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A Systematic Review of Definitions for Neurological Complications and Disease Progression in Patients Treated Surgically for Degenerative Cervical Myelopathy

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Abstract

Study Design: Systematic Review

Objective: This review aims to (1) outline how neurological complications and disease progression are defined in the literature and (2) evaluate the quality of definitions using a novel four-point rating system.

Summary of Background Data: Degenerative cervical myelopathy (DCM) is a progressive, degenerative spine disease that is often treated surgically. Although uncommon, surgical decompression can be associated with neurological complications, such as C5 nerve root palsy, perioperative worsening of myelopathy and longer-term deterioration. Unfortunately, important questions surrounding these complications cannot be fully addressed due to the heterogeneity in definitions used across studies. Given this variability, there is a pressing need to develop guidelines in the reporting of surgical complications in order to accurately evaluate the safety of surgical procedures.

Methods: An electronic database search was conducted in MEDLINE, MEDLINE in Process, EMBASE and Cochrane Central Register of Controlled Trials for studies that reported on complications related to DCM surgery and included at least 10 surgically treated patients. Data extracted included study design, surgical details, and definitions and rates of surgical complications. A four-point rating scale was developed to assess definition quality for each complication.

Results: Our search yielded 2,673 unique citations, 42 of which met eligibility criteria and were summarized in this review. Defined complications included neurological deterioration, late onset deterioration, perioperative worsening of myelopathy, C5 palsy, nerve root or upper limb palsy or radiculopathy, surgery failure, inadequate decompression and progression of ossified lesions. Reported rates of these complications varied substantially, especially those for neurological deterioration (0.2% to 33.3%) and progression of ossified lesions (0.0% to 86.7%).

Conclusions: Reported incidences of various complications vary widely in DCM surgery, especially for neurological deterioration and progression of ossified lesions. This summary serves as a first step for standardizing definitions and developing guidelines for accurately reporting surgical complications.

Key Words: degenerative cervical myelopathy; ossification of the posterior longitudinal ligament; cervical spondylotic myelopathy; complications; C5 palsy; radiculopathy; spinal cord injury; manual muscle test; neurological deterioration; inadequate decompression; surgery failure; progression of ossified lesions

Level of Evidence: 2

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Key Points

1. Surgical decompression for degenerative cervical myelopathy (DCM) can arrest disease progression and improve functional impairment, disability and quality of life.
2. Surgery, however, is associated with complications, including intraoperative spinal cord injury, deterioration of myelopathy, C5 nerve root palsy, new radiculopathy and decreased strength.
3. Reported rates of neurological complications vary considerably across published studies; this is likely due to the heterogeneity of definitions used to characterize these complications.
4. This review outlines how neurological complications and disease progression are defined in the literature and serves as an initial step in unifying terminology.

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Introduction

Degenerative cervical myelopathy (DCM) results from the degeneration of various components of the spinal axis and is the most common cause of spinal cord dysfunction in adults worldwide.[1] The term DCM comprises cervical spondylotic myelopathy (CSM); ossification, calcification or hypertrophy of the spinal ligaments; degenerative disc disease (DDD); and other compressive degenerative pathologies.[2,3] The natural history of DCM is variable: some patients are clinically stable or may even improve over time, while others experience rapid neurological progression.[1,4] Patients with stable and mild myelopathy can be managed non-operatively with close observation, while those with progressive and/or moderate to severe disease typically require surgical intervention.[5] Surgical decompression can be performed anteriorly and/or posteriorly, depending on factors such as cause and extent of compression, cervical alignment, presence of axial neck pain, age, and stability of the spinal column.

Several prospective studies have demonstrated that surgical decompression of the spinal cord can arrest disease progression and improve functional impairment, disability and quality of life.[6,7] Surgery, however, carries a risk of adverse events, including neurological complications such as intraoperative spinal cord injury, deterioration of myelopathy and C5 palsy. Furthermore, patients with ossification of the posterior longitudinal ligament (OPLL) may experience progression of their lesion following surgery.

Reported rates of neurological complications and disease progression vary considerably across published studies. This variation can be partly attributed to differences in surgical expertise but is more likely due to the heterogeneity of definitions used to characterize these complications. For example, in a study by Machino et al, C5 palsy was defined as "paresis of deltoid (manual muscle test (MMT) score of 1 or 2), with or without involvement of the biceps, but no loss of strength in other muscles." The reported incidence of C5 palsy in this

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study was 0.6%.[8] In contrast, Liu et al indicated a much higher incidence (23.1%) using different criteria: "1 grade deterioration on MMT of the deltoid postoperatively, apparent sensory deficits or only pain at the C5 dermatome area."[9] Furthermore, study design and method of data collection may also significantly influence reported rates of complications.

This lack of standardization prevents (1) an accurate assessment of surgical safety, (2) an evaluation of relevant risk factors of neurological complications and (3) an analysis of the impact of adverse events on patient satisfaction, cost, disability and functional impairment. Due to this inconsistency, there is a pressing need to develop high-quality standardized definitions of surgical complications. This review outlines how neurological complications and disease progression are defined in the literature and evaluates the quality of these definitions using a novel four-point rating system.

Methods

Eligibility Criteria

Studies were considered for inclusion if they had 10 or more adult patients (≥18 years of age) with DCM (cord compression caused by spondylosis, disc herniation, OPLL, hypertrophy of the ligamentum flavum (HLF), dynamic factors and/or progressive kyphosis) treated surgically and evaluated postoperatively. Studies also must have defined one or more complications related to surgical intervention.

Studies were excluded if they included patients with isolated radiculopathy or non-degenerative causes of myelopathy such as trauma, tumour and rheumatoid arthritis. Case reports, meta-analyses, systematic reviews, editorials, commentaries, and conference proceedings were also excluded.

Information Sources

An electronic database search was conducted in MEDLINE, MEDLINE in Process,

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EMBASE, and Cochrane Central Register of Controlled Trials for literature published up until January 22nd, 2016.

Search

The search strategy was first developed in MEDLINE and then modified for the other three databases. The following general terms were used to search all databases: (DCM OR CSM OR OPLL) AND surgery AND (adverse events OR complications). Other keywords were also used, including those related to specific neurological complications such as "paralysis", "pals*," "radiculopath*," "worse* adj4 myelopath*," "progress* adj4 myelopath*" and others. Only studies on humans and written in English were considered. Four libraries were used to access the full texts of articles. Articles referenced by relevant studies were also included.

Study Selection

All duplicates, conference abstracts, systematic or literature reviews, commentaries, letters, case reports and studies in other languages were excluded. The remaining abstracts and titles were reviewed and sorted by three independent investigators (L.T., S.C., M.T.K.) as possibly relevant or irrelevant. The full texts of the articles classified as possibly relevant were examined by a fourth reviewer (S.F.L.). Uncertainty about inclusion was resolved through discussion and consensus. Final decisions were reviewed and approved by the senior author (M.G.F).

Data extraction and synthesis

The following data were extracted from each article where available: title, author, year, study design, number of patients, diagnosis, type of surgery, follow-up period/average length of follow-up, and the type, definition, incidence, onset and duration of complications.

When extracting data, two definitions were considered the same if they did not have clinically relevant differences. For example, the following definitions for C5 palsy would be

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considered similar: “paralysis of the deltoid and/or biceps muscle(s)” and “weakness in the muscles corresponding to the C5 myotome”; both imply that there is a loss in strength of the muscles corresponding to the C5 nerve root. In contrast, the definition “upper extremity weakness” would be considered different.

Rating of Individual Definitions

A novel four-point rating system was created to evaluate the quality of a complication definition: “COMP,” Clinical finding, Objective criteria, Modality and Point in time. A single point was granted for each of the following criterion:

A. The complication is linked to a clinical finding and is described qualitatively;
B. The modality of identifying the complication is described (X-ray, magnetic resonance imaging (MRI), computed tomography (CT), lab, patient-reported, etc.);
C. The clinical finding is described quantitatively by a measurement or has been categorized based on objective criteria. If the complication was described quantitatively, a point for Criterion (A) was automatically awarded;
D. The time of evaluation after surgery was defined (days, weeks, months etc.)

This rating scale was developed and modified by consensus among the authors. Each criterion was selected based on trends in current definitions. To score higher, a definition must have a quantitative description; the rationale behind this requirement is that quantitative assessments leave less room for interpretation and should result in a more consistent reporting of the complication. Iterative versions of this system were evaluated for inter-rater reliability. The four-point scale described above demonstrated the highest reliability (93.6%). Table 1 uses C5 palsy as an example to illustrate how definitions are rated using this system.

Reporting

This systematic review was formatted, where applicable, using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[10] For the purpose of this

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review, it was not necessary to evaluate the risk of bias of each individual article or assess the strength of the overall body of evidence. Instead, we rated the quality of each definition using the four-point rating system described above.

Results

Study Selection

Our literature search yielded 2,673 unique citations. We excluded 1,546 articles following abstract and title review. A total of 1,128 studies underwent full text review, 1,086 of which were excluded. Common reasons for exclusion were that the study (1) included patients with only radiculopathy or with myelopathy secondary to trauma, tumour or rheumatoid arthritis, (2) did not discuss neurological complications or disease progression, and (3) did not define reported complications. A total of 42 studies satisfied our inclusion criteria.

Study Characteristics

The 42 articles that discussed neurological complications or progression of ossification were published between 1991 and 2016. Fifteen studies (35.7%) were prospective and 27 (64.3%) were retrospective (Table 2). Sample sizes ranged from 13 to 1,858 patients.

Complication definitions

The reviewed studies included definitions for the following complications: neurologic deterioration (n=5)[11-15], late onset deterioration (n=6)[15-20], perioperative worsening of myelopathy (n=1)[13], progression of ossified lesions (n=10)[16-25], C5 palsy (n=20)[8,9,13,26-42], nerve root/upper limb palsy or new radiculopathy (n=6)[13,43-47], decreased arm strength (n=1)[44], surgery failure (n=1)[48] and inadequate decompression (n=2)[26,49,50]. Table 2 summarizes the included articles and lists complication definitions, study design, timing of follow-up, surgical approach, and incidence. Table 3 displays the reported incidences of surgical complications.

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Neurological deterioration

Ten studies defined neurological deterioration and/or late-onset deterioration.[11-20]

Of the five definitions provided for neurological deterioration, one scored one point and four scored three points on our rating scale. Four studies used quantitative definitions: (1) a decrease in Japanese Orthopaedic Association (JOA) score or an increase in Nurick Grade by 1 point[11]; (2) a decrease of ≥3 points in the JOA score[12]; (3) a decrease of >2 points on the JOA score after initial postoperative recovery;[15] and (4) an increase of ≥1 Nurick grade[14]. Tetreault et al. qualitatively defined deterioration as an "increase of myelopathic signs and symptoms[13]." Reported incidences ranged from 0.2% to 30.8%.

Late-onset deterioration was defined by six studies. Based on our rating scale, three definitions received three points and three scored four points. All definitions were based on a decrease in the total JOA score or subscores of this scale. Quantitative criteria included (1) a decrease by >1[17], >2[18] or >3[16] points on the total JOA; and (2) a decrease in upper extremity and trunk JOA scores by >1[19] or >2[20] points. In two studies, the reference value used to evaluate deterioration was the maximum score of the patient during a 4-year[16] or a 1 to 5 year[19] follow-up. A third study by Goto et al classified late deterioration as a decline following 10 years of postoperative recovery. Reported incidences ranged from 4.5% to 33.3%.

Perioperative Worsening of Myelopathy

Tetreault et al defined perioperative worsening of myelopathy as "signs and symptoms due to cervical myelopathy worsening during the initial four-week postoperative period" (rating = 2).[13] The reported incidence was 0.6% in this prospective cohort of 477 patients.

Progression of Ossified Lesions

Ten studies defined progression of ossified lesions[16-25]. Of these definitions, three scored two points, five scored three points, and one scored four points on our rating scale. The majority

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of studies defined progression of ossification as an increase in the longitudinal or axial extent or sagittal thickness of the lesion. Quantitative definitions for progression included (1) >50% of one vertebral body axially[16,25], (2) longitudinal growth over one vertebral body[22], (3) >2[16,22,25] or ≥2[23,24] mm in thickness, (4) >1 mm in thickness[21] or (5) >2[21] or ≥2[23,24] mm in longitudinal extent. Two studies by Ogawa et al. defined this complication as a progression of the ossified ligament by >2 mm, but did not specify the direction of the progression[19,20]. Finally, the definition by Iwasaki et al. was all-encompassing and included a ≥2 mm increase in the existing lesion, the appearance of a new ossified lesion measuring ≥2 mm and bridging between separate lesions to form a continuous lesion[18].

Chiba et al used computer-assisted measurements to quantify progression of OPLL[17]. This method was originally developed by Chiba and colleagues in 2005 and demonstrated 98% precision to differentiate a 2 mm difference in length or thickness of OPLL[51].

The imaging modality used to assess progression of ossification was lateral radiographs in six studies[16,19-21,23-25] and lateral tomograms in a single study[24].

The studies by Chen et al. reported low incidences of progression between 0.0%[25] and 6.7%[16]. In the remaining studies, incidences ranged from 42.4% to 86.7%.

C5 Palsy

Twenty studies contained 15 definitions for C5 palsy: four scored one point, one scored two points, and eleven scored three points on our rating scale. Twelve definitions used the manual muscle test (MMT) to evaluate muscle weakness or reduction in motor strength. Quantitative definitions of C5 palsy included (1) a deterioration in muscle power or strength by ≥1 grade on the MMT;[9,29,32,36,40-42] and (2) muscle weakness represented by a MMT grade of 1[26], 1 or 2[8,33,34], <3[28,37] or ≤3[38,39]. Reported incidences in studies that used criterion (1) ranged from 3.3% to 23.1% and, in those that used criterion (2), from 0.6% to 6.4%. A single study by Sasai et al. used the MMT to diagnose C5 palsy but did not specify quantitative criteria

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(incidence = 2.7%)[31]. Some definitions specified that this decrease in strength or weakness had to be limited to the deltoid[9,37-39]; the deltoid with or without involvement of the biceps brachii[8,32-34]; the deltoid and biceps brachii[26,40,41]; the deltoid or biceps brachii[36]; or the upper limb[29]. Furthermore, several definitions indicated that this weakness or reduction in strength could not be accompanied by deterioration of neurologic[40,41] or myelopathic symptoms[38,39], aggravation of lower extremity function[36] or loss of strength of other muscles[8,32-34]. A single study by Liu et al also included in their definition of C5 palsy an "apparent sensory deficit or pain in the C5 dermatome area"[9]; the reported incidence of this complication was 23.1%.

Four studies provided more qualitative definitions of C5 palsy, including (1) postoperative symptoms of paresis of the deltoid or biceps brachii muscles[35]; (2) deterioration of muscle or motor strength in the deltoid and/or biceps brachii muscles[27,30]; (3) sensory deficits or increased pain in the C5 nerve root distribution[27,35]; (4) C5 dermatome hypoesthesia[13]; and (5) diminished or absent bicipital reflex[13]. Incidences of C5 palsy reported by these studies ranged from 0.8%[13] to 12.2%[35].

Nerve Root Palsy/Upper Limb Palsy and New Radiculopathy

Six studies featured definitions of nerve root palsy, upper limb palsy, and new radiculopathy. Of these studies, one scored one point, four scored three points, and one scored four points on our rating scale. Four definitions described upper limb palsy or radiculopathy as a loss of motor function defined (1) by a reduction in MMT by ≥1 grade in upper limb muscle strength[44,45] (incidences ranged from 5.0 to 6.2%); (2) by weakness of grade 4 or less in key muscles of the upper extremity[43] (incidence was 15.7%); or (3) using a scale from mild to severe motor paralysis using MMT criteria[46,47] (mild = 4 to 5; moderate = 2 to 3; severe = 0 to 1; incidences ranged from 10.6% to 12.9%). Three of these studies indicated that this reduction in strength could not be accompanied by deterioration in myelopathy symptoms[44]

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or aggravation of lower extremity function[45]. Three studies differentiated between sensory- and motor-dominant palsy. In a study by Dai et al, sensory-dominated palsy was defined as "sensory loss and/or retractable pain with little motor impairment."[47] In a second study by Tsuzuki et al, patients were diagnosed with sensory-dominant palsy if "muscle power improved after pain was relieved by a root block even if the muscle weakness was associated with radicular pain."[46] Finally, in a third study by Hasegawa et al, the appearance of a new sensory disturbance between day 0 and 2 months after surgery was sufficient for a diagnosis of sensory nerve root palsy[45].

The study by Hasegawa et al also specified how the level of neurologic dysfunction was determined: weakness of the deltoid and biceps brachii and/or abnormal reflex of the biceps tendon for C5; weakness of the biceps brachii and wrist extensors and/or abnormal reflex of the brachioradialis tendon for C6; weakness of the triceps and/or abnormal reflex of the triceps tendon for C7; and weakness of the wrist flexors and decrease in grip strength for C8[45]. Furthermore, levels of sensory disturbance were determined using the criteria proposed by Keegan and Garrett.

Finally, a single study by Tetreault et al defined new radiculopathy as "signs and symptoms of other cervical spinal root lesions[13]" (rating = 1). The incidence of this complication was 0.6%.

Decreased Arm Strength

In a study by Takenaka et al, a calibrated hand-held dynamometer was used to assess shoulder abduction, elbow flexion and elbow extension, indicating the strength of the deltoid, biceps brachii and triceps brachii respectively[44]. Additionally, grip strength was evaluated using a grip dynamometer. Decreased arm strength was defined as decreased strength of at least one muscle as determined by one or both of these assessments (rating = 4). The reported incidence in this study was 11.3%.

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Surgery Failure

A single study defined surgery failure (rating = 3).[48] In the study by Saunders et al, improvement was defined as a change of at least two grades in the Nurick classification, and/or resolution of hyperpathia and dysesthesia. A smaller grade of improvement, or regression was considered a failure. The reported incidence of failure was 12.8%.

Inadequate decompression

Three studies defined inadequate decompression.[26,49,50] Two studies by Chen et al considered surgical decompression to be inadequate when the cord flattening ratio (minor axis length of the spinal cord divided by major axis length at the level of maximal cord compression on axial T1-weighted MRI) was less than 0.4 following operation (rating=3). [26,50]

Hirai et al (2011) reported rates of residual anterior compression, defined as (1) effacement of anterior cerebrospinal fluid buffer on T2-sagittal and axial images, or (2) evidence of anterior compression of cord substance on T1-sagittal and axial images (rating=2)[49]. Their radiographic analysis was performed by three independent, blinded spine surgeons. The reported incidence of residual compression increased over time, from 12.8% post-operatively to 37.5% at two years following surgery.

Discussion

An accurate evaluation of complications following surgery for DCM is essential for determining quality of care, comparing outcomes among various surgical approaches, and developing enhanced treatment protocols. Currently, there are no standardized criteria for defining or reporting complications; this knowledge gap prevents an accurate assessment of the safety of surgery, the identification of relevant risk factors and the implementation of appropriate prevention strategies. This systematic review aimed to summarize current definitions of neurological complications and disease progression as a first step in developing

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a unified classification system. Based on our results, reported rates of these complications varied substantially, especially for neurological deterioration and progression of ossified lesions. These wide ranges can likely be attributed to the heterogeneity of definitions used across studies as well as the variability in methods of data collection, study design and timing of evaluation.

Several studies reported rates of neurological deterioration by evaluating changes in either the JOA or Nurick score. Unfortunately, there was no consistency across studies with respect to the extent of decline required for a diagnosis of deterioration. There are certain drawbacks to using a scale like the JOA to evaluate progression of myelopathy. First, although the JOA exhibits high reliability (ICC=0.826)[52], it is possible that a decrease in the JOA by a single point reflects inter- or intra-observer variability. Furthermore, based on the study by Yonenobu et al, inter- and intra-observer agreement is particularly low for certain JOA subscales, namely the lower extremity motor score (62.3% and 62.2%, respectively) and the lower extremity sensory score (62.3% and 57.1%, respectively)[52]. As a result, a diagnosis of neurological deterioration should be based on a decrease of at least two points on the JOA score, which has been accepted as the minimum clinically important (MCID) difference for this scale. Consequently, the study by Chiba et al may have overestimated rates of late neurological deterioration in patients treated surgically for DCM.[17] A second issue is that a decline in a patient's JOA may not necessarily represent progression of myelopathy, but may indicate either concomitant lumbar spinal stenosis or the presence of other co-morbidities that limit a patient's ability to perform certain tasks on the JOA. Finally, the timing of assessment is critical. The onset of new radicular or myelopathic symptoms may occur years after surgical decompression due to progressive kyphosis, progression of ossified lesions or the development of spondylotic changes at levels adjacent to the treated segments. In contrast, "early" neurologic deterioration or worsening of myelopathy are likely not a result of

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adjacent segment degeneration but could be due to surgeon error, inadequate decompression, dynamic cord compression or ischemia reperfusion injury; as such, the etiology of neurologic deterioration should be described. Specific timing thresholds must be defined to effectively differentiate between early and late onset of deterioration.

It is controversial whether progression of an ossified lesion should be considered a complication or a consequence of the natural history of the disease. In this review, reported rates varied widely depending on whether the definition included "progression of more than half of one vertebral body" (0.0% to 6.7%) or just specified an increase in the longitudinal or axial extent of the lesion (42.4% to 86.7%). It is unclear why these incidences differed so drastically, especially since the two studies by Chen et al. also included "progression of more than 2 mm in thickness" as part of their criteria. A possible explanation for these lower rates is that patients were treated with a hybrid posterior procedure that included both a laminoplasty and a lateral mass screw fixation at the unstable levels – this fixation may decrease dynamic causes of myelopathy, stabilize the environment around the spinal cord and ultimately prevent further progression[16,25]. In addition, as duration of follow-up increases, the incidence of this complication would likely also increase. Other issues in determining rates of progression include measurement error, variable quality of radiographs and differences between pre- and post-operative images, including in magnification and contrast characteristics. Chiba et al. developed a rigorous methodology to address some of these issues and accurately evaluate both the length and thickness of ossified lesions[51]. This system used lateral radiographs and a computer-assisted measurement system and was able detect a 2-mm change in length or thickness with 98% of precision.

The onset of radiculopathy (typically at the C5 level) following surgical decompression has been extensively studied. Current hypotheses for this complication include a traumatic surgical procedure, edema of the spinal cord or tethering of the nerve

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root.[53] Another explanation was recently proposed by Karadimas et al using a novel CSM rat model[54]. Based on their results, C5 palsy and other neurological complications may be associated with ischemia reperfusion injury that occurs following surgical decompression. Unfortunately, it is still unclear what the exact incidence of this complication is, whether it is associated with a specific surgical procedure or if there are certain baseline or imaging characteristics that increase a patient's risk. This uncertainty was confirmed in a systematic review of the literature which indicated there was insufficient evidence to determine the association between C5 palsy or upper extremity paresis and cervical alignment, number of compressed segments, position of the superior articular process, cord inclination, high signal intensity on T2-weighted MRI, occupying ratio, number of operated laminae, operative duration, and estimated blood loss[53]. The inability to answer these questions stems from the lack of consistency in definitions across studies. Although almost all definitions of C5 palsy specified a reduction in strength of the deltoid and/or biceps brachii muscles, there was substantial variation in MMT and exclusion criteria. Similar heterogeneity was identified in studies evaluating upper extremity palsy or new radiculopathy. The MCID for the MMT and other relevant scales should be used to identify cases of new radiculopathy.

Finally, none of the definitions for inadequate decompression considered the clinical status of the patient. Instead, all definitions were solely based on MRI findings, including cord flattening ratio, effacement of the anterior cerebrospinal fluid buffer and evidence of anterior cord compression. Given discrepancies between imaging findings and patient presentation, it is also important to consider improvement or regression of myelopathic symptoms when defining inadequate decompression.

This review represents the first part of a larger effort to develop guidelines for reporting surgical complications in the setting of DCM. This process will incorporate results from the current body of literature as well as clinical expertise. Before the development of

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this classification system, we suggest that future research on surgical safety report the following factors: definition of the complication studied, method of data collection (e.g. nurse, surgeon, research coordinator, self-reports), duration of follow-up, rates of mortality and causes, grading system used to evaluate severity, readmission or reoperation and percentage lost at follow-up. This knowledge will allow for more accurate reporting of complications, facilitate improved interpretation of results on surgical safety, and enable integration of larger national and international databases through common data elements.

Conclusion

Reported incidences of neurologic complications and disease progression vary widely in DCM surgery. There is a pressing need to standardize definitions and develop guidelines for accurately reporting surgical complications. In the interim, we suggest that authors define complications in accordance with our four-point rating scale and report methods of data collection, study design and management strategies.

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Table 1. An example on how definitions are scored using a 4-point rating system

Definition	Criterion A	Criterion B	Criterion C	Criterion D
C5 palsy was defined as a decrease in strength of the deltoid or biceps muscle	✓			
C5 palsy was defined as a decrease in strength of the deltoid or biceps muscle as measured by the MMT	✓	✓		
C5 palsy was defined as a decrease in strength of the deltoid or biceps muscle by >1 point on the MMT	✓	✓	✓	
C5 palsy was defined as a decrease in strength in the deltoid or biceps muscle by >1 point on the MMT at 24 hours after surgery (compared to presurgical status)	✓	✓	✓	✓

MMT: manual muscle testing

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Table 2. A Summary of Definitions used for Neurological Complications and Progression of Ossification Posterior Longitudinal Ligament

Complication	Definition	Author (year)	Score	Study Design	Follow-up[#]	Surgical Approach	Patients Available	# of Events	Incidence
(Neurological) Deterioration	A decrease in JOA score or an increase in Nurick grade by ≥1 point	Asgari (2009)	3 (A, B, C)	P	6W, 3-, 6-M, yearly (33M)	Posterior	13	1	7.7%
	A decrease in JOA score by >2 points after initial postoperative recovery	Goto (1993)	3 (A, B, C)	R	>12Y (16.6 Y)	Anterior	52	16[†]	30.8%[†]
	A decrease in JOA score by ≥3 points	Kato (1998)	3 (A, B, C)	R	1-, 5-Y (14.1 Y)	Posterior	44	10	22.7%[^]
	Increase of myelopathic signs and symptoms	Tetreault (2016)	1 (A)	P	<30D	Anterior and/or Posterior	477	1	0.2%
	An increase in Nurick by ≥1 grade	Fessler (1998)	3 (A, B, C)	R	6M, 1-, 2-, 5-Y	Anterior	93	1	1.1%
Late-onset Deterioration	A decline in JOA score by >3 points during the 4 year follow-up, compared to the patient's maximum score	Chen (2013)	4 (A, B, C, D)	R	4Y	Posterior	30	3	10%
	A decline in JOA score by >1 point	Chiba (2006)	3 (A, B, C)	R	<5, 5-10, >10Y	Posterior	80	24	30.0%
	A decrease in JOA score by >2 points	Iwasaki (2007)	3 (A, B, C)	R	5-20Y (10.2 Y)	Posterior	66	3	4.5%
	A decrease in the JOA score by >2 points after ≥10 years of postoperative improvement	Goto (1993)	4 (A, B, C, D)	R	>12Y (16.6 Y)	Anterior	52	13	25.0%
	A decrease in upper-extremity and trunk JOA scores by >1 point at final follow-up compared to the highest score observed 1-5 years after surgery	Ogawa (2005)	4 (A, B, C, D)	R	>7Y	Posterior	57	19	33.3%

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	A decrease in upper-extremity and trunk JOA scores by >2 points	Ogawa (2004)	3 (A, B, C)	R	>5Y (9.5Y)	Posterior	72	11	15.3%
Perioperative worsening of	Signs and symptoms due to cervical myelopathy	Tetreault (2016)	2 (A, D)	P	<30D	Anterior and/or Posterio	477	3	0.6%
Progression of Ossified Lesions	Progression of ossified lesion >50% of one vertebral body axially, or >2 mm in thickness at follow-up, compared with measurements taken just after the operation on lateral radiographs	Chen (2013)	3 (A, B, C)	R	4Y	Posterior	30	2	6.7%
	Ossification of >50% of one vertebral body axially or >2mm in thickness at 4-year follow up compared to immediate post-operative lateral radiographs	Chen (2014)	4 (A, B, C, D)	R	4Y	Posterior	15	0	0.0%
	Computer assisted measurements of the size of the ossified lesions (described by Chiba et al (2005))	Chiba (2006)	2 (A, B)	R	>10Y (14.2 Y)	Posterior	53	35	66.0%
	≥2mm increase in longitudinal extent on radiographs and/or sagittal thickness on lateral tomograms	Kawaguchi (2001)	3 (A, B, C)	R	(13.1 Y)	Posterior	45	33	73.3%
	≥2mm increase in longitudinal extent and/or sagittal thickness on lateral radiographs	Sakaura (2011)	3 (A, B, C)	P	3-, 6-, 9-, 12-M, yearly (5.4Y)	Posterior	11	7	63.6%
	Progression of an ossified lesion >2 mm when comparing preoperative and final follow-up radiographs	Ogawa (2005)	3 (A, B, C)	R	>7Y	Posterior	57	37	64.9%
		Ogawa (2004)		R	>5Y (9.5Y)	Posterior	72	46	63.9%
	Sagittal growth of an ossified mass >2mm or longitudinal growth over one vertebral body	Satomi (1994)	2 (A, C)	R	1-, 3-, 5-Y (8Y)	Posterior	33	14 12	42.4%* 36.4%**
	Longitudinal progression >2 mm on radiographs.	Onari (2001)	3 (A, B, C)	R	>10Y (14.7 Y)	Anterior (26), Combined (4)	30	26	86.7%
	Increase in thickness >1 mm on						30	15	50.0%

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	radiographs								
	≥2 mm increase in existing lesions, a new ossified lesion measuring ≥2 mm, and bridging between separate lesions to form a continuous lesion	Iwasaki (2007)	2 (A, C)	R	>5Y (10.2 Y)	Posterior	52	27	51.9%
C5 palsy	Reduction of MMT by ≥1 grade^^	Ikenaga (2005)	3 (A, B, C)	R	4H-8D	Anterior	544	18	3.3%
	Deterioration of muscle strength of the deltoid and the biceps brachii by ≥1 grade on MMT after surgery, without any deterioration of other neurologic symptoms	Kaneyama (2010)	3 (A, B, C)	P	<2W	Posterior	146	8	5.5%
		Odate (2013)		R	1-21D (5D)	Anterior	459	32	7.0%
	Deltoid muscle weakness (grade ≤3 on MMT) without any deterioration of myelopathic symptoms after surgery	Katsumi (2012)	3 (A, B, C)	P	0-7D	Posterior	282	11	3.9%
		Ohashi (2014)		P	2-, 6-, 12-, 24-M	Posterior	236	10	4.2%
	Deltoid muscle weakness (grade <3 on MMT) after surgery	Katsumi (2013)	3 (A, B, C)	R	0-7D	Posterior	141	9	6.4%
	Deterioration in muscle power of the deltoid or biceps brachii muscle by ≥1 grade on MMT without aggravation of lower extremity function	Kim (2014)	3 (A, B, C)	R	1-18D	Anterior	104	6	5.8%
	Deterioration of the deltoid muscle by ≥1 grade on MMT (5 normal; 0 no muscle contracture) postoperatively and/or apparent sensory deficits or only pain at the C5 dermatome area	Liu (2010)	3 (A, B, C)	R	1-7D	Posterior	91	21	23.1%
	Postoperative symptoms of paresis of the deltoid/biceps brachii muscles and/or pain/sensory deficits of the C5 dermatome	Lubelski (2014)	1 (A)	R	Post-op	Anterior	98	12	12.2%

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	Paresis of deltoid (MMT score 1 or 2), with or without involvement of the biceps, but no loss of strength in other muscles	Machino (2013)	3 (A, B, C)	P	>1Y (2.78 Y)	Posterior	520	3	0.6%
		Machino (2014)		P	>1Y (2.21 Y)	Posterior	505	7	1.4%
		Imagama (2010)		R	1-28D (4.7D)	Posterior	1858	43	2.3%
	Postoperative deterioration of muscle strength in the deltoid muscle by ≥1 grade on the MMT, with or without involvement of the biceps muscle, but no loss of strength in other muscles	Nakashima (2012)	3 (A, B, C)	P	1-10D (2.4)	Posterior	54	8	14.8%
	New decline in deltoid muscle power (evaluated by the MMT) that developed after surgery	Sasai (2003)	2 (A, B)	P	7-8D (7.3)	Posterior	111	3	2.7%
	New deterioration of muscle strength of the deltoid muscle and/or the biceps brachii muscle	Shiozaki (2009)	1 (A)	P	1D	Posterior	19	1	5.3%
	A decrease in upper limb muscle strength by ≥1 grade on postoperative MMT	Yanase (2010)	3 (A, B, C)	R	Post-op	Posterior	153	9	5.8%
	Postoperative MMT <3	Yeh (2014)	3 (A, B, C)	R	<3M	Posterior	104	3	2.9%
	Loss of motor strength in the deltoid and/or biceps brachii muscles, sensory deficit or increased pain in the C5 nerve distribution	Yuan (2015)	1 (A)	P	Post-op	Posterior	38	3	7.9%
	A decrease in strength of deltoid and biceps muscles to a grade of 1 on MMT	Chen (2009)	3 (A, B, C)	R	8-24H	Anterior	138	2	1.4%
	C5 dermatome hypoesthesia, diminished or absent bicipital reflex (not present before surgery),	Tetreault (2016)	1 (A)	P	<30D	Anterior and/or Posterior	477	4	0.8%

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	postoperative deltoid and/or biceps muscle paresis								
Nerve Root/ Upper Limb Palsy	A mild degree of paralysis was defined as a MMT score of 5-4; moderate as 3-2; and severe as 1-0. Motor dominant: muscle weakness with little or no sensory loss. Sensory-dominant: sensory loss and/or intractable pain with little or no motor impairment	Dai (1998)	3 (A, B, C)	R	4H-6D (15H)	Posterior	287	37	12.9%
	A mild degree of paralysis was defined as a MMT score of 5-4; moderate as 3-2; and severe as 1-0. Motor dominant: muscle weakness supervened with little or no sensory loss. Sensory-dominant: muscle power improved after pain was relieved by a root block even in cases where muscle weakness was associated with radicular pain	Tsuzuki (1993)	3 (A, B, C)	R	<1W	Posterior	188	20	10.6%
	Upper limb palsy: A postoperative decrease in upper-limb muscle strength of ≥1 grade on MMT, but no deterioration of myelopathy symptoms	Takenaka (2013)	3 (A, B, C)	R	2W	Posterior	159	8	5.0%
	Upper limb palsy: Deterioration of motor function by ≥1 grade on MMT without aggravation of lower extremity function, the appearance of a new sensory disturbance between postoperative day 0 and 2 months after surgery, or both	Hasegawa (2007)	4 (A, B, C, D)	R	0D-2M	Anterior	424	22	5.2%
						Posterior	433	27	6.2%

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	deterioration of motor function and the appearance of a new sensory disturbance.								
	New radiculopathy: signs and symptoms of other cervical spine root lesions	Tetreault (2016)	1 (A)	P	<30D	Anterior and/or Posterior	477	3	0.6%
	Upper limb palsy: Weakness of key muscles in the upper limb (≤4 grade on MMT) without deterioration of myelopathic symptoms after surgery	Wu (2014)	3 (A, B, C)	R	1-14D (3.4D)	Posterior	102	16	15.7%
Decreased arm strength	The strength of the deltoid, biceps, and triceps brachii muscles was measured by shoulder abduction, elbow flexion, and elbow extension, respectively, using a calibrated hand-held dynamometer before and 2 weeks after surgery. Grip strength was assessed using a grip dynamometer. Decreased arm strength was defined as decreased strength in ≥1 muscle as evaluated by either the hand-held or grip dynamometer (cut-off points based on postoperative/preoperative scores)	Takenaka (2013)	4 (A, B, C, D)	R	2W	Posterior	318[††]	36[††]	11.3%[-]
Surgery failure	Improvement was defined as a change of at least two grades in the Nurick classification, and/or resolution of hyperpathia and dysesthesia. A smaller grade change or regression of improvement was considered a failure	Saunders (1991)	3 (A, B, C)	P	2-, 6-W, 3-, 6-M, yearly	Anterior	39	5	12.8%
Inadequate Decompression	A cord flattening ratio <0.4 after operation on T1-	Chen (2009)	3 (A, B,	R	12-36M (18M	Anterior	138	NR	NR

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	weighted MRI images		C)		)				
		Chen (2009)		P	12-36M (18M)	Anterior	19	NR	NR
	Residual anterior compression of spinal cord: (1) Effacement of anterior CSF buffer on T2 sagittal and axial images; (2) Evidence of anterior compression of cord substance on T1 sagittal and axial images.	Hirai (2011)	2 (A, B)	P	Post-op, 2Y	Posterior	47	16	12.8%[%], 37.5%

P = Prospective, R = Retrospective

[#]Time of diagnosis or onset or period of evaluation (H = hour(s); D = day(s); W = week(s); M = month(s); Y = year(s); (…) = mean follow up)

[^]Extrapolated from Table 5 in Kato et al (1998)

[†]Three patients were categorized as "early deterioration" while ten patients were classified as "late deterioration"

[^^]Extrapolated from Table 3 in Ikenaga et al (2005)

[††]Number of arms assessed and number of arms with decreased strength

[*]Incidence of OPLL progression based on a sagittal growth >2mm

[**]Incidence of OPLL progression based on a longitudinal growth over one vertebral body

[%]Six patients exhibited residual anterior compression of the spinal cord immediately after surgery. At 2, years, 16 patients displayed residual anterior compression, including the six patient who had immediate evidence of inadequate decompression (of the new 10, seven had progression of kyphotic changes and 3 had spondylolisthesis)

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Table 3. An Overview of Reported Incidences of Complications

Complication	Definitions/Studies with Reported Incidences	Mean Incidence at Final Follow Up (range)	Number of Patients
Neurological deterioration	5/5	2.3% (0.2%-30.8%)	679
Late-onset deterioration	6/6	20.4% (4.5%-33.3%)	357
Perioperative worsening of myelopathy	1/1	0.6%	477
Progression of ossified lesions	10/10	56.5% (0.0%-86.7%)	428
C5 palsy	16/20	3.5% (0.6%-23.1%)	6078
Upper limb palsy	6/6	6.4% (0.6%-15.7%)	2070
Decreased arm strength	1/1	11.3%	318
Inadequate decompression	2/3	12.8%	47
Surgery failure	1/1	12.8%	39

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