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# The Natural History of Degenerative Cervical Myelopathy and the Rate of Hospitalization Following Spinal Cord Injury: An Updated Systematic Review

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## Abstract

**Study Method:** Systematic review (update).

**Objective:** Degenerative cervical myelopathy (DCM) is a degenerative spine disease and the most common cause of spinal cord dysfunction in adults worldwide. The objective of this study is to determine the natural history of DCM by updating the systematic review by Karadimas et al. The specific aims of this review were (1) to describe the natural history of DCM and (2) to determine potential risk factors of disease progression.

**Method:** An updated search based on a previous protocol was conducted in PubMed and the Cochrane Collaboration library for studies published between November 2012 and February 15, 2015.

**Results:** The updated search yielded 3 additional citations that met inclusion criteria and reported the incidence of spinal cord injury and severe disability in patients with DCM. Based on 2 retrospective cohort studies, the incidence rate of hospitalization for spinal cord injury is 13.9 per 1000 person-years in patients with cervical spondylotic myelopathy and 4.8 per 1000 person-years in patients with myelopathy secondary to ossification of the posterior longitudinal ligament (OPLL). In a third small prospective study, the risk of being wheelchair bound or bedridden was 66.7% in DCM patients with OPLL.

**Conclusion:** The overall level of evidence for these estimated rates of hospitalization following spinal cord injury was rated as low.

## Keywords

degenerative cervical myelopathy, cervical spondylotic myelopathy, systematic review

## Introduction

Degenerative cervical myelopathy (DCM) is a degenerative spine disease and the most common cause of spinal cord dysfunction in adults worldwide.<sup>1</sup> The term DCM encompasses cord compression secondary to osteoarthritic changes to the spine, disc degeneration, ligamentous aberrations, and progressive kyphosis. Patients with DCM may present with a wide range of neurological signs and symptoms, including pain, lower limb spasticity, decreased hand dexterity, hyperreflexia, and sphincter disturbance.

The pattern of progression in DCM is not well defined. Early reports of the natural history suggest that DCM is a relatively benign disorder and that patients are more likely to

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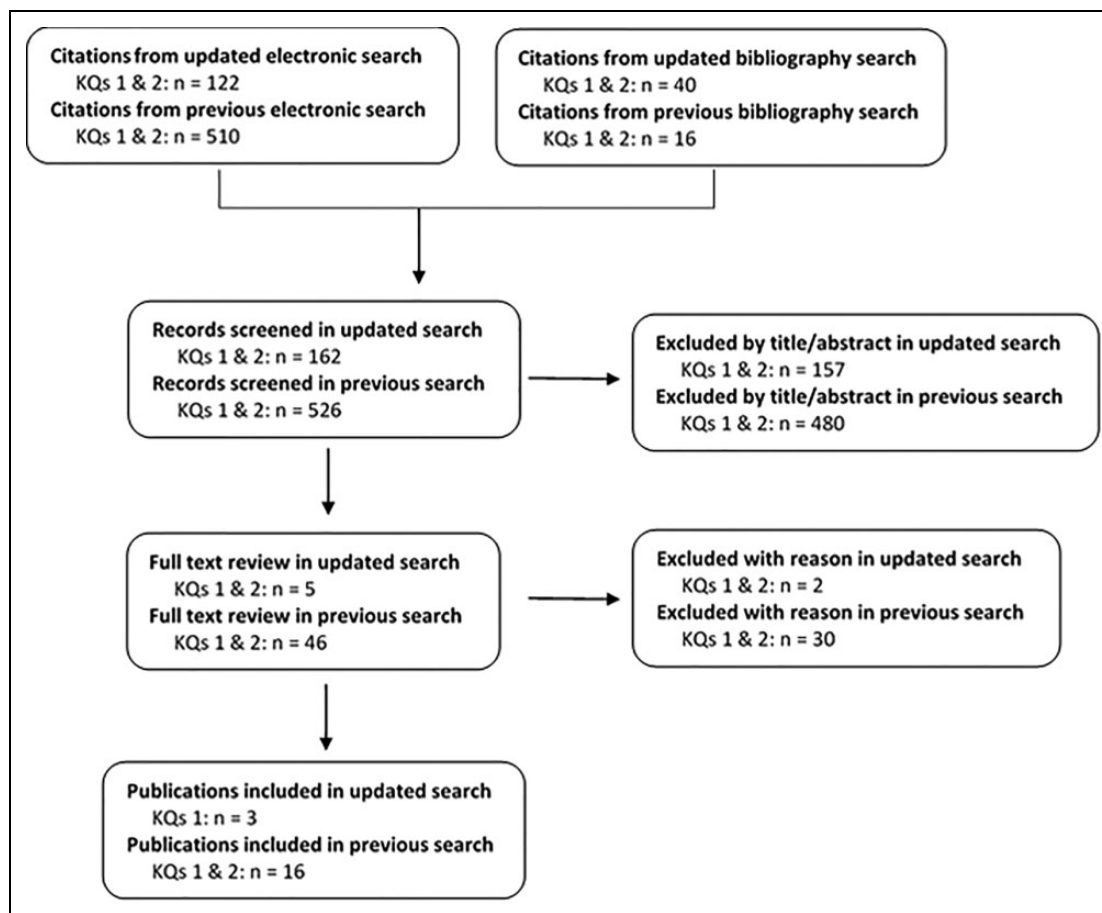
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**Figure 1.** Results of updated and originally published literature searches. KQ = key question.

remain stable over time than to deteriorate.<sup>2</sup> In the most recent systematic review of the literature, there was moderate evidence that 20% to 62% of patients with symptomatic myelopathy will decline by at least 1 point on the Japanese Orthopaedic Association scale if not managed surgically.<sup>3</sup> The objective of this study was to update the systematic review by Karadimas et al<sup>3</sup> that investigated (1) the natural history of DCM and (2) the potential risk factors of disease progression.

## Materials and Methods

### Electronic Literature Search

An updated search based on a previous protocol<sup>4</sup> was conducted in PubMed and the Cochrane Collaboration library for studies published between November 2012 and February 15, 2015. Inclusion and exclusion criteria for the search were previously published, as well as methods for data abstraction, data analysis, evaluation of study quality, and assessment of the overall strength of evidence.

## Results

### Study Selection

The updated electronic search yielded 122 new citations (Figure 1). An additional 40 citations were identified through

**Table 1.** Excluded Studies and Reasons for Exclusion.

Author (Year)	Reasons for Exclusion
Kalb et al (2011)	Surgery study
Matsunaga (2008)	Wrong population: Asymptomatic OPLL

Abbreviation: OPLL, ossification of the posterior longitudinal ligament.

directed manual search. One hundred and fifty-seven studies were excluded following title and abstract review, and 5 studies were further investigated. Following full text review, a single study was excluded because all patients underwent surgery for DCM, and another for including nonmyelopathic patients with ossification of the posterior longitudinal ligament (OPLL; Table 1).<sup>5</sup> Three other studies presented new information relevant to key question 1 and reported the incidence of spinal cord injury and severe disability in patients with DCM.<sup>6-8</sup>

Two retrospective cohort studies used the National Health Insurance Research Database, which contains records for 23 million administered insurants in Taiwan (approximately 99% of the entire population).<sup>7,8</sup> The first study included 14 140 patients hospitalized for cervical spondylotic myelopathy (CSM) with at least 1 year of follow-up (Table 2).<sup>8</sup> The second study consisted of 5604 patients with myelopathy secondary to OPLL and at least 3 years of follow-up.<sup>7</sup> A third prospective

**Table 2.** Characteristics of New Studies Addressing the Natural History of DCM.

Author (Year)/Study Design	Patient Characteristics	Mean Follow-up; % Follow-up	Inclusion Criteria
Wu et al (2013) <sup>8</sup> / Retrospective cohort	N = 14 140; mean age = NR; % male NR	≥ 1 year; % NR	Subjects hospitalized and discharged with the diagnostic ICD-9 code for CSM (721.1) (National Health Research Institute of Taiwan)
Wu et al (2012) <sup>7</sup> / Retrospective cohort	N = 5604; mean age = 60.35 ± 14 years; 70% male	≥ 3 years; % NR	Subjects hospitalized within the study period with a first time discharge summary containing the diagnostic ICD-9 code for OPLL (723.7x) (National Health Research Institute of Taiwan) Patients hospitalized for OPLL who have not received spinal intervention within the previous 6 months (National Health Research Institute of Taiwan)
Matsunaga et al (2004) <sup>6</sup> / Prospective cohort	N = 36 <sup>a</sup> ; mean age = 61.8 years; 59% male	17.6 years (range = 10-30 years); % NR	Patients with DCM from OPLL

Abbreviations: DCM, degenerative cervical myelopathy; ICD-9, International Classification of Diseases, Ninth Edition; CSM, cervical spondylotic myelopathy; NR, not reported; OPLL, ossification of the posterior longitudinal ligament.

<sup>a</sup>N = 450 in study; 36 patients were treated conservatively for myelopathy symptoms.

**Table 3.** Incidence Rate or Risk of Spinal Cord Injury and Disability in Patients Not Treated Surgically.

Outcome	Study	Risk of Bias	Diagnosis	N	Person-Years or Number of Persons	Incidence Rate or Risk <sup>a</sup> (95% CI)
SCI <sup>b</sup>	Wu (2013)	Moderately low	CSM	122	8776.7	13.9 (11.6-16.6)
	Wu (2012)	Moderately low	OPLL <sup>c</sup>	7	1455.2	4.8 (2.3-10.1)
Disability <sup>d</sup>	Wu (2012) <sup>7</sup>	Moderately low	OPLL <sup>c</sup>	5	1463.6	3.4 (1.5-8.0)
	Matsunaga (2004) <sup>6</sup>	Moderately high	OPLL <sup>c</sup>	24	36	66.7%

Abbreviations: CI, confidence interval; SCI, spinal cord injury; CSM, cervical spondylotic myelopathy; OPLL, ossification of the posterior longitudinal ligament; DCM, degenerative cervical myelopathy.

<sup>a</sup>Rate is per 1000 person-years; risk = percentage.

<sup>b</sup>Defined as hospitalizations for SCI.

<sup>c</sup>DCM secondary to OPLL

<sup>d</sup>Wu (2012) defined disability as severe neurological deficits caused by SCI such as paraplegia, tetraplegia, and incontinence; Matsunaga (2004) defined disability as becoming wheelchair bound or bedridden.

cohort study reported outcomes on 450 patients with myelopathy secondary to OPLL; however, only 36 were managed conservatively after refusing surgical treatment.

### Hospitalization for Spinal Cord Injury

Based on 2 retrospective cohort studies, the incidence rate of hospitalization for spinal cord injury was 13.9 per 1000 person-years (95% confidence interval [CI] = 11.6-16.6) in patients diagnosed with CSM<sup>8</sup> and 4.8 per 1000 person-years (95% CI = 2.3-10.1) in patients with myelopathy secondary to OPLL<sup>7</sup> (Table 3). The rate of hospitalization for spinal cord injury in patients with DCM from OPLL was significantly higher than the rate observed in a healthy population (0.18 per 1000 person-years; hazard ratio = 32.2; 95% CI = 10.4-99.0;  $P < .001$ ).<sup>7</sup> These studies both had moderately low risk of bias (Table 4).

### Disability

One large retrospective study evaluated the incidence of severe neurological deficits from spinal cord injury in patients with

**Table 4.** Class of Evidence for Prognostic Studies.

Methodological Principle	Wu (2013) <sup>8</sup>	Wu (2012) <sup>7</sup>	Matsunaga (2004) <sup>6</sup>
Study design			
Prospective cohort study			✓
Retrospective cohort study	✓	✓	
Case-control study			
Case series			
Patients at similar point in the course of their disease or treatment	✓	✓	
Patients followed long enough for outcome to occur	✓	✓	✓
Complete follow-up of ≥80%	✓	✓	
Controlling for extraneous prognostic factors <sup>a</sup>	✓	✓	

<sup>a</sup>Authors must summarize baseline characteristics, and control for those that differ between treatment groups.

CSM, including paraplegia, tetraplegia, and incontinence; the reported rate was 3.4 per 1000 person-years.<sup>7</sup> A second small prospective study reported that the risk of being wheelchair bound or bedridden was 66.7% (24/36) in patients with DCM

**Table 5.** Evidence Summary.

	Strength of Evidence	Conclusions/Comments	Baseline <sup>a</sup>	Upgrade (Levels) <sup>b</sup>	Downgrade (Levels) <sup>c</sup>
<b>What is the natural history of CSM?</b>					
<i>Neurological outcome</i>					
• JOA change compared with baseline	Moderate	• Although mean scores tend to remain constant, there is moderate evidence (2 small prospective <sup>9,10</sup> and 4 small retrospective <sup>10-13</sup> observational studies) that 20% to 62% of patients will deteriorate (at least 1 point on the JOA) 3-6 years after initial assessment. Proportions vary based on definition of deterioration.	High		Risk of bias (1)
• Nurick Grade change compared with baseline	Very Low	• There is very low evidence from one small retrospective observational study (N = 76) <sup>14</sup> that a majority of DCM patients will not experience a change on the Nurick over time with nonoperative treatment. Sixty-seven percent of patients were stable, 20% improved, and 13% deteriorated after 8 years.	Low		Inconsistent (1)
• Spinal cord injury	Low	• There is low-level evidence that the rate of hospitalization for spinal cord injury is 13.9 per 1000 person-years in patients with CSM. <sup>8</sup> The rate is 4.8 per 1000 person-years in patients with DCM from OPLL and 0.18 per 1000 person-years in a healthy population (HR = 32.2; 95% CI = 10.4-99.0). <sup>7</sup>	Low		
• Disability	Low	• There is low-level evidence that the rate of severe disability is 3.4 per 1000 person-years in patients with DCM secondary to OPLL. <sup>7</sup>	Low		
• Conversion to surgery	Very Low	• There is very low evidence (2 small prospective <sup>10,15,16</sup> and 4 small retrospective observational studies) <sup>11,17-19</sup> that the proportion of patients undergoing surgery following worsening of symptoms increases over time. The proportion of patients converting to surgery ranges from 4% to 40% over 3 to 7 years, respectively.	Low		Imprecise (1)
<i>Functional outcome</i>					
• Activities of daily living	Moderate	• There is moderate evidence (2 small prospective studies, N = 31 <sup>20</sup> and N = 33 <sup>21</sup> ) that patients with DCM worsen in performing activities of daily living (ADL) with nonoperative treatment. One study reported 6%, 21%, 28%, and 56% worsening of ADL from baseline values at 1-, 2-, 3-, and 10-years follow-up, respectively.	High		Risk of bias (1)
• Timed 10-meter walk	Very Low	• There is very low evidence (one small prospective study, N = 33 <sup>21</sup> ) that there is no significant difference in 10-meter walking test times between baseline and 1-, 2-, 3-, and 10-years following conservative treatment.	High		Risk of bias (1); Imprecise (1); Inconsistent (1)
• Overall functional status	Very Low	• There is very low evidence (one small prospective observational study, N = 31 <sup>20</sup> ) that the overall functional status improves over time in patients treated conservatively for DCM.	Low		Inconsistent (1)
<b>Are there risk factors that affect the progression of DCM?</b>					
<i>Neurological outcome</i>					
<i>Demographic characteristics</i>					
• Age	Very Low	• There is very low evidence to support the association between age at diagnosis and neurological deterioration based on the JOA. One prospective study reported no association using multivariate analysis; <sup>13</sup> one prospective study reported that older age (mean 58 years) before treatment was a positive predictor for neurological improvement ( $P < .05$ ); <sup>9</sup> and one retrospective study reported that younger age (<52 years) was a positive predictor for neurological improvement using univariate analysis. <sup>17</sup>	Low		Inconsistent (1); Imprecise (1)

(continued)

Table 5. (continued)

	Strength of Evidence	Conclusions/Comments	Baseline <sup>a</sup>	Upgrade (Levels) <sup>b</sup>	Downgrade (Levels) <sup>c</sup>
• Sex	Very Low	• There is very low evidence to support the association between sex and neurological progression of myelopathy on the JOA. One prospective study reported no association using multivariate analysis <sup>10</sup> and one retrospective study indicated that female sex was associated with a progressively worse neurological condition ( $P < .05$ ). <sup>20</sup>	Low		Inconsistent (I); Risk of bias (I)
• Height	Very Low	• There is very low evidence (one prospective study) that lower body height (mean 170 cm) is a positive predictor of JOA improvement ( $P < .05$ ). <sup>9</sup>	High		Imprecise (I); Inconsistent (I)
<b>Radiographic characteristics</b>					
• Circumferential spinal cord compression	Low	• There is low evidence (one prospective study using multivariate analysis) that circumferential spinal cord compression (compared with only partial cord compression) is associated with neurological deterioration (JOA) (adjusted OR = 26.6; 95% CI = 1.7-421.5). <sup>10</sup>	High	Large effect (I)	Risk of bias (I); Imprecise (I); Inconsistent (I)
• Transverse area of the spinal cord; Pavlov's Index	Very Low	• There is very low evidence (one prospective observational study) that a larger transverse area of the spinal cord (mean 76 mm <sup>2</sup> ) ( $P < .05$ ) and a higher Pavlov Index (mean 0.9) ( $P < .05$ ) are associated with improved neurological status (JOA). <sup>9</sup>	High		Risk of bias (I); Imprecise (I); Inconsistent (I)
• Other radiological factors	Very Low	• There is very low evidence (one prospective study using multivariate analysis) that there is no significant association between developmental or dynamic canal factors, high T2WI signal intensity and neurological deterioration (JOA). <sup>10</sup>	High		Risk of bias (I); Imprecise (I); Inconsistent (I)
<b>Clinical characteristics</b>					
• Initial level of disability	Very Low	• There is very low evidence (one prospective <sup>9</sup> and one retrospective <sup>17</sup> observational study) that milder disability before treatment is associated with greater neurological improvement (JOA) ( $P < .05$ ).	Low		Imprecise (I)
• Duration of disease	Very Low	• There is very low evidence (2 retrospective observational studies) that a shorter duration of symptoms is associated with neurological improvement (JOA) ( $P = .001$ ). <sup>13,17</sup>	Low		Inconsistent (I)
• Range of motion	Very Low	• There is very low evidence (one retrospective study) that greater neck range of motion (ROM) ( $P < .05$ ), greater head ROM ( $P < .01$ ), and difference between total head and neck ROM ( $P < .01$ ) are associated with progressively worse neurological condition (JOA). <sup>14</sup>	Low		Inconsistent (I); Imprecise (I)
<b>Conversion to surgery</b>					
<b>Demographic characteristics</b>					
• Age; sex	Very Low	• There is very low evidence (one retrospective study using multivariate analysis) that there is no association between age $\geq 60$ years or sex and conversion to surgery. <sup>19</sup>	Low		Inconsistent (I); Imprecise (I)
<b>Radiographic characteristics</b>					
• Cervical range of motion	Very Low	• There is very low evidence (one small retrospective study, N = 45 using multivariate analysis <sup>19</sup> ) that there is an association between increased risk of surgery and the following factors:	Low	Large effect (I)	Imprecise (I); Inconsistent (I)
• Segmental lordotic angle		• Total cervical range of motion ( $\geq 50^\circ$ ) (adjusted HR = 3.3; 95% CI = 1.03-10.25)			
• Local slip		• Segmental lordotic angle ( $< 0^\circ$ ) (adjusted HR = 4.5; 95% CI = 1.59-12.8)			
		• Presence of a local slip (adjusted HR = 4.7; 95% CI = 1.67-13.0)			

(continued)

**Table 5.** (continued)

	Strength of Evidence	Conclusions/Comments	Baseline <sup>a</sup>	Upgrade (Levels) <sup>b</sup>	Downgrade (Levels) <sup>c</sup>
• Other radiographic factors	Very Low	• There is very low evidence (one small retrospective study, N = 45 using multivariate analysis) that there is no association between increased risk of surgery and C2-7 alignment (<0°), spinal cord diameter (<50%), presence of developmental canal stenosis, and segmental range of motion (≥10°). <sup>19</sup>	Low		Imprecise (1); Inconsistent (1)

Abbreviations: CSM, cervical spondylotic myelopathy; JOA, Japanese Orthopaedic Association; DCM, degenerative cervical myelopathy; OPLL, ossification of the posterior longitudinal ligament; HR, hazard ratio; CI, confidence interval; OR, odds ratio.

<sup>a</sup>Baseline quality: High = majority of articles low/moderately low risk of bias; Low = majority of articles moderately high/high risk of bias.

<sup>b</sup>Upgrade: Large magnitude of effect (1 or 2 levels); dose response gradient (1 level); plausible confounding decreases magnitude of effect (1 level).

<sup>c</sup>Downgrade: Inconsistency of results (1 or 2 levels); indirectness of evidence (1 or 2 levels); imprecision of effect estimates (1 or 2 levels); risk of bias (1 or 2 levels); failure to specify subgroup analysis a priori (1 level); reporting bias (1 level).

secondary to OPLL (Table 3).<sup>6</sup> This study had moderately high risk of bias (Table 4).

## Evidence Summary

The rate of hospitalization due to spinal cord injury was 4.8 per 1000 person-years in patients with DCM secondary to OPLL and 13.9 per 1000 person-years in patients with CSM. The rate of severe disability in DCM patients with OPLL was 3.4 per 1000 person-years. The strength of evidence for these estimates was Low (Table 5).

## Conclusions

The results of this update indicate that the presence of OPLL or CSM may increase a patient's risk of severe disability and hospitalization for spinal cord injury. Although these findings are unlikely to directly influence management strategies, patients should be counseled of the possibility of spinal cord injury when discussing the benefits and risks of various treatment options.

## Declaration of Conflicting Interests

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