

Surgical interventions for cervical spondylosis due to ossification of posterior longitudinal ligament

A meta-analysis

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Abstract

Background: Aim of this study was to evaluate the effectiveness of various surgical interventions for the management of cervical spondylosis due to the ossification of posterior longitudinal ligament (OPLL).

Methods: After a comprehensive literature search in electronic databases, studies were selected by following pre-determined eligibility criteria. Random effects meta-analyses were performed to estimate the effect sizes of various surgical approaches in improving Japanese Orthopedic Association (JOA) scores at latest follow-up and meta-regression analyses were carried out to examine the factors affecting the change in JOA score.

Results: Twenty-three studies [1576 patients; 57.83 (95% confidence interval, 95% CI: 55.98–59.68) years of age; and 73 (70–76) % males; follow-up 55.4 ± 25.7 (range 12–170) months] were included in the meta-analysis. All surgical interventions significantly ($P < .00001$) improved JOA score. Anterior surgical approaches had an effect size of 4.80 [4.10–5.50] and posterior approaches with laminectomy and laminoplasty improved JOA score by 3.57 [2.39–4.75] and 3.99 [3.65–4.32], respectively. Improvement in JOA score was significantly inversely related to the preoperative JOA score ($P < .00001$). Surgical interventions did not significantly affect cervical lordosis at the latest follow-up.

Conclusion: Surgical interventions for cervical spondylosis due to OPLL significantly improve JOA score as observed at the latest follow-up and this is found to be significantly inversely associated with preoperative JOA score.

Abbreviations: CI = confidence interval, CT = computed tomography, JOA = Japanese Orthopedic Association, MeSH = medical subject heading, OPLL = ossification of posterior longitudinal ligament, ROM = range of motion.

Keywords: cervical spine, follow-up, ossification of posterior longitudinal ligament, surgery

1. Introduction

Ossification of the posterior longitudinal ligament (OPLL) is a heterotopic hyperostotic state due to the ectopic calcification^[1] that can develop at various locations of the spine requiring

radiological diagnosis for which computed tomography (CT) has better diagnostic accuracy than plain radiography.^[2] Prognosis and surgical outcomes remain poor in patients with multiple-region OPLL.^[3]

OPLL is one of the main causes of cervical myelopathy and an important factor for disease progression.^[1,4] The prevalence may differ in different geographic regions. Whereas the prevalence of OPLL in Japanese populations is reported to be 1.9% to 4.3%^[1] in the United States, its prevalence is estimated at 0.1% to 1.3%.^[5] Although not fully understood, the etiology of OPLL is multifactorial with both genetic and environmental associations. Genes implicated in its pathogenesis include *BMP4*, *BMP9*, *COL6A1*,^[3–6] *HAO1A*, *HAO1*, *RSPO2*, and *CCDC91*, *RSPH9*, and *STK38L*.^[6–9] Increase in bone mineral density is also reported in patients with OPLL.^[10]

There are no effective conservative treatments for OPLL. Surgical options include anterior corpectomy and fusion, laminectomy and fusion, and laminoplasty.^[11] Anterior decompression to remove OPLL directly is the prime choice, as anterior compression of the spinal cord is the major source of pathology.^[12,13] However, significant complications are associated with anterior corpectomy and fusion.^[14] Moreover, when OPLL spreads over multiple vertebrae or occupies much area of the canal, anterior decompression becomes difficult. Because of these constraints, posteriorly approached procedures including laminoplasty and laminectomy and fusion are frequently used, although their use is also not cost-free. Patients with straight or kyphotic preoperative cervical curvature usually have poor outcomes after laminoplasty and the incidence of progressive

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DW conceptualized and designed the study; CZL and HY extracted and analyzed data, and drafted the manuscript; HL and NC provided technical support in the analyses and writing. All authors agree to be accountable for all aspects of the work.

Ethical approval and informed consents were not required because we neither collected patients' information nor influenced the patient care.

The authors report no conflicts of interest.

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ossification and kyphotic deformity may increase in the long-term follow-up.^[15,16]

Several studies have reported the outcomes of surgical interventions for the treatment of OPLL with anterior or posterior surgical approaches. However, no clear difference in outcomes can be noted from the outcomes of individual studies. We have carried out a systematic review of relevant studies and have performed a meta-analysis of the change in Japanese Orthopedic Association (JOA) score as an outcome measure to assess the overall effect size of the change at the latest follow-up and outcomes with respect to various surgical approaches/techniques. An attempt is also made to identify the factors affecting the change in JOA scores by testing various explanatory variables in the meta-regression analyses.

2. Methods

This systematic review was performed in accordance with the Cochrane Collaboration guidelines^[17] and is reported in accordance with PRSIMA statement.^[18]

2.1. Eligibility and meta-analysis endpoint/variables

Eligible studies of this meta-analysis were those reporting the outcomes of a surgical intervention for the treatment of cervical spondylosis due to OPLL with a follow-up duration of at least 1 year and measured change in JOA score preoperatively, after surgery, and at latest follow-up.

Meta-analysis endpoint (outcome measure) was the change in JOA score from baseline through latest follow-up. For meta-regression analyses, the change in JOA score at the latest follow-up (dependent variable) was tested to evaluate the relationships with several explanatory variables, including the number of subjects in the study, follow-up duration, year of publication, age of subjects at the time of surgery, gender (percentage of males), number of spondylotic levels involved in surgery, duration of surgery, blood loss during surgery, hospital stay duration, preoperative JOA score, and preoperative lordosis.

2.2. Data acquisition

For the acquisition of data, literature search was undertaken in electronic databases (Embase, Google Scholar, Ovid SP, PubMed/Medline, and ASI Web of Science). Medical Subject Headings (MeSH) and keywords specific to this research were used as different combinational phrases. For primary search, “ossification of posterior longitudinal ligament-cervical spondylosis surgery” combination was used. For secondary searches, several MeSH and keywords, including range of motion (ROM), lordosis, myelopathy, radiculopathy, arthroplasty, corpectomy, discectomy, laminectomy, and laminoplasty were used in combination with primary phrase. Search encompassed original research articles published in English language. Bibliographies of retrieved research articles and software indicated corroborations were also considered.

2.3. Data and analyses

Relevant data pertaining to the patients' demography, clinical and orthopedic characteristics, surgery type/technique and device, study population size and follow-up duration, study design and analytical methods, outcome assessment tools and outcomes, and adverse events were obtained from the retrieved research articles and organized in specialized datasheets.

For the estimation of effect size of change in JOA score, data were either extracted raw from the respective research articles or calculated by using latest follow-up and baseline values. Inverse variance weighted effect sizes of overall (all surgical interventions) and subgroups (various surgery types) were obtained under random effects meta-analyses that were carried out with Stata software (version 12; Stata Corporation, College Station, TX). Subgroup analyses were carried out with regards to surgery type, age at surgery, and follow-up (JOA outcomes: postoperative vs latest follow-up).

Meta-regression analyses were also carried out with Stata software by using restricted maximum likelihood method. A *P* value of less than .05 was considered to show a significant relationship. Between-study variance was tested with tau² index and the percentage of between-study heterogeneity (outcome inconsistency) was assessed with I² index. For the assessment of publication bias, Begg funnel plot and Egger precision plot were examined and trim and fill method was used to estimate the number of missing studies.

3. Results

Twenty-three studies^[19–41] reporting surgical interventions in 1576 patients were selected by following the eligibility criteria (Fig. 1). This patient population was followed for 52.60 (95% confidence interval (95% CI) 42.54–62.65] months after surgery. Average age (weighted) was 57.83 (95% CI 55.98–59.68) years and 73 [70–76] % were males. There was no significant publication bias as assessed with Begg test (adjusted Kendall score = −68; *P* = .202; Fig. 2A) and Egger test (coefficient bias = −1.884; *P* = .201; Fig. 2B) as well as with trim and fill method.

Overall, surgical interventions significantly (*P* < .00001) improved JOA score at the latest follow-up (Fig. 3). Anterior surgical approaches involving corpectomy and/or discectomy were associated with an effect size of 4.80 [4.10–5.50], whereas laminectomy and laminoplasty were associated with an improvement of the JOA score of 3.57 [2.39–4.75] and 3.99 [3.65–4.32], respectively. In the subgroup analyses, JOA scores after surgery [4.21 (3.1–5.31)] and at last follow-up [4.04 (3.75–4.32)] were not significantly different.

In the meta-regression analyses, preoperative JOA score was significantly inversely related to the change in JOA score at latest follow-up (coefficient: −0.605; *P* < .00001). Independently, the year of publication was significantly inversely associated with the change in JOA score at latest follow-up (coefficient: −0.13141; *P* = .009). But in the multivariate meta-regression by including preoperative JOA score and follow-up duration, the year of publication had no significant association, but preoperative JOA was still significantly associated with the change in JOA score at latest follow-up. However, the year of publication was also negatively correlated with follow-up duration and the number of subjects in a study (correlation coefficients: −0.444; *P* = .007 and −0.51; *P* = .001, respectively).

None of the other explanatory variables tested, including follow-up duration, sample size, age, gender, number of levels involved, surgery duration, and blood volume loss during surgery, were significantly associated with the change in JOA score at the latest follow-up.

Surgical interventions did not significantly affect cervical lordosis at latest follow-up (Fig. 4). Anterior surgical approaches involving corpectomy and/or discectomy were associated with an effect size of the change in lordosis of −0.21 [−5.28 to 4.86];

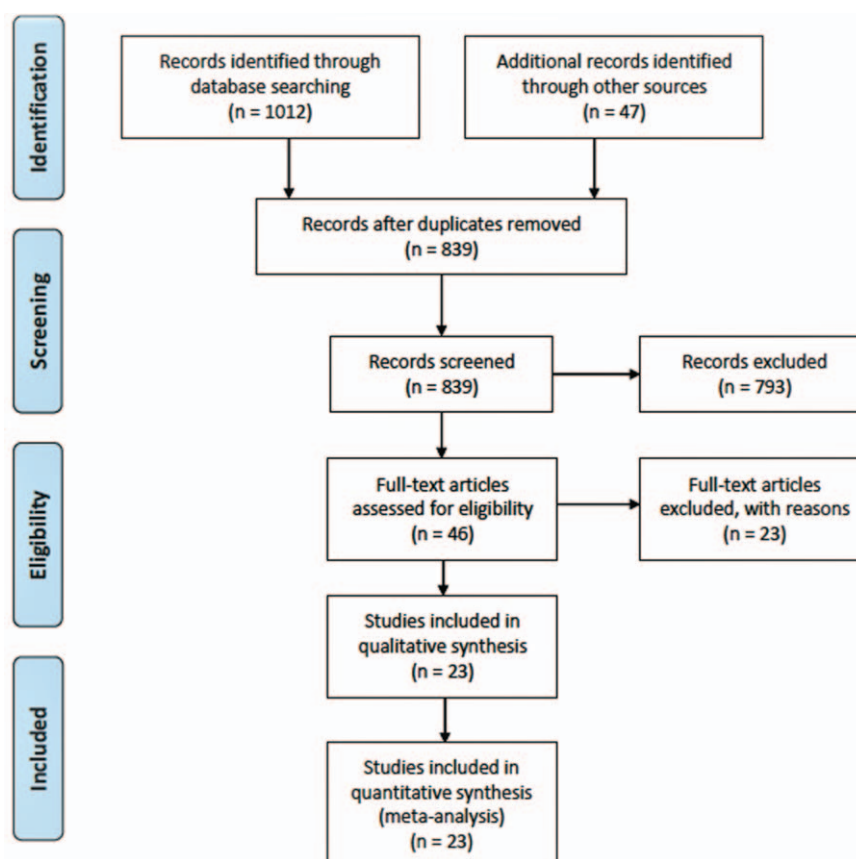


Figure 1. A flowchart of the study screening and selection process.

$P = .935$ degrees, whereas laminectomy and laminoplasty were associated with a change in lordosis of $-1.27 [-6.63$ to $3.82]$; $P = .625$ and $-1.89 [-5.42$ to $1.63]$; $P = .293$ degrees, respectively.

In the meta-regression analyses, none of the other explanatory variables tested, including follow-up duration, sample size, age, gender, number of levels involved, preoperative JOA score, preoperative lordosis, surgery duration, and blood volume loss during surgery, were significantly associated with the change in lordosis at the latest follow-up.

4. Discussion

Surgical interventions for the treatment of cervical spondylosis due to OPLL are found to be associated with significantly improved JOA score at latest follow-up (average 55 months), which was significantly inversely associated with baseline (preoperative) JOA score. The number of levels involved in surgery, although had a negative relationship, but were not significantly associated with the change in JOA score at the latest follow-up (coefficient: -0.282 ; $P = .245$). Similarly, preoperative lordosis was also negatively but not statistically significantly

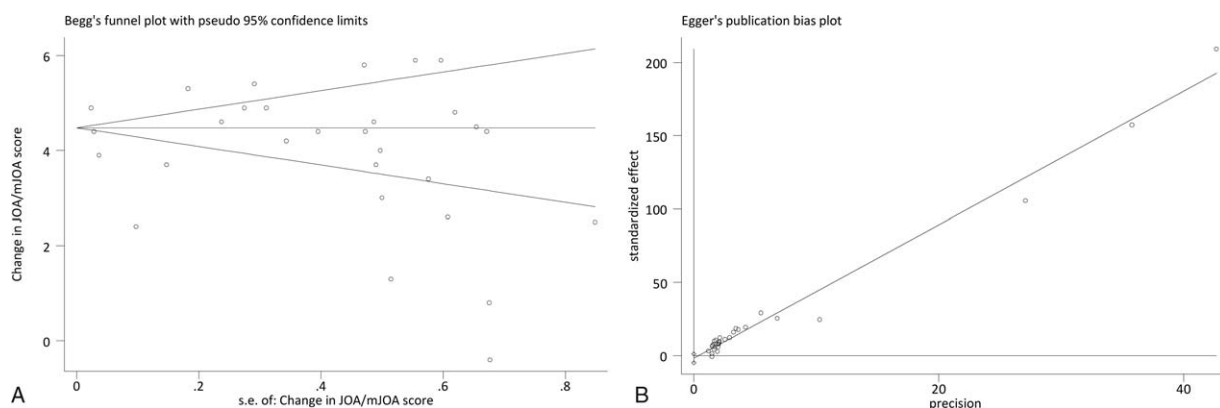


Figure 2. Graphs showing the outcomes of publication bias tests indicative of the absence of a significant publication bias. (A) Begg test's funnel plot, and (B) Egger test precision plot. Both tests were subjected to the meta-analysis of the change in JOA score at latest follow-up.

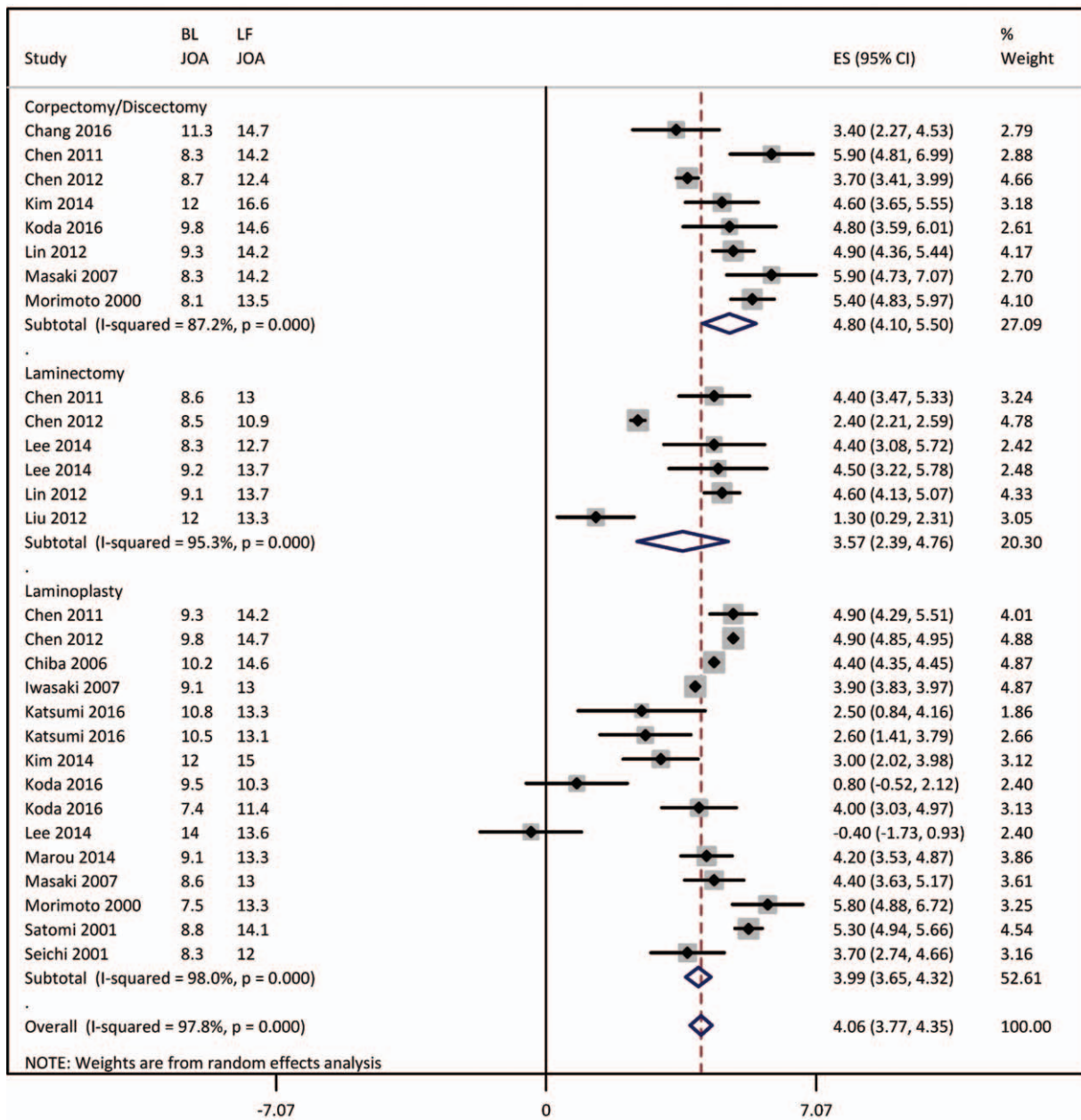


Figure 3. Forest graph showing the overall effect size of the meta-analysis of the improvement in JOA score at the latest follow-up along with subgroup effect sizes.

(coefficient: -3.587 ; $P = .165$) associated with the change in JOA score at latest follow-up. Moreover, surgery did not significantly affect the cervical lordosis.

These results show that surgical interventions were associated with more improvement in patients with relatively lower preoperative JOA score suggesting that the capacity of improvement in JOA score was less in patients with better preoperative JOA score. Surgical interventions are also found to be beneficial irrespective of the number of cervical levels or the follow-up duration, although a nonsignificant negative relationship has been observed for both these explanatory variables, which make it necessary to confirm these results in larger datasets in future.

Majority of the included studies of this meta-analysis reported JOA outcomes at latest follow-up and there was no significant difference between JOA scores after surgery (studies which

reported) and at last follow-up [4.21 ($3.1-5.31$) vs 4.04 ($3.75-4.32$)]. Also, there was no evidence of change of JOA score with increasing duration of follow-up as seen in the meta-regression analyses [coefficient 0.088 (-0.086 to 0.262); $P = .293$].

Our results also suggest that in recent years, there is a trend toward a preference of earlier surgical treatment to cervical spondylosis due to OPLL, as the year of publication (2000 through 2016) was significantly inversely associated with the change in JOA score at latest follow-up (more recent years are associated with less change in JOA score). This trend may be due to advancement in the surgical techniques and better prognosis in recent years. But in the multivariate meta-regression with preoperative JOA score, study population size, and follow-up duration, only preoperative JOA was significantly inversely

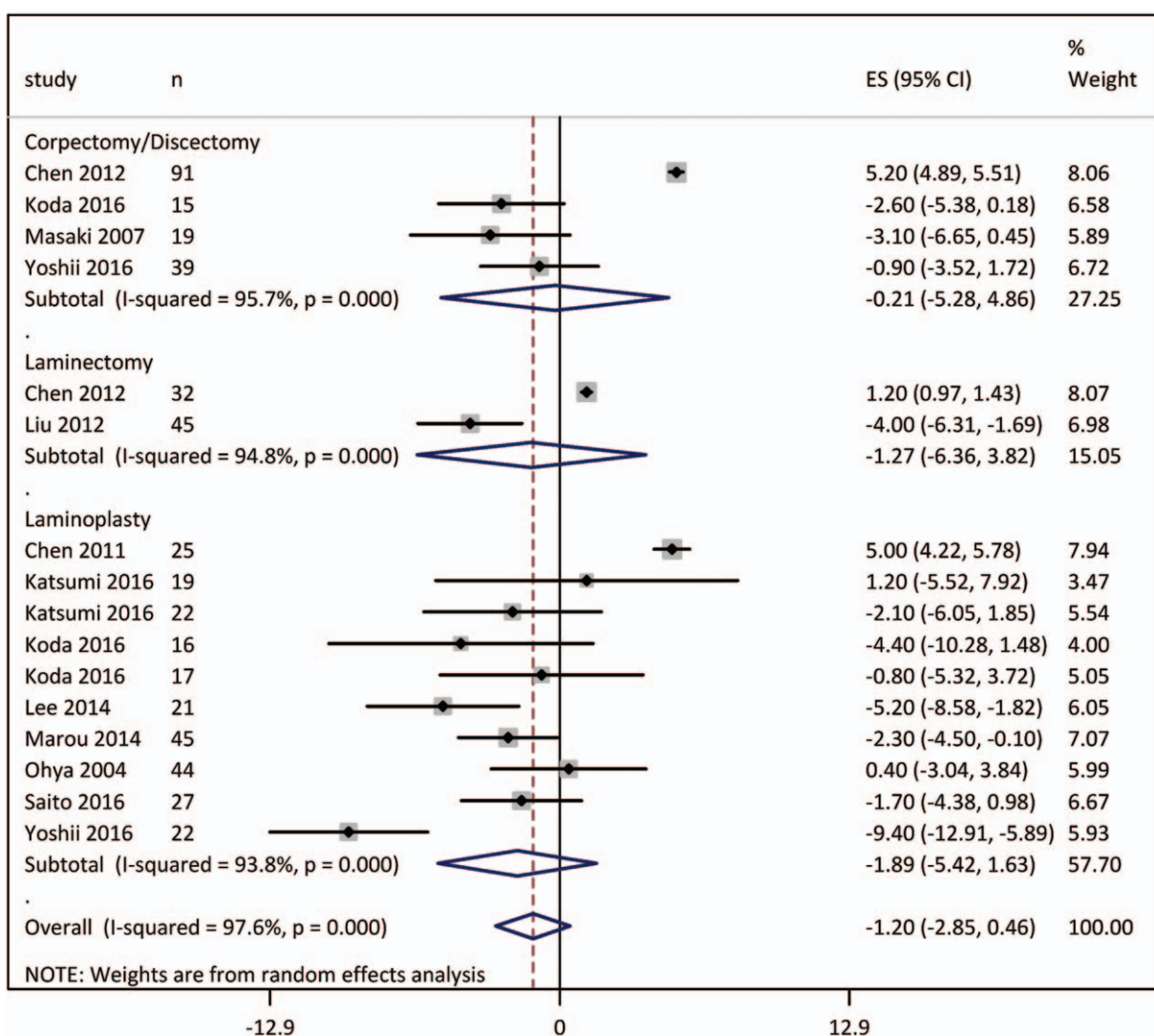


Figure 4. Forest graph showing the overall effect size of the meta-analysis of the change lordosis angle at the latest follow-up along with subgroup effect sizes.

associated with the change in JOA score at latest follow-up. Moreover, more recent studies are also relatively smaller, as the year of publication was negatively correlated with follow-up duration and the number of subjects in a study.

In the present study, age was also not found to be associated with the change in JOA score in the meta-regression analysis. Subgroup analysis by stratifying JOA scores as over and under median age subgroups also did not reveal a meaningful difference. However, majority of the patients in this sample population were below 60 years of age. Only 2 studies recruited relatively older patients (Maruo et al^[31]; age 66.9 ± 8.6 years; change in JOA 4.2 ± 2.3 and Saito et al^[36]; age 67.1 ± 8.2 years; change in JOA: 3.9 ± 1.8), but outcomes were not much different from those of others.

We have also found that there was no notable change in lordosis after surgery. Lordosis of the cervical spine has clinical implications,^[42] as moderate postoperative cervical lordotic curvature is reported to be associated with better surgical outcomes.^[43,44] Therefore, reattainment of cervical lordosis is also considered as an important outcome of surgery that have preventive benefits for possible compression of nervous tissue and

consequent injury.^[45] For successful cervical laminectomy or laminoplasty, it is thought that the presence of preoperative lordosis angle of at least 10° and the preservation of at least 50% facet joints is necessary.^[46,47] This factor may explain the relatively lower improvement in JOA score observed in the present study in laminectomy and laminoplasty subjects, as overall preoperative lordosis angle in this patient population was 5.34 [95% CI: 4.13–6.54] degrees.

In several regions of the world, OPLL is recognized as an important pathological factor for cervical compressive myelopathy.^[48,49] Several unique pathological characteristics of OPLL make the choice of surgical approach debatable. When OPLL affects multilevel cervical spine, anterior decompression involving corpectomy or discectomy and fusion yields direct decompression of the spinal cord,^[50,51] enables reconstruction of the lordotic alignment,^[52] prevents delayed neurologic deterioration,^[53] and permits easier achievement of cervical stability with instrumented arthrodesis.^[54,55] However, there are also some disadvantages of surgeries involving multi-level corpectomy/discectomy such as increased incidence of adjacent-segment degeneration, graft dislodgment, and

complications, including neck stiffness, hoarseness, dysphagia, and pseudomeningocele.^[56–58]

Alternatively, a posterior approach such as laminoplasty can also cope with multi-segmental OPLL and comorbid developmental spinal canal stenosis. Nevertheless, there can be limited surgical outcomes after laminoplasty with risk of kyphotic cervical alignment,^[59,60] the spinal canal occupation,^[61,62] reossification,^[62–64] and hypermobility of the cervical spine.^[65,66] Laminoplasty has been advocated because of its preservation of neck ROM compared with laminectomy with fusion. However, OPLL is different from other etiological factors of myelopathy with respect to neck ROM that may incite further progression of OPLL.^[67] In general, laminoplasty results in long-term decrease in ROM due to unintended autofusion along the lateral margins of the laminoplasty.^[4] It is suggested that progression of OPLL is stimulated by the dynamic factors and ROM stabilization may reduce the progression of OPLL.^[22,68] Because posterior instrumented fusion avoids postoperative cervical instability, it can be a better alternative.^[20]

Among the limitations of the present study, high statistical heterogeneity and less availability of associational data are important considerations. Data regarding ethnicity, education, weight, height, and body mass index (BMI) of the subjects were not sufficiently available in the respective research articles that could further provide associational findings. Moreover, in the included studies of this meta-analysis, only 4 studies measured and reported NDI scores and none of these studies provided Nurick Scale score and therefore it was not possible to have a comparative account of these outcome variables along with JOA score.

5. Conclusion

Surgical interventions for the management of cervical spondylosis due to OPLL significantly improves JOA score without affecting cervical lordosis, as observed at the latest follow-up. The change in JOA score was significantly inversely associated with preoperative JOA score. There may be a trend toward earlier treatment for cervical spondylosis due to OPLL in more recent years that may be attributed to improved diagnostic and surgical techniques.

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