Predictors of outcome in patients with degenerative cervical spondylotic myelopathy undergoing surgical treatment: results of a systematic review

Lindsay A. Tetreault · Alina Karpova ·
Michael G. Fehlings

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Abstract

Purpose To conduct a systematic review of the literature to determine important clinical predictors of surgical outcome in patients with cervical spondylotic myelopathy (CSM).

Methods A literature search was performed using MEDLINE, MEDLINE in Process, EMBASE and Cochrane Database of Systematic Reviews. Selected articles were evaluated using a 14-point modified SIGN scale and classified as either poor (<7), good (7–9) or excellent (10–14) quality of evidence. For each study, the association between various clinical factors and surgical outcome, evaluated by the (modified) Japanese Orthopaedic Association scale (mJOA/JOA), Nurick score or other measures, was defined. The results from the EXCELLENT studies were compared to the combined results from the EXCELLENT and GOOD studies which were compared to the results from all the studies.

Results The initial search yielded 1,677 citations. Ninety-one of these articles, including three translated from Japanese, met the inclusion and exclusion criteria and were graded. Of these, 16 were excellent, 38 were good and 37 were poor quality. Based on the excellent studies alone, a longer duration of symptoms was associated with a poorer outcome evaluated on both the mJOA/JOA scale and Nurick score. A more severe baseline score was related with a worse outcome only on the mJOA/JOA scale. Based on the GOOD and EXCELLENT studies, duration of symptoms and baseline severity score were consistent predictors of

mJOA/JOA, but not Nurick. Age was an insignificant predictor of outcome on any of the functional outcomes considered.

Conclusion The most important predictors of outcome were preoperative severity and duration of symptoms. This review also identified many other valuable predictors including signs, symptoms, comorbidities and smoking status.

Keywords Cervical spondylotic myelopathy · Clinical predictors · Surgical outcome · Systematic review

Introduction

Cervical spondylotic myelopathy (CSM) is the most common cause of spinal cord dysfunction worldwide. The disease is caused by the degeneration of various components of the vertebra, including the vertebral body, the intervertebral disk, the supporting ligaments and the facet joints [1]. Static factors, including the protrusion of osteophytic spurs (spondylosis), disk desiccation, ossification of the posterior longitudinal ligament (OPLL) and hypertrophy of the ligamentum flavum, may lead to the narrowing of the spinal canal and to cord compression [2]. Longstanding compression of the spinal cord can result in irreversible damage including demyelination and necrosis of the gray matter. The onset of CSM is generally insidious and progresses in a stepwise fashion [3, 4]. Upon diagnosis of symptomatic CSM, a physician often recommends surgical treatment to decompress the spinal cord [5]. Surgery has proven to be an effective intervention for the full range of myelopathy severity [6].

Given that CSM is a prevalent cause of spinal cord injury, and since surgery is often an appropriate intervention,

L. A. Tetreault · A. Karpova · M. G. Fehlings (✉)
Krembil Neuroscience Center, Toronto Western Hospital,
University of Toronto, 399 Bathurst St. 4WW449,
Toronto, ON M5T 2S8, Canada
e-mail: Michael.fehlings@uhn.on.ca

it would be useful to identify the most important predictors of surgical outcome. Prediction is a valuable tool in a clinical setting. Knowing a patient's surgical outcome can help determine which patients are most likely to benefit from surgery and help assess their degree of functional improvement [7]. This allows surgeons to provide valuable prognostic information to concerned patients, helping to manage expectations, as well as implement and direct appropriate treatment programs.

Holly et al. [8] conducted a similar systematic review of the literature and found that the most common predictors of surgical outcome for patients with CSM were age, duration of symptoms and severity of myelopathy. These three clinical factors are most frequently reported in the literature. Controversy still remains as to the significance, strength and direction of the relationship between surgical outcome and age, duration of symptoms and baseline severity.

The objective of this paper is to conduct a comprehensive literature search to determine the most important clinical predictors of outcome in surgical CSM-patients. This paper will address whether age, duration of symptoms, baseline severity score are indeed predictors and will also examine other clinical factors including comorbidities, smoking status, signs and symptoms to determine their predictive value.

Materials and methods

A literature search was performed using MEDLINE, MEDLINE in Process, EMBASE and Cochrane Central Register of Controlled Trials. The keywords used for the search were Cervical Spondylotic Myelopathy AND Surgery or Postoperative AND Prediction/Prognosis AND observational studies. The search was limited to humans, aged 18 years or older. The total number of citations found for this review was 1,677.

Articles were included if they were observational studies on patients >18 years with degenerative cervical myelopathy, treated surgically and followed postoperatively. Articles must have either directly or indirectly assessed the ability of a clinical factor to predict surgical outcome. Articles were eliminated if they were review articles or opinions; studies on patients with traumatic spinal cord injuries, thoracic myelopathy, radiculopathy, or non-degenerative cervical myelopathy; studies assessing only radiographic factors as predictors and studies that used complications as an outcome measure. Articles that were not in English or Japanese were excluded. Japanese articles were translated by Dr. Iwasaki and were included in the analysis.

All 1,677 abstracts and titles were reviewed independently by two authors (LAT, AK) and were sorted based on pre-determined inclusion and exclusion criteria. Figure 1 displays the search and review process in detail. Ninety-one articles were included. Three of these were translated from Japanese to English. Each article was assessed for quality with respect to methodology and overall structure. Several rating scales were examined, including Altman [9], Hayden et al. [10], and the Scottish Inter-Collegiate Guidelines Network (SIGN) scale for prognostic studies [11]. A modified version of the SIGN scale was used to rate the articles.

A modified version of the SIGN scoring system was implemented in a systematic review published by Kalsi-Ryan and Verrier [12]. Since the incidence of spinal cord injury is comparatively low, high quality research in this field is challenging. Studies often have small sample sizes with no opportunity for blinded assessment and randomization. Kalsi-Ryan and Verrier modified SIGN so that it was more specific to the nature of literature they were reviewing. We selected the modified SIGN system and further altered it to increase its applicability to literature reporting clinical predictors of surgical outcome in patients with CSM. Questions 15 and 16 were changed from dichotomous scoring to trichotomous scoring as studies may vary greatly in quality of statistical analysis, methodology and bias elimination (Table 1). It was arbitrarily decided that an article whose score was <7 would be classified as POOR, 7–9 as GOOD and 10–14 as EXCELLENT. The results from the EXCELLENT studies were compared to the combined results from the EXCELLENT and GOOD studies which were compared to the results from all the studies.

For each study, the association between various clinical factors and surgical outcome, evaluated by the (modified) Japanese Orthopaedic Association scale (mJOA/JOA), Nurick score or “other” measures, was extracted. A relationship between the outcome and predictor was defined as conditional, if it was significant for certain groups of patients but not others or using one statistical test, but not another.

Results

This review consisted of 37 POOR [13–49], 38 GOOD [50–87] and 16 EXCELLENT [88–103] articles (Table 2).

Fifteen of these studies controlled for confounding variables when looking at the association between outcome and age, duration of symptoms and baseline severity score. The outcome measure used in all EXCELLENT studies was either the Nurick or the mJOA/JOA, with one study commenting on both.

Fig. 1 Search strategy and detailed review process. CSM cervical spondylotic myelopathy

Table 1 Modified Scottish Inter-collegiate Guidelines Network (SIGN) used to rate all articles

Checklist item original	Original scoring	Dichotomous scoring	Comments/interpretations
1. The study addresses an appropriate and clearly focused question	6-point scale	Yes = 1 No = 0	
2. The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation	6-point scale	–	
3. The study indicates how many people were asked to take part did so, in each of the groups being studied	6-point scale	Yes = 1 No = 0	Retrospective studies receive a score of zero
4. The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis	6-point scale	–	
5. What percent (Did any) of individuals or clusters recruited into each arm of the study dropped out before the study was completed?	%	Yes = 0 No = 1	Retrospective studies receive a score of zero unless they commented on drop off rate (>80 %). Prospective studies with a >80 % follow-up receive a 1
6. Comparison is made between full participants and those lost to follow-up, by exposure status	6-point scale	–	
7. The outcomes are clearly defined	6-point scale	Yes = 1 No = 0	
8. The assessment of outcome is made blind to exposure status	6-point scale	–	

Table 1 continued

Checklist item original	Original scoring	Dichotomous scoring	Comments/interpretations
9. Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome	6-point scale	–	
10. The measure of assessment of exposure is reliable	6-point scale	Yes = 1 No = 0	
11. Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable	6-point scale	Yes = 1 No = 0	
12. Exposure level or prognostic factor is assessed more than once	6-point scale	Yes = 1 No = 0	
13. The main potential confounders are identified and taken into account in the design and analysis	6-point scale	Yes = 1 No = 0	The main confounders are age, duration of symptoms and baseline severity score
14. Have confidence intervals been provided?	6-point scale	Yes = 1 No = 0	Have the results been reported using good statistical methods?
15. How well was the study done to minimize the risk of bias or confounders, and to establish a causal relationship between exposure and effect?	Code ++, + or -	Yes = 1 No = 0	Trichotomous rating ^a : 0 = poor 1 = good 2 = excellent
16. Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the exposure being investigated?	Yes/No	Yes = 1 No = 0	Trichotomous rating ^b : 0 = poor 1 = good 2 = excellent
17. Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes/No	Yes = 1 No = 0	

Checklist items in bold are those removed from the original checklist

^a Question 15: To score a perfect 2, the study must be a prospective study with no selection and recruitment bias, must have a follow-up rate >80 % and must have controlled for confounders. A prospective study that met some, but not all of this criteria scores a 1. A retrospective study that has controlled for confounders also scores a 1. A highly biased retrospective or prospective study that has no control receives a score of 0

^b Question 16: A study has sufficient statistical power if, for every predictor evaluated, there are at least 10 participants. Based on the score in question 15, a study can either go up, go down one point or stay the same depending on whether its sample size meets this basic rule

Duration of symptoms

Thirteen articles evaluated duration of symptoms as a predictor of surgical outcome. Nine reported a negative, three a non-significant and one a conditional relationship. It is evident that outcome, assessed on both the mJOA/JOA and Nurick scale, is dependent on preoperative duration of symptoms as indicated by significantly more articles reporting a negative association than a non-significant association. The *R* values for this negative relationship ranged from weak to strong [95] (Table 3).

Baseline severity score

Nine articles reported on the relationship between baseline severity score and surgical outcome. One article suggested a negative, seven a positive and one a non-significant

association. All studies (7) that used JOA as the primary outcome measure demonstrated that more severe preoperative myelopathy is predictive of a worse outcome. When assessing this association on the Nurick scale, there was one article reporting a positive, one a negative and one an insignificant relationship, making it difficult to draw a conclusion as to the predictive value of preoperative severity on Nurick. One study recorded a strong *R* value (0.61) for this positive association [95] (Table 3).

Age

All 16 articles explored the importance of age on surgical outcome. Six studies found a negative, eight a non-significant and two a conditional relationship. Breaking it down by scale, two articles reported a negative and two a non-association between age and Nurick. Four and six studies

Table 2 List of EXCELLENT, GOOD and POOR studies included in systematic review

Rating	Number	Articles	Outcome
Excellent (10–14)	16	Cheng et al. (2009)	Ebersold et al. (1995)
		Furlan et al. (2011)	Kim et al. (2008)
		King et al. (2005)	Nagashima et al. (2011)
		Rajshekhar and Kumar (2005)	Suri et al. (2003)
		Suzuki et al. (2009)	Zhang et al. (2010)
		Zhang et al. (2011)	
	38	Alafifi et al. (2007)	Chen et al. (2001)
		Choi et al. (2005)	Emery et al. (1998)
		Fujimura et al. (1998)	Guidetti and Fortuna (1969)
		Hamanishi et al. (1996)	Heidecke et al. (2000)
		<i>Hirai (1991)</i>	Huang et al. (2003)
		Hukuda et al. (1985)	Kato et al. (1998)
		Kawaguchi et al. (2003)	Koc et al. (2004)
		Koyanagi et al. (1993)	Lyu et al. (2004)
		Masaki et al. (2007)	Nagashima et al. (2006)
		Nagata et al. (1996)	Okada et al. (1993)
Poor (<7)	37	Park et al. (2006)	Singh et al. (2009)
		Singh et al. (2001)	Wada et al. (1999)
		Wiberg (1986)	
		Agrawal et al. (2004)	Amasson et al. (1987)
		Arnold et al. (1993)	Bishara (1971)
		Chagas et al. (2005)	Fessler et al. (1998)
		Gok et al. (2009)	Hamburger et al. (1997)
		Houten and Cooper (2003)	Igarashi et al. (2011)
		Iwasaki et al. (2002)	Kawaguchi et al. (2000)
		Kim et al. (2007)	Lee et al. (1997)
		Magnaes and Hauge (1980)	Matsuoka et al. (2001)
		Moussa et al. (1983)	Naderi et al. (1996)
		Naruse et al. (2009)	Ryu et al. (2010)
		Saunders et al. (1991)	Sinha and Jagetia (2010)
		<i>Sunago (1982)</i>	Wang et al. (2004)
		Yamazaki et al. (2003)	

Italicized articles were the ones translated from Japanese to English
mJOA/JOA (modified) Japanese Orthopaedic Association scale, *EMS* European Myelopathy Score, *NCSS* Neurosurgical Cervical Spine Scale, *SF-36* Short Form-36

Table 3 Evaluation of duration of symptoms, age and baseline severity score as predictors of surgical outcome by excellent, GOOD + EXCELLENT and POOR + GOOD + EXCELLENT studies

Factor	Total (Significant/NS) Significant(+,-) Conditional	Significance by scale	Strength of association	Conclusions
EXCELLENT				
Duration of Symptoms	13(9, 3) → ([90, 94, 95, 97, 99–103], [89, 91, 98]) 9(0, 9) → (0, [90, 94, 95, 97, 99–103]) 1 → [93]	Nurick: 3 mJOA/JOA: 6 Other: 1	$R = -0.231, p = 0.05$ [95] $R = -0.53, p = 0.04$ (diabetic*) [93]	Longer duration of symptoms preoperatively result in a worse surgical outcome on all scales
Age	16(6, 8) → ([88, 94, 95, 99, 102, 103], [89, 90, 92, 96–98, 100, 101]) 6(0, 6) → (0, [88, 94, 95, 99, 102, 103]) 2 → [91, 93]	Nurick: 3 mJOA/JOA: 5 Other: None	$R = -0.38, p = 0.0031$ [95] $R = -0.52, p < 0.01$ (Nurick) [91] $R = -0.43, p < 0.01$ (mJOA) [91]	Age is a potential predictor of outcome evaluated using the Nurick score or the mJOA/JOA
Baseline Severity Score	9(8, 1) → ([89, 94, 95, 97, 98, 101–103], [90]) 8(7, 1) → ([86, 91, 92, 95, 98–100], [94])	Nurick: 2 mJOA/JOA: 7 Other: None	$R = 0.61, p = 0.0001$ [95] $R = -0.65, p < 0.05$ (diabetic*) [93]	More severe preoperative myelopathy results in a worse outcome on the mJOA/JOA scale. The association between Nurick and baseline severity score is unclear
GOOD + EXCELLENT				
Duration of Symptoms	39(25, 10) → ([56–58, 60, 63, 69, 72, 73, 75, 77–79, 83, 85–87, 90, 94, 95, 97, 99–103], [51, 53, 55, 62, 64, 68, 84, 89, 91, 98]) 25(0, 25) → (0, [56–58, 60, 63, 69, 72, 73, 75, 77–79, 83, 85–87, 90, 94, 95, 97, 99–103]) 4 → [54, 59, 76, 93]	Nurick: 4 mJOA/JOA: 21 Other: 5	$R = -0.47, p = 0.000039$ [56] $R = -0.57, p = 0.0001$ (sub-acute*) [58] $R = -0.82, p = 0.0001$ (insidious onset*) [58] $R = -0.60, p < 0.01$ (CSM*) [69] $R = -0.64, p < 0.01$ (OPLL*) [69] $R = -0.231, p = 0.05$ [95] $R = -0.463, p = NA$ (OPLL*) [77] $R = -0.401, p = NA$ (CSM*) [77] $R = -0.459, p = 0.0039$ [78] $R = -0.364, p = NA$ [83] $R = -0.401, p = 0.043$ (elderly*) [59] $R = a0.225, p = 0.041$ [59] $R = -0.53, p = 0.04$ (diabetic*) [93]	Longer duration of symptoms results in worse surgical outcome, evaluated on both the mJOA/JOA and other measures. The association between duration of symptoms and outcome on Nurick was inconclusive

Table 3 continued

Factor	Total (Significant/NS) Significant(+,-) Conditional	Significance by scale	Strength of association	Conclusions
Age	50(17, 27) → ([52, 56, 61, 65, 71, 72, 75, 79, 81, 86–88, 94, 95, 99, 102, 103], [51, 53, 54, 58–60, 62–64, 66, 68, 70, 73, 77, 78, 80, 83–85, 89, 90, 92, 96–98, 100, 101]) 17(16, 1) → ([52, 56, 61, 65, 71, 72, 75, 79, 86–88, 94, 95, 99, 102, 103], [81]) 6 → [57, 69, 74, 76, 91, 93]	Nurick: 3 mJOA/JOA: 19 Other: 2	$R = -0.28, p = 0.000046$ [56] $R = -0.443, p = 0.005$ [71] $R = -0.384, p = 0.0031$ [95] $R = 0.23, p = 0.047$ [81] $R = -0.52, p < 0.01$ (Nurick**) [91] $R = -0.43, p < 0.01$ (mJOA**) [91] $R = -0.65, p = 0.01$ (diabetes*) [93] $R = -0.37, p < 0.05$ (OPLL*) [69] $R = -0.46, p < 0.05$ (CHD*) [69] $R = 0.65, p < 0.001$ (MDI**) [81] $R = 0.64, p < 0.001$ [55] $R = 0.37, p = 0.018$ [67] $R = 0.69, p = 0.009$ [68] $R = 0.611, p < 0.0001$ [95] $R = 0.8412, p = NA$ (CSM*) [82] $R = 0.9261, p = NA$ (OPLL*) [82] $R = 0.387, p = 0.015$ (younger*) [59] $R = 0.333, p = 0.009$ [59]	Age is not a significant predictor of outcome using any measure
Baseline severity score	38(22, 12) → ([50, 52, 54, 55, 62–65, 67, 68, 80–82, 86, 89, 94, 95, 97, 98, 101–103], [51, 56, 58, 71, 72, 77–79, 83–85, 90]) 22(17, 5) → ([50, 52, 54, 55, 63, 65, 67, 68, 82, 86, 89, 94, 95, 98, 101–103], [62, 64, 80, 81, 97]) 4 → [53, 57, 59, 76]	Nurick: 7 mJOA/JOA: 18 Other: 3	$R = 0.65, p < 0.001$ (MDI**) [81] $R = 0.64, p < 0.001$ [55] $R = 0.37, p = 0.018$ [67] $R = 0.69, p = 0.009$ [68] $R = 0.611, p < 0.0001$ [95] $R = 0.8412, p = NA$ (CSM*) [82] $R = 0.9261, p = NA$ (OPLL*) [82] $R = 0.387, p = 0.015$ (younger*) [59] $R = 0.333, p = 0.009$ [59]	More severe preoperative myelopathy is associated with a worse outcome on mJOA/JOA scale. Baseline severity is significantly related to outcome on the Nurick, but the direction of this association is unclear. The association between baseline severity and outcome evaluated using other measures was not evident
POOR + GOOD + EXCELLENT				
Duration of symptoms	63(42,16) → ([13, 16–19, 22, 26, 31, 35–37, 41–45, 49, 56–58, 60, 63, 69, 72, 73, 75, 77–79, 83, 85–87, 90, 94, 95, 97, 99–103], [15, 23, 25, 32, 33, 38, 51, 53, 55, 62, 64, 68, 84, 89, 91, 98]) 42(0,42) → (0, [13, 16–19, 22, 26, 31, 35–37, 41–45, 49, 56–58, 60, 63, 69, 72, 73, 75, 77–79, 83, 85–87, 90, 94, 95, 97, 99–103]) 5 → [48, 54, 59, 76, 93]	Nurick: 11 mJOA/JOA: 28 Other: 11	$R = -0.47, p = 0.000039$ [56] $R = -0.57, p = 0.0001$ (sub-acute*) [58] $R = -0.82, p = 0.0001$ (insidious onset*) [58] $R = -0.60, p < 0.01$ (CSM*) [69] $R = -0.64, p < 0.01$ (OPLL*) [69] $R = -0.597, p < 0.05$ [35] $R = -0.539, p < 0.0001$ [36] $R = -0.231, p = 0.05$ [95] $R = -0.463, p = NA$ (OPLL*) [77] $R = -0.401, p = NA$ (CSM*) [77] $R = -0.459, p = 0.0039$ [78] $R = -0.364, p = NA$ [83] $R = -0.401, p = 0.043$ (elderly*) [59] $R = -0.225, p = 0.041$ [59] $R = -0.53, p = 0.04$ (diabetic*) [93]	Longer duration of symptoms preoperatively results in a worse surgical outcome on all scales

Table 3 continued

Factor	Total (Significant/NS) Significant(+,-) Conditional	Significance by scale	Strength of association	Conclusions
Age	74(28,40) → ([16, 17, 19, 28, 29, 35, 38, 45, 48, 49, 52, 56, 60, 61, 65, 71, 72, 75, 79, 81, 86–88, 94, 95, 99, 102, 103], [14, 15, 18, 21–25, 33, 36, 39, 40, 42, 43, 51, 53, 54, 58–60, 62, 63, 66, 68, 70, 73, 77, 78, 80, 83–85, 89, 90, 92, 96–98, 100, 101]) 28(1,27) → ([81], [16, 17, 19, 28, 29, 35, 38, 45, 48, 49, 52, 56, 60, 61, 65, 71, 72, 75, 79, 86–88, 94, 95, 99, 102, 103]) 6 → [57, 69, 74, 76, 91, 93]	Nurick: 4 mJOA/JOA: 25 Other: 7	$R = -0.28, p = 0.000046$ [56] $R = -0.443, p = 0.005$ [71] $R = -0.384, p = 0.0031$ [95] $R = 0.23, p = 0.047$ [81] $R = -0.52, p < 0.01$ (Nurick**) [91] $R = -0.43, p < 0.01$ (mJOA**) [91] $R = -0.65, p = 0.01$ [93] $R = -0.37, p < 0.05$ (OPLL*) [69] $R = -0.46, p < 0.05$ (CDH*) [69]	Age is not a significant predictor of outcome on any scale
Baseline severity score	56(35,17) → ([18, 20, 22, 24, 26, 28, 29, 31, 32, 36, 40, 45, 46, 50, 52, 54, 55, 62–65, 67, 68, 80–82, 86, 89, 94, 95, 97, 98, 101–103], [14, 21, 34, 35, 43, 51, 56, 58, 71, 72, 77–79, 83–85, 90]) 35(29, 6) → ([18, 20, 24, 26, 28, 29, 31, 32, 36, 40, 45, 46, 50, 52, 54, 55, 63, 65, 67, 68, 82, 86, 89, 94, 95, 98, 101–103], [22, 62, 64, 80, 81, 97]) 4 → [53, 57, 59, 76]	Nurick: 8 mJOA/JOA: 25 Other: 8	$R = -0.65, p < 0.001$ (MDI**) [81] $R = 0.45, p < 0.0001$ [20] $R = 0.64, p < 0.001$ [55] $R = 0.37, p = 0.018$ [67] $R = 0.69, p = 0.009$ [68] $R = 0.38, p = 0.0027$ [36] $R = 0.61, p < 0.0001$ [95] $R = 0.84, p = NA$ (CSM*) [82] $R = 0.93, p = NA$ (OPLL*) [82] $R = 0.39, p = 0.015$ (younger**) [59] $R = 0.33, p = 0.009$ [59]	More severe preoperative myelopathy is associated with a worse outcome on mJOA/JOA scale. Baseline severity is significantly related to outcome on the Nurick, but the direction of this association is unclear

An R value between -1.0 and -0.5 or 0.5 and 1.0 was classified as a strong correlation, between -0.5 and -0.3 or 0.3 and 0.5 as moderate and between -0.3 and -0.1 or 0.1 and 0.3 as weak
mJOA/JOA (modified) Japanese Orthopaedic Association Scale, *CSM* cervical spondylotic myelopathy, *OPLL* ossification of the posterior longitudinal ligament, *NA* not applicable/not given, *CDH* cervical disc herniation, *MDI* Myelopathy Disability Index

* R value and p values reported for specific patient groups

** R value and p value reported for a specific outcome measure when more than one scale was used to evaluate outcome

found a negative and a non-relationship, respectively, between age and JOA/mJOA. It is unclear as to the association between age and outcome evaluated by Nurick, but it is possible to suggest that age may not be predictive of outcome on the JOA/mJOA scale. The two conditional studies were not included in this count. Furlan et al. [91] found that age was a significant predictor of outcome on both scales using multiple regression, but not after dichotomizing the mJOA outcome. In addition, Kim et al. [93] suggested that age was an important predictor, but only in patients with diabetes. The *R* values for this negative relationship ranged from moderate to strong (Table 3).

Most of the GOOD articles were not rated excellent due to flaws in their statistical analysis such as a lack of control for confounding variables. In contrast to the EXCELLENT studies, the GOOD studies used a wider variety of scales and measures to assess outcome such as the Cooper, neurosurgical cervical spine scale (NCSS), neurological assessments, questionnaires and evaluation of symptom improvement.

Duration of symptoms

Thirty-nine articles investigated duration of symptoms as a potential predictor of outcome. Twenty-five reported a negative, ten a non-significant and four a conditional relationship. It is evident that there is a significant negative association between duration of symptoms and outcome evaluated on both the JOA/mJOA scale and other measures: 22 versus 8 articles identified a negative versus a non-significant relationship. Using the Nurick scale, on the other hand, the results were inconclusive: four articles reported a negative and four a non-association. Inclusion of the conditional articles did not alter these results. The *R* values for this negative relationship ranged from weak to strong (Table 3).

Baseline severity score

Thirty-eight studies assessed baseline severity score as a potential predictor of surgical outcome. Five reported a negative, 17 a positive, 12 a non-significant and 4 a conditional relationship. It is evident that outcome, evaluated by mJOA/JOA, is positively dependent on the baseline severity score: 15 papers suggested a positive association, while only 8 reported a non-significant relationship. It is hard to define the relationship between baseline score and Nurick score as two versus four papers reported negative versus positive associations. It is clear that baseline score is a significant predictor of Nurick, but the direction of the relationship is unclear. With respect to all the other outcome measures, two and three studies suggested a negative and a non-significant relationship, respectively.

The *R*-values of this association ranged from moderate to strong (Table 3).

Age

Fifty articles reported on age as a predictor of outcome. Sixteen identified a negative, one a positive, 27 a non-significant and 6 a conditional association between age and outcome. Age was not found to be a predictor of outcome, assessed using either the Nurick, mJOA/JOA or other measures. Two and 14 papers found age had a negative association with Nurick and JOA/mJOA, respectively. Five and 18 studies, on the other hand, reported no relationship with Nurick or JOA/mJOA, respectively. It is important to incorporate the conditional studies into this analysis, especially those that used JOA/mJOA as the primary outcome measure. Both Nagashima et al. and Ogawa et al. [74, 76] identified age as a significant predictor of outcome in more severe myelopathy groups, but not in moderate severity (10–12) groups. Furlan et al. [91] identified age as an important negative predictor using multiple regression, but not stepwise logistic regression. Finally, Koyanagi et al. [69] suggested that age was a significant predictor in patients with OPLL and CDH, but not CSM. Incorporating these results into our assessment of age as a predictor, we still conclude that it is an insignificant predictor. The *R* values of the significant associations ranged from weak to strong (Table 3).

The POOR studies had significant flaws, including study design and poor statistical power and control. In addition, many of these studies used unreliable outcome measures to evaluate surgical improvement and suffered on their ratings as a result.

Duration of symptoms

Sixty-three articles explored duration of symptoms as a predictor of surgical outcome. Forty-two reported a negative, 16 a non-significant and 5 a conditional relationship. The results were clear for all outcome measures: a longer duration of symptoms was predictive of a worse outcome. The *R* value of this association was reported in six studies and ranged from weak to strong (Table 3).

Baseline severity score

Fifty-six papers assessed baseline severity score as a predictor of outcome. Twenty-nine reported a positive, 17 a non-significant, 6 a negative and 4 a conditional association. Baseline severity score was a definite positive predictor of outcome assessed using the JOA/mJOA and other measures. Twenty-two versus ten papers reported a positive versus a non-significant association. The relationship

between baseline severity score and Nurick was inconclusive: three papers identified as a negative, four a positive and two a non-significant association. As in the good/excellent analysis, it is evident that preoperative severity is related to Nurick score, but the direction of this association is unclear. The *R* value of this positive association was reported in six studies and ranged from moderate to strong (Table 3).

Age

Seventy-four studies commented on age as a potential predictor. Twenty-seven identified a negative, 1 a positive, 40 a non-significant and 6 a conditional association. Age was not a significant predictor of outcome, assessed using either the Nurick score or other measures. Nine papers reported a non-significant relationship between age and Nurick, whereas only four suggested a negative relationship. Without looking at the conditional associations, JOA/mJOA was also not dependent on age as indicated by 25 articles reporting no relationship and 20 suggesting a negative one. Five articles identified a conditional association between age and mJOA/JOA. The results from these studies do not affect these conclusions. The *R* values from studies that reported an association ranged from weak to moderate (Table 3).

Other predictors

Articles included in this review also explored the predictive value of other factors including gender, signs and symptoms, disease progression pattern and various comorbidities. The results from these studies are displayed in Table 4. There is no sufficient evidence in the literature to conclude that the presence of a particular sign or symptom or co-morbidity is predictive of outcome.

Discussion

This review compared the results from the EXCELLENT, GOOD + EXCELLENT and POOR + GOOD + EXCELLENT papers (Table 5).

One of the major findings of this review was that patients with a longer duration of symptoms and a more severe baseline score are more likely to have an unfavorable surgical result. The rationale behind this finding is that both severe and chronic, longstanding compression of the spinal cord may lead to irreversible damage due to demyelination and necrosis of the gray matter. Secondly, controversy exists in the literature as to the significance, strength and direction of the relationship between surgical outcome and age. Age was a non-significant predictor on

all the scales when looking at the GOOD + EXCELLENT and the POOR + GOOD + EXCELLENT studies. When looking at only the higher quality studies (modified SIGN ≥ 10), however, age went from a non-significant predictor to a potential predictor. Although most surgeons will not discriminate on the basis of age, they should be aware that the elderly are not able to translate neurological recovery to functional improvement as well as the younger population. Potential explanations for this discrepancy include: (1) the elderly experience age related changes in their spinal cord including a decrease in γ -motoneurons, number of anterior horn cells and number of myelinated fibers in the corticospinal tracts and posterior funiculus, (2) older patients are more likely to have unassociated comorbidities that may affect outcome or (3) the elderly may not be able to conduct all activities on a certain functional scale due to these comorbidities (e.g. walking time may be affected by osteoarthritis) [35, 75, 88, 92, 93]. Finally, our review determined that factors such as signs (hyperreflexia, leg spasticity and Babinski sign), symptoms (gait impairment, clumsy hands and numbness), comorbidities (diabetes and psychological issues), and smoking status do carry some predictive value. Physicians should progressively incorporate predictive modeling into their practices to provide valuable prognostic information to their patients and direct appropriate treatment programs. When evaluating a CSM patient's likely surgical outcome, the surgeon must weigh his/her preoperative severity, duration of symptoms and age accordingly while keeping in mind the ability of other factors to affect the outcome.

As shown in this review, results may differ depending on what scale is used to evaluate surgical outcome. This may be due to limitations in the scales rather than an indication of the actual association between the predictor and outcome. The Nurick score is a scale with lower sensitivity, it is graded out of five and is largely weighted towards lower limb function [104]. When outcome was assessed using the Nurick score, its association with various predictors was less conclusive. For example, duration of symptoms was significantly associated with Nurick score when looking at the EXCELLENT and the POOR + GOOD + EXCELLENT group, but was a questionable predictor in the GOOD + EXCELLENT group. In addition, in the GOOD + EXCELLENT and POOR + GOOD + EXCELLENT studies, there was a significant relationship between preoperative condition and Nurick, but the direction of the association was not evident. The articles that identified a negative association, however, had more biased samples: Gok et al., Huang et al. and Rajshekhar and Kumar [22, 62, 97] all had stricter inclusion criteria. On the other hand, the results were more definite when the outcome was evaluated on either the JOA or mJOA score: a longer duration of symptoms and a more

Table 4 Other prognostic indicators of surgical outcome reported either by EXCELLENT, GOOD or POOR studies

Co-morbidities	
Number of co-morbid diseases	Furlan et al. [91]: number of comorbidities was not associated with postoperative Nurick or mJOA using stepwise logistic regression King et al. [94]: a greater number of comorbid diseases resulted in a worse outcome assessed by the Cooper scale Nagata et al. [75]: a greater number of other health issues contributed to a poor surgical outcome in the older group
Presence of co-morbid disease	Houten and Cooper [25]: presence of comorbidities is not related to outcome
Diabetes	Chen et al., Kawaguchi et al. [30, 51]: diabetes is not a significant predictor of outcome Kim et al., Choi et al. [53, 93]: diabetes is related to a worse outcome
Psychological disorders	Kumar et al. [32]: patients in the poor outcome group had greater emotional problems than those in the good outcome group
Smoking	Kim et al. [93]: smoking status did not affect outcome in control group. In diabetes group, smoking increased the risk of an unfavorable outcome
Signs and symptoms	
Lower extremity dysfunction	Lee et al. [33]: not a significant predictor of outcome Gregorius et al. [23]: presence of lower extremity weakness is associated with a worse outcome
Upper extremity dysfunction	Lee et al. [33]: not a significant predictor of outcome Magnaes and Hauge [34]: presence of arm symptoms is positively associated with leg outcome
Bowel/bladder dysfunction	Houten and Cooper, Lee et al. [25, 33]: not a significant predictor of outcome Gregorius et al., Sinha and Jagetia [23, 45]: presence of bladder/bowel dysfunction is associated with a worse outcome
Babinski sign	King et al. [94]: presence of a Babinski sign was associated with a worse outcome Zhang et al. [102] presence of a Babinski sign was related with a better outcome Alafifi et al. [50]: a positive Babinski sign was predictive of a worse outcome in patients with either a N/Hi or Lo/Hi MRI
Leg spasticity/spastic gait	Gregorius et al. [23]: not a significant predictor of outcome Alafifi et al., Bertalanffy and Eggert [17, 50]: presence of leg spasticity is associated with a worse outcome Chiles et al. [20]: presence of a spastic gait was predictive of a poor outcome using the Wilcoxon rank sum test but not multivariate analysis
Hyperreflexia hand atrophy	Alafifi et al. [50]: both these signs were predictive of a worse outcome in patients with either a N/Hi or Lo/Hi MRI Chiles et al. [20]: hand atrophy was associated with a poorer outcome using multivariate analysis
Sexual dysfunction	Found to be negative predictors of outcome by single studies [45, 46, 50, 94]
Lower extremity numbness	
Hand clumsiness	
Clonus	
Gait impairment	
Upper extremity atrophy	Found to be insignificant predictors of outcome by single studies [23, 33]
Radicular pain	
Lower cervical pain	
Cervical ROM	
Long tract signs	
Other	
Gender	17 articles reported that gender is not a significant predictor of outcome [19, 22–24, 29, 33, 40, 51–54, 58, 59, 71, 81, 85, 91] Emery et al. [55]: males showed greater improvement following surgery than females
Race	Race is not a predictor of outcome [23]
Onset of symptoms	Patients with a gradual onset of symptoms have a worse outcome [17]
Disease progression	Patients with a slower progressing disease have a better outcome [37]

mJOA modified Japanese Orthopaedic scale, *N/Hi* normal/high, *Lo/Hi* low/high, *MRI* magnetic resonance imaging

Table 5 Summary of results: percentages of articles reporting a negative, positive, non-significant or conditional association between surgical outcome and duration of symptoms, baseline severity score or age

	Negative	Positive	Non-significant	Conditional
Excellent				
Duration of symptoms	69 %	NA	23 %	8 %
Baseline severity score	11 %	78 %	11 %	NA
Age	37.5 %	NA	50 %	12.5 %
Good + excellent				
Duration of symptoms	65 %	NA	26 %	10 %
Baseline Severity Score	13 %	45 %	31.5 %	10.5 %
Age	32 %	2 %	54 %	12 %
Poor + good + excellent				
Duration of symptoms	67 %	NA	25 %	8 %
Baseline severity score	11 %	52 %	30 %	7 %
Age	36.5 %	1.5 %	54 %	8 %

Bold values indicate the relationship between predictor and outcome with the highest percentage

severe baseline severity score were associated with a worse outcome. The mJOA and JOA are widely accepted standards for CSM assessment and separately evaluate lower and upper limb, sphincter and sensory function. Although JOA has been validated and shown to have high inter- and intra-rater reliability [105], its modified version has not.

In a research setting, when looking at a relationship between various factors and outcome, it is important to control for the confounders baseline severity score and duration of symptoms. When assessing statistical control in our review to rate the articles, we ensured that the studies controlled for age, duration of symptoms and baseline severity as these were identified as important predictors by Holly et al. [5]. According to this review, age may be a less important confounder. Few articles reported on the *R* values for the significant associations between various clinical factors and outcome. This makes it difficult for clinicians and researchers to evaluate the strength of these correlations.

Holly et al. [5] indicated that the limitations of their review were that there were very few prospective studies, that many studies assessed the outcome using un-validated measures and that it was hard to analyze functional outcome due to the use of different scales between studies. Our study had much larger pool of articles and consisted of higher quality literature, including some prospective studies that evaluated outcome using the validated JOA scale or Nurick score. There was also a sufficient number of articles to compare predictors on the same scale. In addition, the differences in our methodology, including a comparison of results among the three groups, also allowed for the incorporation of quality assessment in the analysis. Since, the Japanese have had a substantial contribution to research

in the field of spinal cord injury, including the creation of the JOA scale, we also translated all Japanese articles into English and incorporated them into our analysis. Finally, our systematic review differed from Holly et al.'s as it included a preliminary analysis of other predictors including signs and symptoms, comorbidities, gender and smoking status to determine their predictive value.

There are limitations to our study: (1) we did not separate studies based on length of follow-up time; (2) articles that dichotomized a predictor might have done it differently (e.g. age) and (3) some of the articles with relevant abstracts or titles were excluded because they were not available or in another language other than Japanese or English. Future systematic reviews should address these limitations to provide a completely unbiased evaluation of important predictors of outcome.

The results from this review should encourage further exploration in this area. Even though many studies have examined important predictors of surgical outcome in CSM, there still remains a lack of evidence in the form of high quality, prospective studies using validated outcome measures. A large prospective analysis is required to reemphasize the predictive value of duration of symptoms and baseline severity score, to settle the controversy surrounding age and to confirm that signs, symptoms and comorbidities do impact surgical results.

Conflict of interest None.

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