decisions.

Keywords
guidelines, degenerative cervical myelopathy, cervical spondylotic myelopathy, spinal cord compression

Summary of Recommendations

We recommend surgical intervention for patients with severe DCM
Quality of Evidence: Moderate
Strength of Recommendation: Strong

We recommend surgical intervention for patients with moderate DCM.
Quality of Evidence: Moderate
Strength of Recommendation: Strong

We suggest offering surgical intervention or a supervised trial of structured rehabilitation for patients with mild DCM. If initial nonoperative management is pursued, we recommend operative intervention if there is neurological deterioration and suggest operative intervention if the patient fails to improve.
Quality of Evidence: Very low to low
Strength of Recommendation: Weak

We suggest not offering prophylactic surgery for non-myelopathic patients with evidence of cervical cord compression without signs or symptoms of radiculopathy. We suggest that these patients be counseled as to potential risks of progression, educated about relevant signs and symptoms of myelopathy, and be followed clinically.
Quality of Evidence: No identified evidence; based on clinical expert opinion
Strength of Recommendation: Weak

Nonmyelopathic patients with cord compression and clinical evidence of radiculopathy with or without electrophysiological confirmation are at a higher risk of developing myelopathy and should be counselled about this risk. We suggest offering either surgical intervention or nonoperative treatment consisting of close serial follow-up or a supervised trial of structured rehabilitation. In the event of myelopathic development, the patient should be managed according to the recommendations above.
Quality of Evidence: Low
Strength of Recommendation: Weak

Introduction

Degenerative cervical myelopathy (DCM) is a progressive spine disease and the most common cause of spinal cord dysfunction in adults worldwide.[1] With the aging of the global population, clinicians will be required to manage an increasing number of patients with degenerative changes to their spine and varying stages of myelopathy.[2] Currently, there are no guidelines that outline how to best manage patients with mild (defined as a modified Japanese Orthopedic Association (mJOA) score of 15-17), moderate (mJOA = 12-14), or severe (mJOA $\leq$ 11) disease, or nonmyelopathic patients with evidence of cord compression.[3] This guideline provides evidence-based recommendations to specify appropriate treatment strategies for these four patient populations. The systematic reviews aimed to (1) help identify patients at high risk of neurological deterioration, (2) define the role of non-operative and operative management in each patient group, and (3) determine which patients are most likely to benefit from surgical intervention. The ultimate goal of these guidelines is to improve outcomes and reduce morbidity in patients with DCM by promoting standardization of care and encouraging

clinicians to make evidence-informed decisions. An introductory article in this focus issue provides further background information on DCM and summarizes the rationale, scope, and specific aspects of care covered by this guideline. This article is titled "A Clinical Practice Guideline for the Management of Degenerative Cervical Myelopathy: Introduction, Rationale and Scope."

Methods

This guideline was developed under the auspices of AOSpine North America and the Cervical Spine Research Society. A multidisciplinary guideline development group (GDG) was formed and consisted of clinicians from a broad range of specialties. The GDG was solely responsible for guideline development and was editorially independent from all funding sources. Members were required to disclose financial and intellectual conflicts of interest (Appendix, Chapter 2). A guideline development protocol, based on the Conference on Guideline Standardization (COGS) checklist,[4,5] was created to outline the rationale and scope of the guideline and to direct its development. Systematic reviews were conducted based on accepted methodological standards to summarize the evidence informing the recommendations. Details of specific methods used for each topic are outlined in the individual reviews included in this focus issue. Methods outlined by the Grading of Recommendation, Assessment, Development and Evaluation (GRADE) Working Group were used to assess the overall quality (strength) of evidence for critical outcomes.[6,7] The GRADE Guideline Development Tool was used to document the process, rank the importance of outcomes, weigh the benefits and harms of various options, and determine the strength of recommendation.[8-11] Methodologists with no financial or intellectual conflicts of interest worked closely with clinical authors to conduct the systematic reviews and provided methodological expertise on the guideline development process. Guideline development methods are provided in another article included in this focus issue: "Guidelines for the Management of Degenerative Cervical Myelopathy and Acute Spinal Cord Injury: Development Process and Methodology."

Clinical Recommendations

Part 1. Clinical Population: Patients With Severe DCM

Population Description: Patients with mJOA = 0 to 11
Key Question: Should operative management be used to treat patients with severe DCM?
Recommendation: We recommend surgical intervention for patients with severe DCM
Quality of Evidence: Moderate
Strength of Recommendation: Strong

Evidence Summary

A systematic review of the literature was conducted to determine (1) the expected functional, disability and pain outcomes following surgical intervention, (2) whether these expected outcomes depend on preoperative disease severity or duration of symptoms, and (3) what are the complications associated with surgery. Thirty-two studies met inclusion criteria and were summarized in this review: 9 prospective comparative studies, 4 randomized controlled trials, and 19 prospective case series. Of these, 21 reported on change in JOA or mJOA (low/moderately low risk of bias in 14, moderately high risk of bias in 7), 7 on neck disability index (NDI) (low/moderately low risk of bias in 4, high/moderately high risk of bias in 3), 5 on Nurick score (low/moderately low risk of bias in 2, high/moderately high risk of bias in 3), and 5 on visual analog scale (VAS) (low/moderately low risk of bias in 3, moderately high risk of bias in 2). The studies with moderately high risk of bias either had undefined or poor follow-up rates (<80%).

Based on our results, pooled standard mean differences showed a large effect for improvement in JOA or mJOA from baseline at short-, medium-, and long-term follow-up: 6 to 12 months (1.92; 95% CI = 1.41-2.43), 13-36 months (1.40; 95% CI = 1.12-1.67), and ≥36 months (1.92; 95% CI = 1.14-2.69); all *P*s <.00001. Patients also exhibited clinically meaningful improvements in the NDI and Nurick scores from baseline at short-, medium-, and/or long-term follow-up: 6 to 12 months (Nurick = 1.42; 95% CI = 1.11-1.74; NDI = 18.02; 95% CI = 11.02-25.02), 13 to 36 months (Nurick = 1.06; 95% CI = 0.69-1.43; NDI = 19.71; 95% CI = 14.01-25.42), and ≥36 months (NDI = 23.21; 95% CI = 11.84-34.58); all *P*s <.0001). Pooled standard mean differences for the VAS were also large at all 3 follow-up periods: 6 to 12 months (32.74; 95% CI = 18.39-47.10), 13 to 36 months (32.55; 95% CI = 21.37-43.72), and ≥36 months (40.00; 95% CI = 37.01-42.99); all *P*s <.0001. The majority of studies included in the systematic review on operative treatment consisted of patients with moderate to severe myelopathy: mJOA/JOA (7.4-12.9), NDI (26.35-55.20), Nurick (2.85-3.3), and VAS (32-71.6). Only 1 study by Fehlings et al[12] evaluated surgical outcomes in patients with mild, moderate and severe disease using the criteria set by these guidelines. Based on their results, patients with a mJOA<12 improved by 4.91 (95% CI = 4.34-5.49) on the mJOA, by 12.53 (95% CI = 8.05-17.02) on the NDI, and by 1.74 (95% CI = 1.41-2.08) on the Nurick score. All of these changes were statistically significant and exceeded reported minimal clinically important differences (MCIDs) of these metrics.

The cumulative incidence of complications is low for patients treated surgically for DCM (14.1%; 95% CI = 10.1%-18.2%). Specific complications include axial pain (5.6%; 95% CI = 3.8%-7.5%), laryngeal nerve injury/dysphagia (2.2%; 95% CI = 1.4%-3.0%), instrumentation/graft complication (2.0%; 95% CI = 1.3%-2.7%), C5 radiculopathy or palsy (1.9%; 95% CI = 1.4%-2.4%), pseudoarthrosis (1.8%; 95% CI = 0.9%-2.6%), infection (1.5%; 95% CI = 1.0%-2.1%), adjacent segment disease (1.5%; 95% CI = 0.3%-2.7%), dural tear/cerebrospinal fluid leak (1.4%; 95% CI = 0.8%-1.9%), worsening of myelopathy (1.3%; 95% CI = 0.5%-2.1%), hematoma (0.9%; 95% CI = 0.4%-1.4%), new radiculopathy/palsy (not C5) (0.9%; 95% CI = 0.0%-1.7%),

neurologic deterioration (0.9%; 95% CI = 0.3%-1.5%), delayed wound healing (0.8%; 95% CI = 0.0%-1.7%), dysphonia (0.7%; 95% CI = 0.1%-1.2%), postoperative deformity (0.5%; 95% CI = 0.0%-1.2%), and bed sores (0.8; 95% CI = 0.0%-2.3%). Cumulative incidences of major complications are also low: death (0.3%; 95% CI = 0.0%-0.5%), stroke/transient ischemic attack (0.3%; 95% CI = 0.0%-0.7%), esophageal injury (0.0%; 95% CI = 0.0%-2.9%), cardiopulmonary events (3.3%; 95% CI = 1.3%-5.3%), fracture (2.1%; 95% CI = 0.0%-4.5%), and reoperation/revision surgery (1.4%; 95% CI = 0.6%-2.1%). Unfortunately, studies did not report rates of complications based on preoperative myelopathy severity.

A second systematic review was conducted to determine (1) the change in function, pain and quality of life following structured non-operative treatment, (2) the variability of change in function, pain and quality of life following different types of structured nonoperative treatments, (3) the differences in outcomes observed between certain subgroups (eg, baseline severity score, duration of symptoms), and (4) negative outcomes and harms resulting from structured non-operative treatment. Eight studies (1 randomized controlled trial, 3 prospective cohort studies, and 4 retrospective cohort studies) met the inclusion criteria and were summarized in this review. The mean preoperative JOA scores ranged from 11.1 to 14.6; the evidence from this review is therefore more applicable for patients with moderate and mild myelopathy. Furthermore, the GDG agreed that the results of nonoperative management are less clinically relevant in the severe population.

In summary, there is moderate strength of evidence that surgical intervention for DCM results in significant improvements in clinical status as assessed by the mJOA or JOA at short-, medium-, and long-term follow-up. Based on low strength of evidence, rates of C5 radiculopathy or palsy and infection were low following surgery for DCM. Furthermore, very low strength of evidence suggested low pooled cumulative incidences of dural tear/cerebrospinal fluid leak, worsening of myelopathy, death, pseudoarthrosis, and implant complications.

With regard to cost-effectiveness, 2 studies were identified that evaluated the cost-utility of surgery in Canadian patients enrolled in the AOSpine North America and/or International studies. The first study (based on the North America study) estimated the cost of surgery to be $21 066.44, with an incremental cost-utility ratio (ICUR) of $32 916 per quality-adjusted life year (QALY).[13] A second study by Witiw et al[14] (based on the North America and International studies) conducted a more rigorous cost-utility analysis using a 2-arm, Markov State Transition model where values for subjects undergoing surgery were compared with estimated counterfactual outcomes of initial conservative management.[14] In a primary model, the lifetime ICUR was determined to be $11 496/QALY gained for surgical intervention, an estimate considered very cost-effective according to criteria defined by the World Health Organization (WHO). Further testing using a Monte Carlo probabilistic sensitivity analysis revealed that 97.9% of estimates fell within the WHO threshold, suggesting robustness to variability in the parameter estimates. To supplement this testing, a highly conservative assumption that individuals undergoing initial nonoperative management would not experience any neurologic decline over their lifetime was added to the model. In this scenario, the ICUR was calculated as $20,548/QALY gained with 94.7% of estimates falling within the WHO threshold; this finding further supports the cost-effectiveness of surgical intervention. Unfortunately, these analyses only explored the cost-effectiveness of surgery in Canada and did not stratify their samples based on preoperative myelopathy severity. This lack of generalizable evidence on cost-effectiveness highlights a significant knowledge gap in the literature; as a result, much of the discussion related to resource requirements was based on professional opinion.

Rationale for Recommendation

The outcomes most critical for decision-making were change in mJOA or JOA following surgery and rates of major complications. Major complications were defined as any surgery-related adverse event that resulted in permanent morbidity, prolongation of hospital stay, or reoperation. The GDG agreed that the results from the systematic review on nonoperative treatment are less relevant to answer this question as most studies did not evaluate outcomes in severe patients. The majority of the GDG selected that the overall certainty of the evidence was moderate given the large effect size of the pooled estimate from several prospective studies.

The GDG believed that there was no important uncertainty or variability about how much key stakeholders value the main outcomes. Patients and clinicians would similarly value improvement in functional status and a low risk of complications. Although the cost-effectiveness of surgery in these patients is largely unknown, the GDG agreed that payers would also value these main outcomes due to a likely reduction in future management costs and financial burden.

The GDG agreed that the anticipated desirable effects (ie, improved mJOA or JOA) were probably large and the anticipated undesirable effects (ie, treatment complications) were probably small. Pooled standard mean differences showed a large effect for improvement in functional status and disability from baseline at short-, medium-, and long-term follow-up. Furthermore, the rates of overall complications and of major complications are low following surgery in this population. The GDG acknowledges that the studies included in the systematic review on operative treatment did not stratify their sample based on preoperative myelopathy severity and that the risk of complications may be slightly higher in patients with more extensive degenerative pathology. Given these explanations, the GDG agreed that the desirable effects are probably large relative to the undesirable effects.

In the absence of evidence, the GDG used their clinical expertise to discuss the resources required to surgically manage patients with severe myelopathy. Although the GDG confirmed the resources are probably not small, they also agreed that

surgery may result in substantial cost savings due to long-term improvements in quality of life, impairment, and disability. As a result, the majority of the GDG (n = 14) agreed that the incremental cost is probably small relative to the net benefit of surgery. Twelve members, however, argued that, in the absence of evidence on cost-effectiveness, the cost-benefit ratio is uncertain.

The GDG believed that a recommendation for surgery in patients with severe myelopathy would probably reduce health inequities; this decision was made under the assumption that policy makers would fund initiatives to ensure patients with severe myelopathy have improved access to surgical intervention. The GDG agreed that the option of surgery would probably be acceptable to the majority of stakeholders due to anticipated positive outcomes, a low risk of complications and a likely reduction in overall management costs (probably yes = 16, yes = 11). Finally, the option of surgical intervention for patients with severe myelopathy is probably feasible to implement (probably yes = 12, yes = 11); potential barriers include an accurate diagnosis of myelopathy, a timely referral for surgical consultation, patient access to care and high costs.

Considering all these factors, the GDG voted that the desirable consequences probably outweigh the undesirable consequences in most settings (probably outweigh = 16, outweigh = 9); this led to the formation of a strong recommendation for surgery in patients with severe myelopathy.

Part 2. Clinical Population: Patients With Moderate DCM

Population Description: Patients with a mJOA = 12 to 14
Key Questions: Should operative management be used to treat patients with moderate DCM?
Recommendation: We recommend surgical intervention for patients with moderate DCM.
Quality of Evidence: Moderate
Strength of Recommendation: Strong

Evidence Summary

The evidence used for this recommendation was derived from the systematic reviews on the efficacy and safety of nonoperative and surgical management for the treatment of DCM. Pooled mean improvements on the mJOA or JOA, Nurick, NDI, and VAS following surgery are provided in the evidence summary for part 1. Unfortunately, only 1 study by Fehlings et al[12] compared surgical outcomes between patients with mild, moderate, and severe disease using the criteria set by this guideline. Based on their results, patients with a mJOA between 12 and 14 improved by 2.58 (95% CI = 2.07-3.09) on the mJOA, by 9.79 (95% CI = 5.90-13.68) on the NDI, and by 1.51 (95% CI = 1.22-1.81) on the Nurick score. All these changes were statistically significant and exceeded the reported MCIDs for these metrics. Cumulative incidences of surgical complications are also low and are reported in part 1. Unfortunately, studies did not report rates of complications based on preoperative myelopathy severity.

The systematic review on operative management also evaluated whether surgical outcomes were influenced by duration of symptoms or preoperative disease severity. Three studies evaluated differences in functional recovery based on the mJOA or JOA between patients with varying duration of symptoms ($\leq$12 and >12 months; <6, 6-12, >12 months).[15-17] Based on their results, the degree of improvement was not significantly different between these patient subgroups. In contrast, a fourth study reported that a longer duration of symptoms was associated with reduced odds of achieving a mJOA score $\geq$16 at 1-year follow-up (odds ratio [OR] = 0.78, 95% CI = 0.61-0.997, P = .048).[18] Four studies evaluated the relationship between preoperative myelopathy severity and postoperative neurological outcomes.[12,18-20] In a study by Fehlings et al,[12] patients with severe myelopathy (mJOA<12) demonstrated the greatest improvement (4.91; 95% CI = 4.34-5.49) on the mJOA, while patients with mild disease (mJOA $\geq$ 15) improved the least (1.29; 95% CI = 0.70-1.87).[12] Conversely, Chibbaro et al[19] reported that a similar percentage of patients with either moderate (mJOA = 10-13) or severe (mJOA = 5-9) myelopathy exhibit neurological improvement on the mJOA score. Two other studies determined that patients with more severe myelopathy are less likely to achieve a score $\geq$16 or a postoperative improvement of 2 or more points on the mJOA.[18,20]

In the systematic review on non-operative treatment, the mean preoperative JOA scores ranged from 11.1 to 14.6. Response to treatment was minimal, with change scores ranging from 0 to 2.3. Only a single study by Matsumoto et al[21] reported a mean change in JOA score of $\geq$2 points at final follow-up (mean = 47 months); their sample, however, only consisted of patients with myelopathy secondary to soft disc herniation. The proportion of patients who converted to surgery following failed nonoperative care ranged from 23% to 54%. The GDG agreed that the results from the systematic review on nonoperative management are less relevant in patients with moderate myelopathy and that these outcomes are not critical for decision making.

In summary, there is moderate strength of evidence that surgical intervention for DCM results in significant improvements in clinical status as assessed by change in mJOA or JOA scores at short-, medium-, and long-term follow-up. Based on low strength of evidence, rates of C5 radiculopathy or palsy and infection were low following surgery for DCM. Furthermore, very low strength of evidence reported low pooled cumulative incidences of dural tear/cerebrospinal fluid leak, worsening of myelopathy, death, pseudoarthrosis, and implant complications.

It is also crucial to consider important predictors of outcomes when devising appropriate treatment strategies. Based on a study by Tetreault et al,[18] the odds of achieving a postoperative mJOA score $\geq$16 (1) decreased by 22% (OR = 0.78, 95% CI = 0.61-0.997, P = .048) when a patient moved from a shorter to a longer duration of symptoms group ($\leq$3 months; >3 but $\leq$6 months; >6 but $\leq$12 months; >12 but $\leq$24 months; >24 months) and (2) were 1.22 times greater (OR = 1.22; 95% CI = 1.05-1.41, P = .0084) for every 1-point increase in

preoperative mJOA. Furthermore, patients with more severe preoperative impairment were less likely to exhibit a postoperative improvement of 2 or more points on the mJOA scale at 18-months follow-up (OR: 0.72; 95% CI = 0.66-0.92).[20] The rationale behind this finding is that severe and long-standing compression of the spinal cord may result in histological damage that cannot be reversed through decompression. In contrast, moderate strength of evidence suggested that the improvement in mJOA score from baseline is smaller for patients with mild myelopathy (1.29; 95% CI = 0.70-1.87) preoperatively than those with moderate (2.58; 95% CI = 2.07-3.09) or severe (4.91; 95% CI = 4.34-5.49) impairment. This association, however, likely reflects the ceiling effect of the mJOA and the fact that patients with a lower mJOA have larger room for improvement. Finally, a recent study by Tetreault et al[22] indicated that patients with severe myelopathy must make larger gains (3 points) to achieve a MCID on the mJOA than patients with moderate (2 points) or mild (1 points) disease. These results indicate that patients should be operated on in a timely fashion and before they progress to a more severe disease state.

Rationale for Recommendation

The voting for each question in the "evidence-to-recommendation" framework was similar to the results presented in part 1 on severe myelopathy. The exception was that there was more uncertainty with regard to whether the incremental cost of surgery in moderate patients was small relative to the net benefit (uncertain = 12, probably yes = 10, yes = 2). This uncertainty arises from the lack of evidence on the cost-effectiveness of surgical intervention in varying myelopathy severities; however, given that surgery significantly improves function and reduces disability, there may be substantial cost savings as these patients may require less future care and be able to return to work.

The justifications for selecting these answers were also similar to those presented in part 1. In addition to the efficacy and safety of surgery, the associations between outcomes and duration of symptoms and preoperative myelopathy severity were also considered when weighing the desirable and undesirable effects. Patients with more severe myelopathy and a longer duration of symptoms are less likely to achieve a score $\geq$16 on the mJOA. As a result, it is favorable to operate in a timely fashion and before the patient progresses to a more severe disease state.

Considering all these factors, the GDG voted that the desirable consequences probably outweigh the undesirable consequences in most settings (probably outweigh = 20, outweigh = 5); this led to the formation of a strong recommendation for surgery in patients with moderate myelopathy.

Part 3. Clinical Population: Patients With Mild DCM

Population Description: Patients with mJOA 15 to 17

Key Questions: (1) Should nonoperative management be used to treat patients with mild DCM? (2) Should operative management be used to treat patients with mild DCM?

Recommendation: We suggest offering surgical intervention or a supervised trial of structured rehabilitation for patients with mild DCM. If initial nonoperative management is pursued, we recommend operative intervention if there is neurological deterioration and suggest operative intervention if the patient fails to improve.

Quality of Evidence: Very low

Strength of Recommendation: Weak

Evidence Summary

The GDG agreed it was important to consider the following when developing a recommendation for the treatment of mild myelopathy: (1) disease natural history; (2) the comparative effectiveness of nonoperative versus operative intervention; (3) the change in impairment, disability, and quality of life following operative and nonoperative treatments; (4) the associated risks of surgical and non-operative management; and (5) important predictors of outcomes and disease progression. Furthermore, patient preferences must be taken into account as patients with mild symptoms may be hesitant to consent to surgery.

Four systematic reviews were conducted to summarize the evidence required for this guideline. In 2013, Karadimas et al[23] published a systematic review on the natural history of DCM and on important predictors of disease progression. This review was updated for the purpose of this guideline and expanded to include data on the rate of hospitalization due to spinal cord injury in patients with myelopathy. Based on their results, there was moderate evidence from 2 small prospective and 4 retrospective observational studies that 20% to 62% of patients with symptomatic myelopathy deteriorate by at least 1 point on the JOA at 3 to 6 years after initial assessment.[23] Furthermore, patients with DCM increasingly worsen at performing activities of daily living at 1-year (6%), 2-year (21%), 3-year (28%) and 10-year (56%) follow-up. Finally, the rate of hospitalization due to spinal cord injury is 4.8 per 1000 person-years in patients with myelopathy secondary to ossification of the posterior longitudinal ligament (OPLL) and significantly higher than the rate in a healthy population (0.18 per 1000 person-years) (hazard ratio [HR] = 32.2; 95% CI = 10.4-99.0). The rate of spinal cord injury in individuals with CSM is 13.9 per 1000 person-years. Overall, the GDG agreed these rates are low and less important for driving the recommendation for mild patients.

A systematic review by Rhee et al[24] aimed to define the role of nonoperative treatment in patients with DCM by evaluating the comparative effectiveness and safety of nonoperative versus operative management. Furthermore, Rhee et al[24] also examined the relationship between minor traumatic events and worsening of myelopathy. This review was updated for the purpose of this guideline and also presented information on the relative hazard of spinal cord injury in patients treated

nonoperatively versus surgically. The majority of conclusions for this review were derived from a single randomized controlled trial by Kadanka et al.[25] This randomized controlled trial reported that, in patients with "milder" myelopathy (mJOA $\geq$ 12), (1) there was no difference in mJOA scores at 1-, 2-, 3- and 10-year follow-up between patients that received operative versus nonoperative care; (2) surgery resulted in a slower 10-m walk test than nonoperative treatment; and (3) there was no difference between treatment groups in the proportion of patients with worsened or improved clinician-based or patient reported daily activity scores (low level evidence).[25,26] However, no improvements in the mJOA were observed in the operative cohort of this trial, which differs from the results reported in other series of myelopathic patients undergoing surgical decompression[12,19,27-34]; this may partially explain their finding of no difference between treatment groups. Finally, based on low level evidence, rates of hospitalization for subsequent spinal cord injury were significantly higher in patients undergoing initial conservative treatment compared to those managed operatively (HR (ref = operative treatment) = 1.57; 95% CI = 1.11-2.22, $P = .011$).

Given the paucity of comparative effectiveness studies, we conducted 2 additional systematic reviews to evaluate the change in impairment, quality of life and disability following nonoperative and operative treatments. It is important to interpret the results of these studies in terms of the MCID of various assessment tools. Based on a study by Tetreault et al,[22] the overall MCID of the mJOA is between 1.11 and 2.0 and varies by myelopathy severity (severe = 3 points, moderate = 2 points, mild = 1 point). The MCID for the NDI in a degenerative spine population is 7.5. Although the MCID of the Nurick scale has not been defined, a 1-grade change likely reflects substantial improvement in impairment.

The studies included in the systematic review on structured nonoperative treatment consisted mostly of patients with moderate myelopathy (range of mJOA between 11.1 and 14.6); no studies were identified that discussed outcomes in only patients with mild myelopathy. Types of structured nonoperative treatment varied across studies and were not well defined; treatments included bed rest, cervical traction, cervical immobilization, thermal therapy, physical therapy, and/or nonsteroidal anti-inflammatory drugs. Based on very low-level evidence, there were no statistically significant differences between mJOA or JOA scores at baseline and following structured nonoperative treatment. Improvements on the mJOA or JOA did not exceed the MCID (0-2.3) for this metric except in the study by Matsumoto et al.[21] The greatest reported gain in functional status following nonoperative care was reported in studies involving patients with myelopathy due to soft disc herniation and dynamic cervical myelopathy. These etiologies might be expected a priori to respond better to nonoperative care, since soft disc herniation may spontaneously regress, and immobilization may at least temporarily decrease cord irritation if the primary mechanism of compression is dynamic rather than static. In contrast, nonoperative treatment had less effect in patients with DCM due to static spinal cord compression, or etiologies that do not tend to regress spontaneously over time. Furthermore, the proportion of patients who underwent surgical intervention following failed structured nonoperative treatment ranged from 23% to 54%.

In a systematic review on the efficacy of operative treatment, only 1 study by Fehlings et al[18] evaluated surgical outcomes in patients with mild, moderate and severe disease using the criteria set by this guideline. Based on their results, patients with a preoperative mJOA 15 to 17 improved by 1.29 (0.70-1.87) on the mJOA, by 12.05 (7.76-16.34) on the NDI and by 1.54 (1.22-1.86) on the Nurick scale. All of these changes were statistically significant and exceeded the reported MCID for these metrics. The cumulative incidence of complications is also low for patients treated surgically for DCM. Rates of specific complications are reported in part 1; unfortunately, studies did not report rates of complications based on preoperative myelopathy severity.

These 2 systematic reviews also aimed to determine whether outcomes differ in various subgroups (eg, based on baseline severity score or duration of symptoms). In a study on nonoperative treatment by Fukui et al,[35] 80% of patients with a duration of symptoms less than 3 months improved by $\geq$1 point on the JOA, whereas only 46% of patients with a duration of symptoms greater than 3 months exhibited this gain in functional status. Furthermore, a retrospective study by Li et al[36] reported a significant correlation between JOA recovery rate and disease duration in a combined nonoperative and surgical cohort ($R = 0.888$, $P < .01$).

In the systematic review on operative treatment, low-level evidence suggested that the odds of achieving a postoperative mJOA $\geq$16 decreased by 22% (OR = 0.78; 95% CI = 0.61-0.997; $P = .048$) when a patient moved from a shorter to longer duration of symptoms group ($\leq$3 months; >3 but $\leq$6 months; >6 but $\leq$12 months; >12 but $\leq$24 months; >24 months). Furthermore, baseline severity score was also associated with postoperative outcomes: (1) the odds of achieving an optimal outcome (mJOA $\geq$ 16) were 1.22 times greater (OR = 1.22; 95% CI = 1.05-1.41, $P = .0084$) for every 1-point increase in preoperative mJOA and (2) patients with more severe preoperative impairment were less likely to exhibit a postoperative improvement of 2 or more points on the mJOA scale at 18-months follow-up (OR = 0.72; 95% CI = 0.66-0.92). In contrast, moderate strength of evidence suggested that the improvement in mJOA score from baseline is smaller for patients with mild myelopathy (1.29; 95% CI = 0.70-1.87) preoperatively than those with moderate (2.58; 95% CI = 2.07-3.09) or severe (4.91; 95% CI = 4.34-5.49) impairment. This association, however, likely reflects the ceiling effect of the mJOA and the fact that patients with a lower mJOA have larger room for improvement.

Rationale for Recommendation

To develop a final recommendation, 2 key questions were addressed: (1) Should nonoperative treatment be used to manage patients with mild DCM? (2) Should operative treatment be used to manage patients with mild DCM?

For the question on nonoperative treatment, the outcomes most critical for decision making were change or improvement in mJOA, rate of conversion to surgery, disease natural history and incidence of hospitalization for spinal cord injury or severe disability following a traumatic event. The GDG agreed that the overall certainty of the evidence was either very low (n = 14) or low (n = 10). The majority of studies that directly answered this question were retrospective case series. A single randomized controlled trial by Kadanka et al[25,26] included a heterogeneous population and did not use the same cutoff for mild myelopathy as this guideline (mJOA $\geq$ 12 instead of mJOA $\geq$ 15). Another limitation in the current body of evidence is that "nonoperative management" was not uniformly defined and consisted of a wide variety of treatments, including medication, immobilization, and physical therapy.

The majority of the GDG (n = 10) agreed that there was probably no important uncertainty or variability about how much stakeholders value the main outcomes. Eight members, however, argued that there was possibly important uncertainty or variability. Patients and clinicians would similarly value the main outcomes: improvement in functional status, prevention of disease progression and reduced risk of spinal cord injury. In contrast, it is uncertain how much payers would value some of these main outcomes given the lack of studies that discuss the cost-effectiveness of nonoperative management in patients with mild myelopathy. These values were assessed through discussion among the GDG and based primarily on expert opinion.

Fourteen members of the GDG agreed that the anticipated desirable effects were probably not large (n = 14). Based on the results from 5 studies, patients do not achieve clinically significant improvements on the mJOA or JOA following various types of nonoperative treatments. Nine members, however, were uncertain whether the anticipated desirable effects were large; their rationale was that the studies that evaluated the efficacy of nonoperative treatment did not stratify their sample based on myelopathy severity.

The GDG was uncertain as to whether the anticipated undesirable effects were small. The undesirable effects of nonoperative treatment include disease progression, suboptimal outcomes and hospitalization for spinal cord injury. Conversion to surgery was not considered an undesirable effect as this may reflect patient or clinician preferences. Based on the evidence (1) 20% to 62% of symptomatic patients progress if not treated surgically, (2) improvements in outcomes are suboptimal as they do not exceed the MCID of various metrics, and (3) the incidence of hospitalization for spinal cord injury is higher in patients treated conservatively than those managed operatively (HR (ref = operative treatment) = 1.57; 95% CI = 1.11-2.22; P = .011). Despite this evidence, the GDG were still uncertain as these results were derived from studies that included patients with varying myelopathy severities. Furthermore, the GDG was uncertain whether the desirable effects were large relative to the undesirable effects.

In the absence of evidence, the GDG used their clinical expertise to discuss the resources required to manage patients nonoperatively. The group agreed that the resources required for non-operative management are uncertain and likely vary based on the type of non-operative management. For example, the "rigorous" treatment protocol defined by Yoshimatsu et al[37] likely requires substantial resources as it consists of 3 to 4 hours of continuous cervical traction per day for 1 to 3 months, combined with immobilization by cervical orthosis, exercise therapy, drug therapy and thermal therapy. Follow-up monitoring may also involve significant resources.

The majority of the GDG were also uncertain on the impact of a recommendation for nonoperative management on health inequities, as well as the acceptability of this option to key stakeholders. This uncertainty likely arises from the uncertainty surrounding the relative size of desirable versus undesirable effects and the lack of data on the cost-effectiveness of various interventions. The option of nonoperative management for the treatment of mild myelopathy is probably feasible to implement; however, potential barriers include access to care, the requirement for patients to independently fund their treatment, and an accurate and timely diagnosis of myelopathy.

Considering all these factors, the GDG agreed that the desirable and undesirable consequences are closely balanced or uncertain; this led to the formation of a suggestion of nonoperative treatment as an option for the management of patients with mild myelopathy. Patient preferences are important considerations in the decision-making process, as patients with mild symptoms may be hesitant to undergo surgery and prefer to pursue an initial trial of nonoperative treatment.

For the question on operative treatment, the outcomes most critical for decision making were change in mJOA or JOA and risk of major complications. It is also important to consider the impact of duration of symptoms and preoperative myelopathy severity on surgical outcomes. The GDG agreed that the overall certainty of the evidence was low. Although there is moderate evidence that suggests surgery results in clinically meaningful improvements, only 1 study stratified their population based on preoperative myelopathy severity. Furthermore, the heterogeneity of the patient sample across studies further reduces our certainty in the overall evidence.

The GDG selected that there was probably no important uncertainty or variability about how much stakeholders value the main outcomes. Patients and clinicians would similarly value the main outcomes: clinically meaningful improvements in functional status and low rates of major complications. It is uncertain how much payers would value the main outcomes given the lack of cost-effectiveness data on operative management for mild patients; however, there is also a potential that surgery may reduce future management costs.

The majority of the GDG (n = 14) felt that the desirable anticipated effects are probably large. However, several of the studies included in the systematic review on operative treatment consisted of patients with moderate and severe myelopathy. The results must therefore be interpreted cautiously in the context of mild DCM; only a single study stratified its sample by preoperative myelopathy severity. Twelve members of the GDG were uncertain as to whether the anticipated desirable

effects were large; their rationale was that the highest quality study, a randomized controlled trial by Kadanka et al,[25,26] reported that there was no difference in mJOA scores between patients that received operative versus non-operative care. Similar to the questions on moderate and severe myelopathy, the undesirable effects of surgery are probably small due to a low cumulative incidence of overall complications as well as rates of reoperation, death, worsening of myelopathy, stroke, and cardiopulmonary events.

There was a split in the voting as to whether the anticipated desirable effects were large relative to the undesirable effects (probably yes = 12, uncertain = 16).

The resources required to surgically manage mild patients vary based on health care systems and are probably not small. Furthermore, the cost-effectiveness of surgical treatment is largely unknown. In patients with moderate myelopathy, surgical intervention may afford significant cost-savings as patients may be able to return to work following improvement in functional impairment. It is unlikely that patients with mild myelopathy and disability pose as much financial burden on society as those with more advanced disease. The GDG was uncertain about the impact of a recommendation for surgery on health inequities and whether this option would be acceptable to key stakeholders. Furthermore, the option is probably feasible to implement; potential barriers include access to care, costs, and an accurate and timely diagnosis of myelopathy.

Given these points, the desirable and undesirable effects are closely balanced or uncertain; this led to the formation of a suggestion for operative treatment in patients with mild myelopathy.

Based on these 2 recommendations, we suggested offering either surgical intervention or a supervised trial of structured rehabilitation in patients with mild myelopathy. If patients experience neurological deterioration during their course of nonoperative treatment, we strongly recommended conversion to surgery. A key factor considered for this recommendation is that both a longer duration of symptoms and more severe myelopathy reduce a patient's odds of achieving a score $\geq$16 on the mJOA[18]; it is therefore advised that patients with progressive myelopathy be referred immediately for surgical consultation regardless of baseline severity in order to halt neurological deterioration and potentially reverse some of their disability. Given the evidence that surgery results in clinically significant gains, we formed a weaker recommendation for operative intervention in patients who fail to improve following nonoperative treatment. Since the undesirable and desirable consequences of both nonoperative and operative treatments are closely balanced, patient preferences must be strongly considered as patients may be reluctant to undergo surgery for mild myelopathy, especially if they have not deteriorated over time. Furthermore, factors that influence the risk-benefit ratio of either operative or nonoperative management must be weighed when determining the optimal treatment strategy in these patients; these include age, comorbidities, duration of symptoms, and smoking status. Thus, the GDG recommends a process of shared decision making between the surgeon and patient, with the surgeon providing his or her best estimate of the risks and benefits of operative and non-operative management for that particular individual.

Part 4. Clinical Population: Nonmyelopathic Patients Without Symptoms of Radiculopathy

Population Description: Nonmyelopathic patients with imaging evidence of cord compression without signs or symptoms of radiculopathy

Key Question: Should operative management be used to treat non-myelopathic patients with evidence of cord compression without signs or symptoms of radiculopathy?

Recommendation: We suggest not offering prophylactic surgery for nonmyelopathic patients with evidence of cervical cord compression without signs or symptoms of radiculopathy. We suggest that these patients be counseled as to potential risks of progression, educated about relevant signs and symptoms of myelopathy, and be followed clinically.

Quality of Evidence: No identified evidence; based on clinical expert opinion

Strength of Recommendation: Weak

Evidence Summary

The GDG agreed that it was important to consider the following when developing a recommendation for the treatment of nonmyelopathic patients with evidence of cord compression: (1) disease natural history, (2) rates of disease progression and myelopathy development, and (3) risks of operative intervention. A systematic review was conducted by Wilson et al[38] to determine, in nonmyelopathic patients with radiographic evidence of cervical spinal cord compression, spinal canal narrowing and/or OPLL, (1) the frequency and timing of symptom development and (2) the clinical, radiographic, and electrophysiological predictors of symptom development. This review focused on longitudinal cohort studies that followed these patients over time and observed whether they developed signs and symptoms of myelopathy. We attempted to update this systematic review; however, there were no studies published after 2013 that satisfied our inclusion criteria.

Based on the original review, 8% of subjects with evidence of cord compression or canal stenosis developed myelopathy by 12 months and 22.6% at a median of 44 months.[38] This data was derived from 2 large prospective cohort studies by Bednarik et al, which did not segregate their population based on whether patients had clinical evidence of radiculopathy. Furthermore, in asymptomatic patients with OPLL, the frequency of myelopathy development ranged from 0% to 61.5% across 3 studies; however, the overall body of evidence was rated as insufficient for this finding.[38] The cumulative incidence of complications is low for patients treated surgically for myelopathy; however, studies have not evaluated rates of complications following prophylactic surgery in nonmyelopathic patients.

The GDG agreed that there were no studies that directly addressed the question of whether operative, nonoperative treatment or a "wait-and-see" approach should be used to manage nonmyelopathic patients with evidence of cord compression without signs or symptoms of radiculopathy. As a result, our recommendation will be based on clinical expertise, resource demand and indirect evidence. Furthermore, the acceptability of our recommendation and patient preferences must also be considered as nonmyelopathic individuals may be hesitant to undergo prophylactic surgery.

Rationale for Recommendation

The GDG agreed that there were no included studies that evaluated the comparative effectiveness of operative versus conservative treatment in nonmyelopathic patients with evidence of cord compression without signs or symptoms of radiculopathy. As a result, this recommendation was primarily based on clinical expertise and on indirect evidence surrounding rates of myelopathy development.

Given that the main outcome is to prevent the development of myelopathy, the GDG agreed that there is no important uncertainty or variability about how much key stakeholders value this outcome. Based on professional opinion, the GDG agreed that clinicians, patients, and stakeholders would not want patients to develop myelopathy due to the associated impairment and disability, reduced quality of life, costs and financial burden.

The GDG selected that the anticipated desirable effects of prophylactic surgery in these patients are probably not large. Based on the review by Wilson et al,[38] only 22.6% of patients with evidence of cord compression ultimately develop myelopathy; furthermore, this estimate includes all patients, including those at a higher risk of disease development. Similar to the previous three questions, the undesirable effects of surgery are probably small as the cumulative incidence of complications is low. This evidence on the safety of surgery was derived from studies on patients with myelopathy; no studies have explored complication rates in a nonmyelopathic population. As a result, the GDG voted that the desirable effects are probably not large relative to the undesirable effects, especially in patients who are not at a high risk of developing myelopathy; prophylactic surgery puts these patients at a risk of complications with little known benefit.

The resources required to surgically manage these patients vary based on health care system and are probably not small. Furthermore, the cost-effectiveness of prophylactic surgical intervention is largely unknown. Based on professional opinion, the GDG selected that the incremental cost is probably not small relative to the net benefit. As a result, this option is likely not acceptable to key stakeholders since prophylactic surgery is likely costly with limited benefit. The feasibility of this option is uncertain and likely depends on location; potential barriers include access to care, long surgical wait times and low surgical priority compared with myelopathic patients.

As a result of the above explanations, the GDG confirmed that the undesirable consequences probably outweigh the desirable consequences in most settings and that the option of surgery should not be offered in this population.

Part 5. Clinical Population: Nonmyelopathic Patients With Radiculopathy

Population Description: Nonmyelopathic patients with imaging evidence of cord compression and clinical and/or electrophysiological evidence of radiculopathy.

Key Question: Should operative management be used to treat nonmyelopathic patients with evidence of cord compression and clinically/electrophysiologically diagnosed radiculopathy?

Recommendation: Nonmyelopathic patients with cord compression and clinical evidence of radiculopathy with or without electrophysiological confirmation are at a higher risk of developing myelopathy and should be counselled about this risk. We suggest offering either surgical intervention or nonoperative treatment consisting of close serial follow-up or a supervised trial of structured rehabilitation. In the event of myelopathic development, the patient should be managed according to the recommendations above.

Quality of Evidence: Low

Strength of Recommendation: Weak

Evidence Summary

This question differs from part 4 because the population of interest includes nonmyelopathic patients with evidence of cord compression and radiculopathy. In formulating this recommendation, the GDG not only focused on the evidence presented in part 4 but also considered whether clinical and electrophysiological signs of radiculopathy are important predictors of myelopathy development.

The systematic review by Wilson et al[38] summarized existing evidence on significant clinical, radiographical and electrophysiological predictors of symptom development. Important findings included that (1) the presence of symptomatic radiculopathy was a significant clinical predictor of myelopathy development in univariate analysis (risk ratio [RR] = 3.0; 95% CI = 2.0-4.4) and (2) prolonged somatosensory (RR = 2.9; 95% CI = 1.7-5.1) and motor-evoked potentials (RR = 3.2; 95% CI = 1.9-5.6), as well as electromyography evidence of anterior horn cell lesions (RR = 2.4; 95% CI = 1.5-3.9) were significant electrophysiological predictors of myelopathy development in univariate analysis (low level evidence).[38] Furthermore, based on a multivariate analysis, clinically symptomatic radiculopathy ($P = .007$; moderate level evidence) and prolonged somatosensory ($P = .007$; moderate level evidence) and motor-evoked potentials ($P = .033$; moderate level evidence) were significantly associated with early ($\leq$12 months) myelopathy development.[38] Specifically, clinical radiculopathy was diagnosed in 62.5% of patients who developed

myelopathy by 12 months versus in 26.3% of those who did not. Furthermore, prolonged somatosensory and motor-evoked potentials were present in a higher percentage of patients who developed myelopathy (43.8% and 37.5%, respectively) than those who did not (16.4% and 16.9%, respectively).

The GDG agreed that there were no studies that directly addressed the question of whether operative, nonoperative treatment or a "wait-and-see" approach should be used to manage nonmyelopathic patients with evidence of cord compression and radiculopathy. As a result, our recommendation will be based on clinical expertise, resource demand, and indirect evidence. Furthermore, acceptability of our recommendation and patient preferences must also be considered, as nonmyelopathic individuals may be hesitant to undergo prophylactic surgery.

Rationale for Recommendation

Similar to part 4, the main outcome driving this recommendation is the prevention of myelopathy. Unfortunately, there were no identified studies that discussed the comparative effectiveness of surgery versus conservative treatment in halting disease development. In contrast to question 4, however, it is also important to consider whether the presence of radiculopathy increases a patient's risk of myelopathy; the systematic review provided low to moderate evidence to answer this question. As a result, the GDG agreed that the overall certainty of the evidence was low given that the class II prognostic studies do not directly specify whether these patients should undergo prophylactic surgery.

Similar to question 4, the GDG confirmed that (1) there is no important uncertainty or variability about how much key stakeholders value the main outcomes (ie, prevention of myelopathy), (2) the resources required for surgery are probably not small, (3) the incremental cost is probably not small relative to the net benefit, and (4) the impact of this recommendation on health inequities and the acceptability and feasibility of this option are uncertain.

In contrast to question 4, the GDG agreed that the anticipated desirable effects are uncertain. Based on the systematic review by Wilson et al,[38] patients with symptomatic and/or electrophysiological evidence of radiculopathy are at a higher risk of myelopathy development. This finding may provide a compelling argument for prophylactic surgery in these patients; however, there is no evidence to suggest whether the size of the anticipated desirable effects is large. Similar to the other questions, the anticipated undesirable effects are probably small since surgery is associated with a low rate of complications. These results were derived from studies on myelopathic patients and should be interpreted with caution. The GDG was uncertain whether the anticipated desirable effect of preventing myelopathy outweighed the potential risks associated with surgery. Furthermore, the feasibility of prophylactic surgery is uncertain and likely varies based on health care system; potential barriers include access to care, long wait times and low surgical priority for nonmyelopathic patients.

Considering these factors, the GDG acknowledged that the anticipated desirable and undesirable effects were closely balanced or uncertain. As a result, the GDG suggested that patients should be offered either surgery or a trial of structured nonoperative treatment. Again, we advocate a shared decision-making process that takes into account individual preferences and other factors that may influence surgical risk. In the case of myelopathy development, the patient should be treated according to the recommendations proposed in sections 1 to 3; rapidity of disease onset and disease severity must be considered when devising an appropriate management strategy. This recommendation considered patient preferences as nonmyelopathic patients might be hesitant to undergo surgery, as well as the acceptability of this option to payers and clinicians.

Evidence Gaps and Future Research Recommendations

This guideline has identified important knowledge gaps in the literature and areas of future research. These include (1) a limited understanding of the natural history of DCM; (2) controversy surrounding the comparative effectiveness of surgical versus nonoperative treatment, especially in patients with mild myelopathy; (3) a lack of research on structured therapies; (4) a lack of studies that stratified their sample based on preoperative disease severity when evaluating the efficacy and safety of nonoperative and surgical management; (5) limited evidence surrounding the cost-effectiveness of surgical and nonoperative management in patients with varying myelopathy severities; and (6) uncertainty surrounding patient preferences, acceptability, and the impact of these recommendations on health inequities, particularly in a population of patients with mild myelopathy.

Methodological limitations in the existing body of evidence include (1) the lack of standardized definitions of DCM, mild, moderate, and severe myelopathy and types of complications; (2) poorly defined treatment protocols for nonoperative management; (3) the use of outcome measures with unknown reliabilities (eg, mJOA); (4) heterogeneous patient populations and varying surgical approaches; and (5) loss to follow-up. Furthermore, many of our recommendations considered the association between duration of symptoms and surgical outcomes; however, the reliability of this factor is unknown and is likely subject to recall bias. Finally, reported rates of disease progression varied from 20% to 62% and conversion to surgery from 23% to 54%; these wide ranges indicate that the natural history of DCM is likely variable and differs among patients.

Unfortunately, randomized controlled trials in a surgical setting are largely unfeasible; it is unethical to deny a patient surgical intervention when there is not clinical equipoise between operative and nonoperative treatment. Further prospective observational studies may help to ascertain the efficacy and safety of surgical and non-operative treatment in patients with mild, moderate, and severe disease. These studies should use a wide variety of outcome assessment tools, including the Graded Redefined Assessment of Strength Sensibility and Prehension, indices of quality of life (eg, Short-Form 36) and measures of patient satisfaction.[39] Furthermore, in order to

accurately compare the safety of various treatment options, there is a need to first standardize definitions of adverse events and complications. The development of a classification system will require a thorough systematic review of existing definitions, a modified Delphi process and an evaluation of differences in functional and quality-of-life outcomes, costs and satisfaction between patients who do and do not experience a complication following treatment.

Based on our recommendation for mild patients, it is critically important to distinguish between patients in a stable disease state and those at a high risk of deteriorating from mild to moderate myelopathy. According to several previous studies, risk factors of neurologic progression include circumferential cord compression on axial magnetic resonance imaging (MRI); an angular-edged spinal cord, defined as an acute angled or lateral corner at one or both sides; greater range of preoperative neck and head motion; lower segmental lordotic angle and greater percentage of vertebral slip; segmental instability; and reduced diameter of the cerebrospinal fluid column.[40-44] Future studies are required to determine important predictors of disease progression and to better differentiate between types of DCM; genetic or biomarker studies may help address this knowledge gap.

According to the review by Wilson et al,[38] hyperintensity on a T2-weighted MRI is a significant predictor of myelopathy development (RR = 1.7; 95% CI = 1.0-2.7). Specifically, T2-hyperintensity was observed in 35.6% of patients who developed myelopathy versus in 21.4% of those who did not. For the purpose of this guideline, the GDG decided not to segregate the asymptomatic population based on presence/absence of T2-signal change. Future high-quality evidence on this topic, however, should be incorporated when updating this guideline.

The cost-effectiveness of surgery and nonoperative treatment is largely unknown and should be evaluated across medical systems worldwide. In doing so, it is important to consider direct medical and life time costs (including revision surgery) and health utility gained. Although challenging to evaluate, resource utilization (eg, primary care visits, prescription drugs) and indirect costs (eg, forgone productivity, care taker burden) must also be taken into account.

Beyond the scope of this guideline, other areas of interest in the field of DCM include (1) the comparative efficacy of various surgical (eg, laminectomy with fusion vs laminoplasty) and nonoperative treatments (eg, physiotherapy vs immobilization); (2) the impact of neuroprotective agents on treatment outcomes; (3) an evaluation of the incidence and prevalence of DCM; (4) the role of advanced imaging techniques in the diagnosis of myelopathy and prognosis; and (5) an assessment of the factors that delay either nonoperative or surgical management in these patients.

Implementation Considerations

It is expected that this guideline will influence clinical practice and facilitate evidence-based decision making. Dissemination of the knowledge from this guideline is of critical importance and will be accomplished at multiple levels:

- Presentation at international spine surgery, neurology, rheumatology, and primary care meetings
- Scientific and educational courses in symposium format
- Webinar dissemination of information to a broad audience in an interactive format
- Publication of a focus issue in a peer-reviewed journal
- Submission to the National Guideline Clearinghouse
- AOSpine International Degenerative Knowledge Translation Forum

Internal Appraisal and External Review of This Guideline

The vice-chair of the GDG conducted an internal appraisal of the final guideline using Appraisal of Guidelines for Research & Evaluation II (AGREE II) standards.[45] A multidisciplinary group of stakeholders, including patients, were invited to externally review the final draft prior to publication. Additional details of these processes and a summary of conflict of interests for external reviewers are found in the accompanying methods article.

Plans for Updating

The guidelines will be reviewed by the primary sponsor and the vice-chair at three years to a maximum of five years following publication. The guideline will be updated when new evidence suggests the need to modify our recommendations. An earlier update will be considered if there are changes in (1) the evidence related to harms and benefits, (2) outcomes which would be considered important for decision making; (3) ranking of current critical and important outcomes, and (4) available interventions and resources.[46]

Authors' Note

The guideline development group did not include a patient representative or a public member. Committee positions: Co-Chair: Michael G. Fehlings, MD, PhD; Vice-Chair/Systematic Review Coordinator: Lindsay A. Tetreault, PhD; General Member of Leadership Group: Daniel Riew, MD; General Member of Leadership Group: James Middleton, MD; Co-Chair: Jeffrey C. Wang, MD.

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Declaration of Conflicting Interests

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References

1. Fehlings MG, Tetreault LA, Wilson JR, Skelly AC. Cervical spondylotic myelopathy: current state of the art and future directions. *Spine (Phila Pa 1976)*. 2013;38(22 suppl):S1-S8. doi:10.1097/BRS.0b013e3182a7e9e0.
2. Fehlings MG, Tetreault L, Nater A, et al. The aging of the global population: the changing epidemiology of disease and spinal disorders. *Neurosurgery*. 2015;77(suppl 4):S1-S5 doi:10.1227/NEU.0000000000000953.
3. Tetreault L, Kopjar B, Nouri A, et al. The modified Japanese Orthopaedic Association scale: establishing criteria for mild, moderate and severe impairment in patients with degenerative cervical myelopathy. *Eur Spine J*. 2017;26:78-84. doi:10.1007/s00586-016-4660-8.
4. Shiffman RN, Michel G. Toward improved guideline quality: using the COGS statement with GEM. *Stud Health Technol Inform*. 2004;107:159-163.
5. Shiffman RN, Shekelle P, Overhage JM, Slutsky J, Grimshaw J, Deshpande AM. Standardized reporting of clinical practice guidelines: a proposal from the Conference on Guideline Standardization. *Ann Intern Med*. 2003;139:493-498.
6. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011;64:401-406.
7. Agency for Healthcare Research and Quality. *Methods guide for Effectiveness and Comparative Effectiveness Reviews (AHRQ Publication No. 10(14)-EHC063-EF)*. Rockville MD: Agency for Healthcare Research and Quality; 2013.
8. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. *J Clin Epidemiol*. 2013;66:719-725. doi:10.1016/j.jclinepi.2012.03.013.
9. Andrews JC, Schunemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol*. 2013;66:726-735. doi:10.1016/j.jclinepi.2013.02.003.
10. Schunemann HJ, Oxman AD, Akl EA, et al. Moving from evidence to developing recommendations in guidelines: article 11 in Integrating and coordinating efforts in COPD guideline development. An official ATS/ERS workshop report. *Proc Am Thorac Soc*. 2012;9:282-292. doi:10.1513/pats.201208-064ST.
11. Wu JC, Ko CC, Yen YS, et al. Epidemiology of cervical spondylotic myelopathy and its risk of causing spinal cord injury: a national cohort study. *Neurosurg Focus*. 2013;35:E10. doi:10.3171/2013.4.FOCUS13122.
12. Fehlings MG, Wilson JR, Kopjar B, et al. Efficacy and safety of surgical decompression in patients with cervical spondylotic myelopathy: results of the AOSpine North America prospective multicenter study. *J Bone Joint Surg Am*. 2013;95:1651-1658. doi:10.2106/JBJS.L.00589.
13. Fehlings MG, Jha NK, Hewson SM, Massicotte EM, Kopjar B, Kalsi-Ryan S. Is surgery for cervical spondylotic myelopathy cost-effective? A cost-utility analysis based on data from the AOSpine North America prospective CSM study. *J Neurosurg Spine*. 2012;17:89-93. doi:10.3171/2012.6.aospine111069.
14. Witiw CD, Tetreault LA, Smieliauskas F, Kopjar B, Massicotte EM, Fehlings MG. Surgery for degenerative cervical myelopathy: a patient centered quality of life and health economic evaluation. *Spine J*. 2017;17:15-25. doi:10.1016/j.spinee.2016.10.015.
15. Suzuki A, Misawa H, Simogata M, Tsutsumimoto T, Takaoka K, Nakamura H. Recovery process following cervical laminoplasty in patients with cervical compression myelopathy: prospective cohort study. *Spine (Phila Pa 1976)*. 2009;34:2874-2879. doi:10.1097/BRS.0b013e3181bb0e33.
16. Karpova A, Arun R, Davis AM, et al. Predictors of surgical outcome in cervical spondylotic myelopathy. *Spine (Phila Pa 1976)* 2013;38:392-400. doi:10.1097/BRS.0b013e3182715bc3.
17. Cheung WY, Arvinte D, Wong YW, Luk KD, Cheung KM. Neurological recovery after surgical decompression in patients with cervical spondylotic myelopathy: a prospective study. *Int Orthop*. 2008;32:273-278. doi:10.1007/s00264-006-0315-4.
18. Tetreault LA, Kopjar B, Vaccaro A, et al. A clinical prediction model to determine outcomes in patients with cervical spondylotic myelopathy undergoing surgical treatment: data from the prospective, multi-center AOSpine North America study. *J Bone Joint Surg Am*. 2013;95:1659-1666. doi:10.2106/JBJS.L.01323.
19. Chibbaro S, Mirone G, Makiese O, George B. Multilevel oblique corpectomy without fusion in managing cervical myelopathy: long-term outcome and stability evaluation in 268 patients. *J Neurosurg Spine*. 2009;10:458-465. doi:10.3171/2009.1.spine08186.
20. Setzer M, Vrionis FD, Hermann EJ, Seifert V, Marquardt G. Effect of apolipoprotein E genotype on the outcome after anterior cervical decompression and fusion in patients with cervical spondylotic myelopathy. *J Neurosurg Spine*. 2009;11:659-666. doi:10.3171/2009.7.spine08667.
21. Matsumoto M, Chiba K, Ishikawa M, Maruiwa H, Fujimura Y, Toyama Y. Relationships between outcomes of conservative treatment and magnetic resonance imaging findings in patients with mild cervical myelopathy caused by soft disc herniations. *Spine (Phila Pa 1976)*. 2001;26:1592-1598.
22. Nouri A, Tetreault L, Zamorano JJ, et al. Role of magnetic resonance imaging in predicting surgical outcome in patients with cervical spondylotic myelopathy. *Spine (Phila Pa 1976)*. 2015;40:171-178. doi:10.1097/BRS.0000000000000678.

23. Karadimas S, Erwin W, Ely C, Dettori JR, Fehlings MG. Pathophysiology and natural history of cervical spondylotic myelopathy. *Spine (Phila Pa 1976)*. 2013;38(22 suppl 1):S21-S36. doi:10.1097/BRS.0b013e3182a7f2c3.
24. Rhee JM, Shamji MF, Erwin WM, et al. Nonoperative management of cervical myelopathy: a systematic review. *Spine (Phila Pa 1976)*. 2013;38(22 suppl 1):S55-S67. doi:10.1097/BRS.0b013e3182a7f41d.
25. Kadanka Z, Bednarik J, Novotny O, Urbánek I, Dušek L. Cervical spondylotic myelopathy: conservative versus surgical treatment after 10 years. *Eur Spine J*. 2011;20:1533-1538.
26. Kadanka Z, Mares M, Bednanik J, et al. Approaches to spondylotic cervical myelopathy: conservative versus surgical results in a 3-year follow-up study. *Spine (Phila Pa 1976)*. 2002;27:2205-2210; discussion 2210-2211.
27. Fehlings MG, Ibrahim A, Tetreault L, et al. A global perspective on the outcomes of surgical decompression in patients with cervical spondylotic myelopathy: results from the prospective multicenter AOSpine international study on 479 patients. *Spine (Phila Pa 1976)*. 2015;40:1322-1328. doi:10.1097/BRS.0000000000000988
28. Hirai T, Okawa A, Arai Y, et al. Middle-term results of a prospective comparative study of anterior decompression with fusion and posterior decompression with laminoplasty for the treatment of cervical spondylotic myelopathy. *Spine (Phila Pa 1976)* 2011;36: 1940-1947 DOI: 10.1097/BRS.0b013e3181feeeb2
29. Hu W, Shen X, Sun T, Zhang X, Cui Z, Wan J. Laminar reclosure after single open-door laminoplasty using titanium miniplates versus suture anchors. *Orthopedics*. 2014;37:e71-e78.
30. Kimura A, Endo T, Inoue H, Seichi A. Preoperative predictors of patient satisfaction with outcome after cervical laminoplasty. *Global Spine J*. 2014;4:77-82. doi:10.1055/s-0034-1366973.
31. Lian XF, Xu JG, Zeng BF, Zhou W, Kong WQ, Hou TS. Noncontiguous anterior decompression and fusion for multilevel cervical spondylotic myelopathy: a prospective randomized control clinical study. *Eur Spine J*. 2010;19:713-719.
32. Moussellard HP, Meyer A, Biot D, Khiami F, Sariali E. Early neurological recovery course after surgical treatment of cervical spondylotic myelopathy: a prospective study with 2-year follow-up using three different functional assessment tests. *Eur Spine J*. 2014;23:1508-1514 doi:10.1007/s00586-014-3315-x.
33. Ohashi M, Yamazaki A, Watanabe K, Katsumi K, Shoji H. Two-year clinical and radiological outcomes of open-door cervical laminoplasty with prophylactic bilateral C4-C5 foraminotomy in a prospective study. *Spine (Phila Pa 1976)*. 2014;39:721-727. doi:10.1097/brs.0000000000000251.
34. Ying Z, Xinwei W, Jing Z, et al. Cervical corpectomy with preserved posterior vertebral wall for cervical spondylotic myelopathy: a randomized control clinical study. *Spine (Phila Pa 1976)*. 2007;32:1482-1487. doi:10.1097/BRS.0b013e318068b30a.
35. Fukui K, Kataoka O, Sho T, Sumi M. Pathomechanism, pathogenesis, and results of treatment in cervical spondylotic myelopathy caused by dynamic canal stenosis. *Spine (Phila Pa 1976)*. 1990;15:1148-1152.
36. Li FN, Li ZH, Huang X, et al. The treatment of mild cervical spondylotic myelopathy with increased signal intensity on T2-weighted magnetic resonance imaging. *Spinal Cord*. 2014;52:348-353. doi:10.1038/sc.2014.11.
37. Yoshimatsu H, Nagata K, Goto H, et al. Conservative treatment for cervical spondylotic myelopathy, prediction of treatment effects by multivariate analysis. *Spine J*. 2001;1:269-273.
38. Wilson JR, Barry S, Fischer DJ, et al. Frequency, timing, and predictors of neurological dysfunction in the nonmyelopathic patient with cervical spinal cord compression, canal stenosis, and/or ossification of the posterior longitudinal ligament. *Spine (Phila Pa 1976)*. 2013;38(22 suppl 1):S37-S54. doi:10.1097/BRS.0b013e3182a7f2e7.
39. Kalsi-Ryan S, Singh A, Massicotte EM, et al. Ancillary outcome measures for assessment of individuals with cervical spondylotic myelopathy. *Spine (Phila Pa 1976)*. 2013;38(22 suppl 1):S111-S122. doi:10.1097/BRS.0b013e3182a7f499.
40. Shimomura T, Sumi M, Nishida K, et al. Prognostic factors for deterioration of patients with cervical spondylotic myelopathy after nonsurgical treatment. *Spine (Phila Pa 1976)*. 2007;32:2474-2479.
41. Sumi M, Miyamoto H, Suzuki T, Kaneyama S, Kanatani T, Uno K. Prospective cohort study of mild cervical spondylotic myelopathy without surgical treatment. *J Neurosurg Spine*. 2012;16:8-14. doi:10.3171/2011.8.spine11395.
42. Barnes MP, Saunders M. The effect of cervical mobility on the natural history of cervical spondylotic myelopathy. *J Neurol Neurosurg Psychiatry*. 1984;47:17-20.
43. Oshima Y, Seichi A, Takeshita K, et al. Natural course and prognostic factors in patients with mild cervical spondylotic myelopathy with increased signal intensity on T2-weighted magnetic resonance imaging. *Spine (Phila Pa 1976)*. 2012;37:1909-1913. doi:10.1097/BRS.0b013e318259a65b.
44. Kong LD, Meng LC, Wang LF, Shen Y, Wang P, Shang ZK. Evaluation of conservative treatment and timing of surgical intervention for mild forms of cervical spondylotic myelopathy. *Exp Ther Med*. 2013;6:852-856. doi:10.3892/etm.2013.1224.
45. Brouwers MC, Kho ME, Browman GP, et al. Development of the AGREE II, part 2: assessment of validity of items and tools to support application. *CMAJ*. 2010;182:E472-E478. doi:10.1503/cmaj.091716.
46. Shekelle P, Woolf S, Grimshaw JM, Schünemann HJ, Eccles MP. Developing clinical practice guidelines: reviewing, reporting, and publishing guidelines; updating guidelines; and the emerging issues of enhancing guideline implementability and accounting for comorbid conditions in guideline development. *Implement Sci*. 2012;7:62.